



AMERICAN SOCIETY OF
PLASTIC SURGEONS®

Evidence-Based Clinical Practice Guideline: Breast Reconstruction with Expanders and Implants

INTRODUCTION

The American Cancer Society estimates that nearly 230,000 American women were diagnosed with invasive breast cancer in 2011.¹ Many of these individuals will require mastectomy and total reconstruction of the breast. The diagnosis and subsequent process can create significant confusion and distress for the affected persons and their families and, consequently, surgical treatment and reconstructive procedures are of utmost importance in the breast cancer care continuum. In 2011, the American Society of Plastic Surgeons® (ASPS) reported an increase in the rate of breast reconstructions, citing nearly 100,000 procedures, of which the majority employed expanders/implants.² The 3% increase in reconstructions over the course of just one year highlights the significance of maintaining patient safety and optimizing surgical outcomes.

Rationale and Goals

These guidelines were developed from a comprehensive review of the scientific literature and reflect the consensus of the Post-Mastectomy Expander/Implant Breast Reconstruction Guideline Work Group of the American Society of Plastic Surgeons.

Scope

These guidelines specifically address the risk factors, treatment, anticipated outcomes, and follow-up of patients undergoing breast reconstruction with expanders/implants for the treatment of cancerous defects. Graded practice recommendations can be found in Appendix A.

Intended Users

This guideline is intended to be used by the multidisciplinary team that provides care for patients with breast cancer through the use of breast cancer treatment, mastectomy and breast reconstruction. Healthcare practitioners should evaluate each case individually and treat patient preference as a key role in decision making. This guideline is also intended to serve as a resource for healthcare practitioners and developers of clinical practice guidelines and recommendations.

Disclaimer

Evidence-based guidelines are strategies for patient management, developed to assist physicians in clinical decision making. This guideline was developed through a comprehensive review of the scientific literature and consideration of relevant clinical experience, and describes a range of generally acceptable approaches to diagnosis, management, or prevention of specific diseases or conditions. This guideline attempts to define principles of practice that should generally meet the needs of most patients in most circumstances.

However, this guideline should not be construed as a rule, nor should it be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the appropriate results. It is anticipated that it will be necessary to approach some patients' needs in different ways. The ultimate judgment regarding the care of a particular patient must be made by the physician in light of all the circumstances presented by the patient, the available diagnostic and treatment options, and available resources.

This guideline is not intended to define or serve as the standard of medical care. Standards of medical care are determined on the basis of all the facts or circumstances involved in an individual case and are subject to change as scientific knowledge and technology advance and as practice patterns evolve. This guideline reflects the state of current knowledge at the time of publication. Given the inevitable changes in the state of scientific information and technology, this guideline will be reviewed, updated and revised periodically.

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Conflict of Interest

All contributors and preparers of the guideline, including ASPS staff and consultants, disclosed all relevant conflicts of interest via an on-line disclosure reporting database. In accordance with the Institute of Medicine's recommendations for guideline development, members with a conflict of interest represented less than half of the Breast Reconstruction Guideline Work Group.³

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METHODOLOGY

Work Group Selection Process

ASPS Members were invited to apply to the Work Group via society email and fax communication. All applicants were also required to submit an online conflict of interest disclosure form for membership consideration. Members of the Health Policy Committee reviewed and selected work group members to ensure a diverse representation of United States regions, practice type (large multispecialty group practice, small group practice, solo practice, and academic practice), and clinical, research, and evidence-based medicine experiences and expertise. Three stakeholder organizations, including the American Society of Breast Surgeons, American College of Radiology, and American Society of Clinical Oncology, were also invited to participate in the guideline development process by nominating one member from their respective organizations to serve on the work group.

Clinical Question Development

Work Group Members utilized the Nominal Group Technique to reach consensus on the clinical questions to be addressed in the evidence-based guideline. The Nominal Group Technique is ideal for face-to-face meetings and is designed to encourage equal participation in Work Group discussions and project contributions. The Work Group completed five rounds of the consensus process. Before the Introductory Meeting, all Work Group Members submitted ninety-seven potential clinical questions, which were compiled and dispersed at the Introductory Meeting for consideration and discussion.

The clinical questions were ranked according to the following criteria to assess for potential impact: 1) relevance to guideline scope; 2) addresses a gap in care; 3) can be developed into an actionable recommendation; 4) can be developed into an implementable recommendation; 5) is controversial or of significant interest; 6) is important to public health. The Work Group agreed on the

following clinical questions to address in this evidence-based guideline, including:

1. In patients undergoing surgical treatment for breast cancer, what is the optimal time to discuss breast reconstruction options?
2. In patients undergoing mastectomy for the treatment of breast cancer, what is the optimal time for implant-based reconstruction (i.e., immediate versus delayed) when radiation treatment is not required?
3. In patients undergoing mastectomy for the treatment of breast cancer, what is the optimal time for implant-based reconstruction (i.e., immediate versus delayed) when radiation treatment is required?
4. In patients undergoing breast reconstruction following mastectomy, what are the risk factors when undergoing immediate implant-based reconstruction?
5. In patients requiring radiation therapy and undergoing immediate breast reconstruction after mastectomy, when is the optimal time for radiation therapy?
6. In patients undergoing implant-based reconstruction after mastectomy, what is the optimal duration of antibiotic prophylaxis for prevention of postoperative infections?
7. In patients undergoing mastectomy and implant-based breast reconstruction, what are the outcomes associated with utilizing acellular dermal matrix during reconstruction?
8. In patients undergoing mastectomy and implant-based breast reconstruction, what are the screening recommendations to monitor for cancer recurrence?
9. In patients undergoing breast reconstruction following mastectomy, what are the oncologic outcomes associated with undergoing immediate implant-based reconstruction?

The systematic review process yielded relevant evidence for six questions. The questions on radiation therapy were combined based on available evidence. Additionally, three clinical questions were addressed through supplemental research and cumulative work group clinical expertise.

Literature Search and Admission of Evidence

Published studies were sought by using electronic and manual search strategies. The primary search, executed from December 2011 to February 2012, was conducted in PubMed with the following keywords, MEDLINE Medical Subject Headings (indicated as [MeSH]), publication types (indicated as [ptyp]), Boolean operators, and limits:

1. (Mammoplasty[MeSH] AND reconstruction) OR "breast reconstruction"
2. Case reports[ptyp] OR Editorial[ptyp] OR Comment[ptyp] OR Letter[ptyp] OR News[ptyp] OR Newspaper article[ptyp] OR In Vitro[ptyp] OR Legal Cases[ptyp] OR Legislation[ptyp]
3. #1 NOT #2; Limits: English, Humans

Recent studies that may not have been indexed (e.g. publisher-supplied and pre-MEDLINE citations) were sought using a keyword search strategy similar to item 1 above, without MeSH terms or limits on publication type, up through the search cut-off date of December 31, 2011. Supplemental electronic searches were performed in the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and the Cochrane Library. In addition, a manual review of reference lists from the previous two years and studies accepted per the conditions designated for the literature search, supplemented the electronic searches.

Study selection for each clinical question was accomplished through two levels of study screening. Level I screening was performed by a single reviewer and involved a review of the titles and abstracts downloaded from the literature search noted above. At Level II screening, the full article was obtained, and the study was reviewed for fit with inclusion and exclusion criteria as outlined in Appendix B. The reason for exclusion (e.g. no outcomes of interest) was noted for all articles reviewed at Level II that were ultimately found ineligible for inclusion in the guideline. Work Group Members reviewed the list of excluded articles and the reasons for exclusion to determine whether articles should be excluded or reconsidered for inclusion.

Articles were selected for inclusion if they were relevant to clinical questions about risk factors, treatment options, and postoperative complications and if they were deemed high or moderate quality per the critical appraisal process, which is described below. The literature search identified a total of 2,749 articles that were subject to Level I screening, for a total of 295 remaining articles. After Level II screening and critical appraisal, the results were narrowed to 178 articles, of which ultimately 62 studies were deemed relevant and of high to moderate quality. These studies were used to develop practice recommendations. Additional references were included if considered

necessary for discussion; however, these references were not critically appraised and are clearly documented in the guideline text. Details of literature search terms and search results are provided in Appendix B.

Critical Appraisal of the Literature

The ASPS evidence-based process includes a rigorous critical appraisal process. Each study is appraised by at least two reviewers. If a discrepancy exists between the reviewers, the literature is appraised by a third reviewer, and the level of evidence is determined by consensus. Studies are appraised and assigned levels of evidence according to the ASPS Evidence Rating Scales for therapy, risk, and diagnosis, which can be found in Appendix C. Checklists appropriate for the clinical question (therapy, prognosis/risk, or diagnosis) and study design (randomized controlled trial, cohort/comparative, case-control, etc) are employed. The checklists used by ASPS are similar to commonly used appraisal tools, (e.g., checklists developed by the Critical Appraisal Skills Programme (CASP) and the Centre for Evidence Based Medicine (CEBM)). Evidence ratings are not assigned to studies with inadequately described methods and/or worrisome biases.

Development of Clinical Practice Recommendations

Recommendations were developed through a consensus process. After a thorough review of the evidence, Guideline Work Group Members jointly drafted statements for each recommendation during conference call meetings and online discussions. After each meeting, members had an opportunity to individually comment and revise the draft recommendations via an email discussion. Guideline Work Group Members participated in several rounds of revisions until unanimous consensus was achieved on each recommendation statement. Each recommendation in this guideline is accompanied by a grade indicating the strength of supporting evidence, taking into account the overall level of evidence and the judgment of the guideline developers. Grading is determined as follows:

Grade	Descriptor	Qualifying Evidence	Implications for Practice
A	Strong Recommendation	Level I evidence or consistent findings from multiple studies of levels II, III, or IV	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
B	Recommendation	Levels II, III, or IV evidence and findings are generally consistent	Generally, clinicians should follow a recommendation but should remain alert to new information and sensitive to patient preferences.
C	Option	Levels II, III, or IV evidence, but findings are inconsistent	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role.
D	Option	Level V: Little or no systematic empirical evidence	Clinicians should consider all options in their decision-making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role.

Peer Reviewer Process

The American Society for Therapeutic Radiology and Oncology (ASTRO) and The National Accreditation Program for Breast Centers (NAPBC) were invited to peer review this guideline. In addition, a total of 30 physicians and surgeons were invited to peer review the guideline. Peer review was also performed by volunteers from the ASPS Healthy Policy, Patient Safety, Coding and Payment Policy, and Quality and Performance Measurement Committees. Peer reviewers were given two weeks to review this guideline using an abbreviated version of the Appraisal of Guidelines Research & Evaluation Instrument developed by the AGREE Collaboration.

Guideline Approval Process

After the peer review process, the guideline draft was reviewed and modified by the Post-Mastectomy Expander/Implant Breast Reconstruction Guideline Work Group to address peer review comments. The final guideline was approved by the ASPS Executive Committee during its March 2013 meeting.

Plan for Updating Guideline

In accordance with the National Guideline Clearinghouse's inclusion criteria, this guideline will be updated within five years to reflect changes in scientific evidence, practice parameters, and treatment options.

BACKGROUND

Definitions

- Immediate breast reconstruction is defined as: A breast reconstruction procedure performed at the time of the mastectomy.
- Delayed breast reconstruction is defined as: A breast reconstruction procedure performed any time after the mastectomy.
- Acellular dermal matrix is defined as: A dermal graft used primarily to provide support and/or additional soft tissue coverage with expander/implant breast reconstruction.

Diagnostic Criteria

The patient usually presents to the plastic surgeon's office with a history of prior diagnosis and/or treatment for breast cancer. Patients who have had breast cancer may have had only a biopsy of the mass, a lumpectomy, or a simple mastectomy (alone or with axillary lymph node sampling or removal). Any of these surgical treatments may have been supplemented with radiation treatment to the breast and/or regional lymph nodes. Other cancer related treatments may include a modified radical mastectomy, chemotherapy and/or radiation, which may have an effect on the reconstructive site.

Physical Examination

Physical examination of the breast defect should include documentation of the size and configuration of the missing tissue. The presence of scarring and radiation changes and the condition of the pectoralis major muscle, nipple areola complex, and the contralateral breast should also be noted.

RECOMMENDATIONS

Considerations for Surgical Planning

Patient Education

The systematic literature search process did not retrieve any studies meeting inclusion criteria. Consequently, other widely accepted sources contributed to the creation of an expert clinical opinion for best practice.

While existing federal law through the 1998 Women's Health and Cancer Rights Act mandates insurance coverage for reconstructive surgery, there are limited additional mandated provisions that ensure women have the necessary information to be able to make an informed decision about their reconstructive options. In 2005, the American College of Surgeons created the National Accreditation Program for Breast Centers (NAPBC), which is a consortium of national and professional organizations that have developed standards for breast cancer care. Section 2.18 of the Standards for accreditation specifies that all appropriate patients undergoing mastectomy be offered a preoperative referral to a board certified reconstructive/plastic surgeon.⁴ Despite this standard being applied at many breast centers throughout North America, disparities in access to reconstructive surgery remain.⁵⁻⁸ Key national studies conducted at the University of Michigan and Dana Farber Cancer Institute have analyzed why many women did not receive reconstruction. They found that the two main limiting factors were the patient's ability to understand their options and breast surgeons' failures to refer their patients to a reconstructive surgeon.^{7,9} In response, New York enacted a law known as the Information and Access to Breast Reconstruction Surgery Act, that went one step further to ensure that patients were made aware of their options and coverage for breast reconstruction. This law mandates that hospitals providing mastectomy or lumpectomy surgery must provide the patient written information on breast reconstruction prior to obtaining consent for oncologic surgery. The law also details the minimum amount of information that must be provided including: a description of the various reconstructive options and the advantages and disadvantages of each, information assuring the coverage by both public and private insurance plans, instructions on how a patient may access reconstructive care including the potential transfer of care to a facility that provides reconstructive care and any other information as may be required by the commissioner.¹⁰ Following suit, New Mexico and California also enacted similar patient-communication measures. Additionally, in 2012, a bipartisan effort led to the introduction of the Breast Cancer Education Act in the US House of Representatives. The bill would require the Department of Health and Human Services to plan and implement an education campaign to inform mastectomy patients of breast reconstruction availability and coverage, and of prostheses and other replacement options.¹¹ In the ideal situation, the patient would meet with both the oncology and reconstructive surgeon at the same time. Realistically, given time constraints and scheduling conflicts of both parties, as long as the above requirements are met, the patient will be able to make an informed decision.

Recommendation: Patients undergoing mastectomy should be offered a preoperative referral to a plastic surgeon. The adoption of this approach by practicing surgeons would benefit breast cancer patients nationwide and would result in enhanced patient education of reconstructive options.

Recommendation Grade: D

Immediate versus Delayed Reconstruction

The decision to start reconstruction at the time of the mastectomy should consider the psychosocial benefits to the patient of expediting the reconstructive process balanced by the potential increased surgical risk of starting reconstruction prior to the completion of adjuvant therapy. Beginning the reconstructive process at the time of the mastectomy has the advantage of preserving the skin envelope and shape, as well as maintaining the inframammary fold definition. Immediate reconstructions have the potential to help patients more quickly recover from the psychological impact of the breast amputation and can result in a smaller burden on patients' work or home life as fewer operations are required to reconstruct their breasts.

Commonly, the decision for immediate versus delayed reconstruction hinges on whether post-mastectomy radiation is indicated. Although studies comparing immediate versus delayed reconstruction and radiation therapy versus no radiation therapy have been published, randomized control trial data is not available. In one case series, logistic regression analysis identified timing of reconstruction to be an independent risk factor for postoperative complications, with a higher complication rate among those with immediate procedures.¹² Likewise, a retrospective cohort study found that patients who received immediate breast reconstruction were twice as likely to experience a postoperative complication compared with those who received delayed breast reconstruction (odds ratio 2.06 [95% CI 1.21-3.52]; $p=0.008$). In addition, patients who received immediate breast reconstruction were 5.2 times more likely to have a Baker Grade II, III, or IV capsular contracture compared to patients who received delayed breast reconstruction ($p<0.001$). It is important to note that ten percent of the total sample size received radiation therapy either before or after breast reconstruction in this study.¹³

In contrast, a case series identified delayed reconstruction as a statistically significant independent predictor of infection ($p<0.05$). When analyzed in the multivariate regression model, however, delayed reconstruction did not retain statistical significance.¹⁴ Several other studies found no statistically significant associations between the timing of reconstruction and total complications, reconstruction failure, and infection.¹⁵⁻¹⁷

The timing, and in particular, the staging process of implant-based reconstruction is rapidly evolving. The increased acceptance of nipple-sparing mastectomy has created an opportunity for patients to receive immediate, one-stage implant reconstruction. These

procedures may result in greater patient satisfaction due to the obvious benefits of fewer surgical procedures. However, high-level comparative studies are currently unavailable to assess clinical or patient-reported outcomes among patients undergoing these types of expedited reconstructive operations.

Recommendation: Evidence is varied and conflicting on the association between postoperative complications and the timing of post-mastectomy expander/implant breast reconstruction and is often confounded by the use of radiation. The inconsistent research findings and a lack of definitive evidence should alert physicians to evaluate each case individually.

Level II, III, IV Evidence

Recommendation Grade: C

Risk Factors for Post-Operative Complications with Expander/Implants

Smoking

The current evidence indicates that smoking increases the risk of postoperative complications in patients undergoing immediate expander/implant breast reconstruction. Among nine studies, six univariate and six multivariate analyses found nicotine use to be significantly correlated with increased postoperative complications. One study did not find nicotine use to be associated with postoperative infections,¹⁴ and two studies did not find nicotine to be associated with overall complication rates.^{16, 18} However, all nine studies suggested that smoking has a profoundly negative impact on expander/implant postoperative outcomes.

Complications associated with nicotine use ranged from wound complications to implant loss. Overall complication rates were found to be 2.2 to 3.07 times higher among smokers than non-smokers.¹⁹⁻²¹ Smokers were 2.9 times more likely than nonsmokers to develop wound necrosis ($p=0.003$)²² and 5.9 times more likely to experience reconstruction failure ($p=0.001$).²³ One retrospective case series indicated that smokers were at a 3 times higher risk of implant loss compared to nonsmokers (odds ratio 3.02 [95% CI 1.61-5.57]; $p=0.001$),²⁴ but the same study noted that nicotine use was not found to be significantly associated with overall complications that included seroma, hematoma, skin problems and infection. However, it is important to note that the number of smokers in this study is unknown; thus the power of the study to address these associations is unclear.

Recommendation: Smoking is associated with an increased risk of complications and an increased risk of reconstructive failure in patients undergoing post-mastectomy expander/implant breast reconstruction. Patients should be informed of the increased risks and advised on smoking cessation as means to decrease surgical complications. Additionally, it should be recognized that the decision to proceed with surgery may preclude timely smoking cessation.

Level II, III, IV Evidence

Recommendation Grade: A

Obesity

Evidence indicates that obesity increases the risk of postoperative complications in patients undergoing post-mastectomy expander/implant breast reconstruction. The global obesity definition – body mass index (BMI) greater than 30 – was used for these analyses. The majority of the eight studies addressing the association between BMI and postoperative expander/implant complications concluded that obesity was significantly associated with postoperative complications.^{20-22, 25-27}

The incidence of wound infections and expander/implant failures were directly correlated to increasing BMI. Wound infections among patients with first stage expander/implant reconstructions were 3.3 times higher among patients with a BMI of 25-30 ($p=0.002$) and 18.5 times higher among those with a BMI greater than 30 when compared to patients with a BMI of less than 25 ($p<0.001$). The risk of implant loss was 3 times higher for those with a BMI of 25-30 (odds ratio 3.1 [95% CI 1.0-9.3]; $p=0.043$) and almost 6 times higher for those with a BMI greater than 30 when compared to those with BMI less than 25 (odds ratio 5.9 [95% CI 1.2-29.5]; $p=0.032$).²² Several studies found a statistically significant link between obesity and an increased risk of overall reported complications including mastectomy skin flap necrosis, fat necrosis, wound dehiscence, infection, seroma, hematoma, and implant extrusion.^{20-21, 25-27} Obese patients were almost twice as likely as patients of a normal weight to develop an expander/implant complication (odds ratio 1.8 [95% CI 1.1-3.0]; $p=0.02$).²¹

One retrospective case series did not find a significant association between BMI and overall complications, which included seroma, hematoma, skin problems and infection.²⁴ However, it is unknown how many patients were in the obese category and whether the study was adequately powered to address this association. Additionally, one retrospective case series did not find a significant association between BMI and infection,¹⁴ but it is important to note that a large sample size would be required to adequately evaluate this association.

Recommendation: A BMI of 25 or greater is associated with an increased risk of postoperative complications and reconstructive failure among patients undergoing post-mastectomy expander/implant breast reconstruction. These risks are even higher among patients with a BMI greater than 30. Obese patients should be informed of their increased surgical risks with expander/implant reconstructions and advised on practical weight loss solutions. Additionally, it should be recognized that the decision to proceed with surgery may preclude timely weight management.

Level III, IV Evidence

Recommendation Grade: A

Breast Size

Evidence suggests that patients with a preoperative breast cup size of C or larger may be at an increased risk for postoperative complication with immediate expander/implant breast reconstructions compared to those with a preoperative breast cup size of A or B. In a retro-

spective case series, large preoperative breast size was significantly associated with higher infection rates in both the univariate and multivariate analyses. In the univariate analysis, 28% of patients with a preoperative breast cup sizes of D and DD had an infection compared to 13% of those with a breast cup sizes of A, B, and C ($p<0.001$). In the multivariate analysis, preoperative breast cup size larger than C remained a statistically significant risk factor for infection; patients with a breast cup size of D or DD were nearly 3 times more likely than patients with smaller breasts to experience an infection (odds ratio 2.89 [95% CI 1.59-5.26]; $p<0.001$).¹⁴ A retrospective comparative study observed a greater rate of skin necrosis in breasts larger than 600 grams (> C cup) compared with breasts smaller than 600 grams (A or B cup) (19% vs. 1.8%, respectively; $p<0.01$).²⁸ Similar results were also reported in a multivariate analysis, which indicated for every 100-cc increase in final implant volume, the risk of developing a complication increases by 1.32 times ($p<0.001$).²⁷ One retrospective case series, however, found the exact opposite. The association between breast size and incidence of implant failure in an univariate statistical analysis demonstrated that patients with preoperative cup sizes of A and B were more likely to experience implant failure than patients with cup sizes of C and D (35.9% vs. 16.7%, respectively; $p=0.009$). However, a multivariate analysis could not be conducted due to small sample size; therefore, it is unclear if this association would have remained significant when controlling for the effects of other confounding factors.²³

Recommendation: Preoperative breast size, specifically C or larger, may be associated with an increased risk of complication and an increased risk of reconstructive failure in patients undergoing post-mastectomy expander/implant breast reconstruction. However, much of the currently available evidence does not control for BMI, which is associated with both preoperative breast size and complication rates. Given the limited evidence and contradictory literature, physicians should be aware of this potential complicating factor.

Level III, IV Evidence

Recommendation Grade: D

Diabetes

Evidence suggests that among patients with expander/implant breast reconstructions, diabetes is not a significant risk factor for postoperative complications, including implant failure, pulmonary embolism, seroma, necrosis, wound dehiscence, mastectomy flap necrosis, infection, and capsular contracture^{14,16,18,21} or reconstructive failure, defined as the premature removal of expander or implant.^{16, 21} Among the five studies that analyzed the impact of diabetes on surgical outcomes, one retrospective comparative study suggested that diabetes negatively impacted postoperative outcomes. In a univariate analysis, diabetes was shown to be a significant independent risk factor for development of total complications. Patients with diabetes had a higher rate of complications than patients without diabetes (56.7% vs. 30.8%, respectively; $p<0.004$). However, diabetes was not a statistically significant risk factor when controlling for other variables in a multivariate logistic regression model.²⁶

Recommendation: There is no evidence to indicate that diabetes is a significant independent risk factor for the development of either postoperative complications or reconstructive failure in patients undergoing post-mastectomy expander/implant breast reconstruction. However, this information should not deter surgeons from continuing to practice glycemic control in the peri-operative period for breast cancer patients.

Level II, III, IV Evidence

Recommendation Grade: B

Radiation Therapy

Overview

Research has found that radiation therapy is an independent risk factor for postoperative complications in patients undergoing immediate expander/implant breast reconstruction. Complications associated with radiation therapy include infection, wound dehiscence, necrosis, seroma, hematoma, capsular contracture, extrusion, implant loss and reconstruction failure.^{12, 17-18, 26, 29, 30-32} A retrospective cohort study found that 40.7% of patients who received radiation therapy experienced a postoperative complication compared with only 16.7% of patients who received no radiation therapy ($p < 0.01$).¹⁸ Using multivariate logistic regression analysis, other studies revealed similar disparities in total complication rates depending on radiation status when controlling for comorbidities and other confounding factors. The risk of total complications increased by 3.3 times¹² and 4.99 times²⁶ in patients who received radiation therapy compared with patients who did not receive radiation therapy ($p < 0.05$). The use of postoperative radiation therapy significantly increased the risk of most implant associated complications among patients with immediate expander/implant reconstructions.³¹ Compared with patients who received no adjuvant radiation therapy, those who received postoperative radiation therapy had higher rates of infection (3.8% vs. 20.5%, respectively), Baker Grade III and IV capsular contracture (2.7% vs. 15.4%, respectively), and implant loss (9.4% vs. 41%, respectively) (all $p < 0.05$).³¹

Level III, IV Evidence

Recommendation Grade: B

Previous Radiation

Retrospective studies suggest an increased risk of postoperative complications among patients who receive radiation therapy prior to expander/implant breast reconstruction.^{14, 33} Complication rates reported in two studies that evaluated expander/implant patients with and without radiation prior to reconstruction were 25% vs. 13.9%, respectively ($p < 0.01$),¹⁴ and 30% vs. 14%, respectively ($p = 0.007$).³³ Furthermore, a multivariate analysis that controlled for confounding factors found that expander/implant patients were 2.55 times as likely to have an infection as patients without radiation ($p = 0.002$).¹⁴ Results also suggest that previous radiation therapy may increase the risk of capsular contracture. Among the 20 patients who received whole-beam external radiation therapy, 40% experienced a Baker Grade III/IV capsular contracture compared with only 6.9% of patients

not receiving radiation therapy ($p = 0.03$).³⁴ A retrospective study comparing major and minor complication rates between patients with and without radiation therapy found that complications were more frequent in the radiation group, but the difference did not achieve statistical significance.³⁵ Other retrospective case series findings suggest that pre-reconstruction radiation therapy did not have a significant impact on overall complications, infection rates, and necrosis.³⁶

Level III, IV Evidence

Recommendation Grade: C

Radiation Therapy to Expander

Surgical outcomes were evaluated among three studies of patients who did and did not receive radiation during the expansion process. Two out of the three studies suggest that radiation therapy leads to higher rates of postoperative complications, including infection, mastectomy flap necrosis, seroma, hematoma, implant exposure, and explantation, although these differences did not reach statistical significance.³⁷⁻³⁸ The third study found that 51% of patients who received radiation to expanders experienced a complication compared with only 14% of patients who did not receive radiation ($p = 0.005$).³⁹ Radiation therapy could not be placed into the multivariate logistic regression model for further statistical analysis, however, due to small sample size. Furthermore, the optimal time between radiation to the expander and exchange of expander for a permanent implant is a clinically relevant question but one without supporting data to guide clinical decision-making.

Level III, IV Evidence

Recommendation Grade: B

Radiation Therapy to Implant

In nine studies, postoperative outcomes of patients who received radiation therapy following implant exchange were compared with patients who did not receive radiation therapy. Several of these studies found postoperative radiation therapy to be a significant risk factor for the development of capsular contracture ($p < 0.05$).^{34, 40-42} A prospective cohort study, which controlled for confounding factors in multivariate logistic regression analysis, demonstrated that postoperative radiation therapy was associated with a six-fold increase in risk of complications compared with no radiation therapy (odds ratio 6.4 [95% CI 1.6-25.0]) Patients who received postoperative radiation therapy were also 5.1 times more likely than patients who received no radiation therapy to experience reconstructive failure ($p = 0.02$).¹⁶ Additionally, a five year follow-up retrospective cohort study found that implant patients with radiation had a 61% total complication rate compared to only 21% among patients without radiation ($p = 0.003$).⁴⁴ Other studies also found an association between radiation to implant and higher postoperative complications rates; however, these differences were not statistically significant.^{21, 33, 43}

Level II, III, IV Evidence

Recommendation Grade: B

Optimal Timing of Radiation and Reconstruction

Evidence to support a recommendation on the appropriate timing of radiation therapy to a patient undergoing expander/implant breast reconstruction is limited. In a retrospective cohort study, no significant differences were found in the incidence of major or minor complications between patients who received external beam radiation therapy to the expander compared with those who received radiation therapy to the implant.⁴⁵ Likewise another retrospective cohort study found no significant differences in complication rates by timing of radiation.¹⁸ A small subgroup analysis of patients who received radiation therapy during the expansion process versus after implant exchange found that patients who received radiation therapy to expanders had numerically higher rates of capsular contracture; however, the difference was not statistically significant.⁴² A prospective cohort study evaluated the impact of radiation therapy to expanders versus implants to determine the outcome of implant failure and capsular contracture. The rate of implant reconstruction failure was 40% among patients who received radiation therapy to expanders and 6.4% among those who received radiation therapy to implants ($p < 0.0001$). The rate of Baker Grade IV capsular contracture was significantly higher in patients who received radiation therapy during the expansion process compared with patients who received radiation therapy to the implant or no radiation therapy at all (13.3% vs. 10.1% vs. 0%, respectively; $p < 0.001$).⁴⁶ An additional clinically important question is the impact of reconstruction on the delivery of radiation. Currently, there is no evidence that reconstruction delays the administration of radiation. The optimal time for radiation is within eight weeks of the mastectomy. Patients who receive radiation later than eight weeks post-mastectomy have higher five-year local recurrence rates.⁴⁷

Level II, III Evidence

Recommendation Grade: C

Overall Recommendation: The optimal timing of radiation is within eight weeks of the mastectomy. Radiation is associated with an increased risk of complications and reconstructive failure among patients undergoing post-mastectomy expander/implant breast reconstruction. Patients should be counseled in regards to these increased risks.

Level II, III, IV Evidence

Recommendation Grade: B

Chemotherapy

Most of the evidence regarding the impact of chemotherapy on complications with post-mastectomy expander/implant breast reconstructions does not address outcomes based on the timing of the chemotherapy. A retrospective case series found similar infection rates between patients who received chemotherapy before or after implant exchange compared to those without chemotherapy.¹⁷ Another case series did not find a significant association between chemotherapy and implant failures.²³ However, a prospective cohort study found higher infection rates among patients who received chemotherapy

after mastectomy but before breast reconstruction compared to those without chemotherapy (44% vs 25%, respectively; $p = 0.05$). It should be noted that one-third of patients included in this study received an autologous breast reconstruction and two-thirds underwent an expander/implant technique. No information was provided on the infection rate among those with autologous procedures and chemotherapy; therefore, it is unclear if this subgroup of patients experienced a higher or lower rate of infections compared to patients who received expander/implant reconstructions and chemotherapy.⁴⁸

Small studies suggest that chemotherapy before breast reconstruction may not be a significant risk factor for the development of surgical complications.^{36, 48-49} Complications evaluated in these statistical assessments included implant explantation, seroma, necrosis, infection, and hematoma. A study that separated neoadjuvant from adjuvant therapy among mastectomy patients with immediate expander/implant reconstruction showed no difference in rates of implant loss based on timing of chemotherapy or due to chemotherapy.⁴⁸ Also, neoadjuvant chemotherapy was not recognized as a significant risk factor for total complications in patients undergoing mastectomy and immediate expander/implant breast reconstructions.⁴⁹ Additionally, a case series found no significant relationship between neoadjuvant chemotherapy and early complications or prosthesis removal,³⁶ and another case series had similar findings although patients receiving either neoadjuvant or adjuvant therapy were not stratified by chemotherapy timing.²¹

The impact of reconstruction on the delivery of chemotherapy is an important question with potential impact on disease-free survival. A 12 week or greater delay in starting chemotherapy after mastectomy adversely impacts disease-free and overall survival.⁵⁰ Among patients treated at a National Comprehensive Cancer Network (NCCN) facility, 98% of breast cancer patients regardless of surgical treatment received chemotherapy within 12 weeks of definitive surgery.⁵¹

Recommendation: Preoperative chemotherapy does not appear to be a significant risk factor for either postoperative complications or implant failure in patients undergoing post-mastectomy expander/implants breast reconstruction.

Level II, III, IV Evidence

Recommendation Grade: C

Hormonal Therapy:

Evidence is limited regarding the impact of adjuvant hormonal therapy on breast reconstruction outcomes. When looking specifically at capsular contracture, a retrospective case series found that the use of hormonal therapy was not a significant risk factor for capsular contracture, and multivariate analysis confirmed these findings.²³ A prospective cohort study that looked at a broader definition of implant reconstruction failure was able to demonstrate a significantly higher rate of implant reconstruction failure in patients who received tamoxifen compared with patients who did not receive this therapy

(28% vs. 5%, respectively; $p=0.01$). On multivariate analysis, when controlling for the effect of radiation therapy and other confounding factors, the use of tamoxifen was found to be a statistically significant risk factor for the development of reconstructive failure (odds ratio 6.4; $p=0.03$).¹⁶ However, the analysis did not include clinically relevant factors such as age and incidence of hormonally sensitive disease.

Recommendation: Hormonal therapy may increase the risk of postoperative complications and reconstruction failure in patients undergoing post-mastectomy expander/implant breast reconstruction. However, inconsistent research findings and a lack of definitive evidence should alert physicians to evaluate each case individually.

Level II, IV Evidence

Recommendation Grade: D

Collagen Vascular Disease

Although the authors were interested in collagen vascular disease and associated outcomes, the systematic literature search process did not retrieve any studies meeting inclusion criteria.

Previous Breast Surgery

Although a history of previous breast surgery is not uncommon and despite the authors' interest in the relationship between previous breast surgery and reconstructive complications and/or failure, the systematic literature search process did not retrieve any studies meeting inclusion criteria.

Treatment

Antibiotic Prophylaxis

The systematic literature search process did not retrieve any studies meeting inclusion criteria. Consequently, other widely accepted sources contributed to the creation of an expert clinical opinion for best practice.

The Surgical Care Improvement Project (SCIP), which began in 2005, is a national effort to substantially reduce surgical morbidity and mortality and may be the best, most well-researched guideline available. It is a national partnership coordinated through a steering committee of 10 national organizations with technical expertise panels from more than 20 other organizations.⁵² The SCIP guidelines for antibiotics are three-fold. The purpose of these measures is to establish therapeutic antibiotic serum and tissue levels at the time of incision while minimizing risks to the patient and population. The guidelines state that 1) the antibiotics must be administered within one hour prior to incision, although two hours is acceptable for medications with longer infusion times such as fluoroquinolones and vancomycin; 2) the antibiotics must be appropriately selected for the surgical site; 3) the antibiotics should be discontinued within 24-hours of the end of the surgical procedure.⁵³ For breast cancer reconstruction cases, a first or second-generation cephalosporin would meet these requirements.⁵⁴ When patients are allergic to beta-lactams, appropriate antibiotics include vancomycin, fluoroquinolones, or clindamycin.⁵⁵

Preoperative antibiotic use, as defined by SCIP, is standard of care regardless of the type of breast reconstruction being performed. However, patients with implant-based breast reconstruction have a feature that distinguishes them from most other surgical patients: an external surgical drain in proximity to the implant that remains for an extended, and highly variable, period of time postoperatively.

To date there is a paucity of data on the appropriate length of postoperative antibiotic use when surgical drains are used in the setting of implants.

Recommendation: Patients undergoing post-mastectomy expander/implant breast reconstruction should receive a preoperative dose of an appropriate IV antibiotic initiated sixty minutes or less from the time of incision (within two hours for antibiotics with longer infusion times). Unless a drain is present, antibiotics should be discontinued within 24-hours of the completion of the procedure. If a drain is present, the role of antibiotics is less clear and should be left to physician preference. Of note, documenting a drain in proximity to the implant as a reason for continuation of IV antibiotics beyond the 24-hour postoperative period or switching to postoperative antibiotics within 24-hours of procedure completion is compliant with current SCIP guidelines. Presently, there is limited evidence on post-operative antibiotic prophylaxis. Overall, surgeons should adhere to their specific state and hospital guidelines on antibiotic administration.

Recommendation Grade: D

Acellular Dermal Matrix (ADM)

Current evidence suggests that the use of acellular dermal matrix (ADM), although increasingly common in post-mastectomy expander/implant breast reconstruction, can result in increased risk of complications in the presence of certain risk factors. In a retrospective review of immediate two-stage breast reconstructions that compared complication rates between an ADM cohort and two non-ADM cohorts (concurrent and consecutive), patients who received ADM had increased complications, particularly seroma (7.2% vs. 1.6%, respectively) and reconstructive failure, most commonly due to infection, (5.9% vs. 1.9%, respectively). Multivariate analysis showed these complications to be further exacerbated in the presence of risk factors such as smoking ($p=0.054$), older age ($p=0.041$), higher BMI ($p=0.023$), and axillary dissection ($p=0.002$).²⁵ Additionally, in a retrospective comparative study, it was found that the use of ADM in immediate two-stage implant-based reconstructions was associated with a significant increase in major complications compared to those without ADM (15.3% vs. 5.4%, respectively; respectively). These complications included infection requiring antibiotics (8.6% vs. 2.7%, respectively; $p = 0.001$), flap necrosis requiring excision (6.7% vs. 2.7%, respectively; $p = 0.015$), and explantation of the tissue expander (7.7% vs. 2.7%, respectively; $p = 0.004$).⁵⁶ In a retrospective review of immediate prosthesis-based reconstruction with and without ADM, the overall surgical complication rate was significantly higher in the ADM group (19.5 vs. 12.3, respectively; $p<0.001$). This was most relevant to overall wound infection, which was statistically significant in the univariate analysis ($p=0.031$) but not significant in the multivariate

analysis ($p=0.097$). The use of ADM did not significantly increase the incidence of minor wound infection, mastectomy flap necrosis, seroma, and hematoma. When overall surgical complications were examined in a univariate analysis, the use of ADM, smoking, higher BMI, higher initial volume, and larger implant size were statistically associated with a significantly higher rate of overall surgical complications; these remained statistically significant in the multivariate analysis. The authors hypothesized that the increased incidence of surgical complications in the ADM cohort may be attributable to other significant risk factors.²⁰ Results from a retrospective review of immediate two-stage reconstructions with and without ADM indicated that the ADM cohort had a significantly higher rate of infection ($p=0.022$), reoperation ($p=0.11$), expander explantation ($p=0.020$), and overall complications ($p=0.007$). However, when reconstructed breasts were stratified by size, ADM use was not associated with higher complication rates in patients with breasts weighing less than 600g; whereas, ADM use was significantly associated with higher infection rates in breasts larger than 600g. These results suggest that high BMI and high breast volume in conjunction with ADM use are factors that could increase the risk of postsurgical complications.²⁸

Six additional retrospective studies suggest that use of ADM is not associated with increased complication rates. The only exception was in a systematic review of nine studies that found a significantly higher rate of seroma in the ADM compared to the non-ADM group ($p=0.03$). Otherwise, both ADM and non-ADM cohorts had similar rates of infection leading to expander/implant explantation ($p=0.18$), incidence of cellulitis or wound infection not requiring surgical intervention ($p=0.09$), incidence of reported hematoma ($p=0.11$), and incidence of partial mastectomy flap necrosis ($p=0.08$).⁵⁷ Likewise, a previous study by the same authors found no significant difference in total complication rates between ADM and non-ADM cohorts ($p=0.79$).⁵⁸ A retrospective cohort study found similar complication rates between an ADM cohort (immediate single-stage reconstruction) and non-ADM (immediate two-stage reconstruction) cohort (14.8% vs. 19.6%, respectively; $p=0.18$). Initially, the non-ADM cohort was perceived to be more susceptible to complications than the ADM cohort, but this was attributed to the presence of irradiation, which when controlled for, resulted in similar complication rates between both groups. Irradiation and inexperience with surgical technique were the only two variables that appeared to be significantly associated with the incidence of a complication.³³ A retrospective cohort study further supported the use of ADM. Compared with patients without ADM, those with ADM reconstructions had fewer overall complications, such as seroma/hematoma, infection and wound complications; ADM use was also associated with lower rates of capsular contracture (odds ratio 0.16 [95% CI 0.73-0.38]; $p<0.001$) and fewer overall complications (odds ratio 0.61 [95% CI 0.38-0.97]; $p=0.038$).⁵⁹ Another retrospective review also found no significant difference in complications between the ADM and non-ADM cohorts.⁶⁰

Recommendation: Evidence on acellular dermal matrix (ADM) in post-mastectomy expander/implant breast reconstruction is varied and conflicting. Surgeons should evaluate each clinical case individually and objectively determine the use of ADM.

Level III Evidence

Recommendation Grade: C

Outcomes

Monitoring for Cancer Recurrence

The systematic literature search process did not retrieve any studies meeting inclusion criteria. Consequently, other widely accepted sources contributed to the creation of an expert clinical opinion for best practice.

Current guidelines for detecting local recurrence of post-mastectomy breast cancer, with or without breast reconstruction, recommend clinical examination alone. The American Society of Clinical Oncology (ASCO) advises clinical exam every 3-6 months in years 1-3, every 6-12 months in years 4-5, and then annually.⁶¹ The National Comprehensive Cancer Network (NCCN) recommends clinical exam every 4-6 months for 5 years, and then annually.⁶² There is no data to support screening for local recurrence following implant or tissue-based breast reconstruction by any imaging method, including mammography, ultrasound, or MRI. Additionally, a review of the evidence for surveillance mammography following breast reconstructions illustrates wide variation in the reporting of stage at diagnosis, use of radiotherapy, systemic treatment, length of follow-up, mammography regimen, and concurrent clinical findings. Although not consistently reported, it appears that most local recurrences found by mammography were also apparent on clinical exam.⁶³

Recommendation: Clinical examination is sufficient to detect local cancer recurrence in patients undergoing post-mastectomy expander/implant breast reconstruction. Imaging studies are not required as part of routine surveillance. On the basis of clinical suspicion, imaging studies can be used for clinical indications on a case by case basis. Diagnostic imaging is indicated if there is any clinical concern for recurrence.

Recommendation Grade: D

Effect of Implant-Based Reconstruction on Oncologic Outcomes

Evidence indicates that local control and survival are related for breast cancer. An overview of randomized trials found that the 10 year risk of local recurrence with and without post-mastectomy radiotherapy was 3.1% and 8%, respectively, for node-negative breast cancer, and 7.5 vs. 27.6%, respectively for node-positive disease. This reduction in risk of local recurrence was associated with a statistically significant 5-7% improvement in survival at 15 years, a benefit that was apparent only when the absolute reduction in local recurrence was more than 10%.⁶⁴ The aim of post-mastectomy radiation therapy is to minimize local recurrence in those patients at greatest risk, typically patients with T3 tumors and/or greater than 3 positive axillary nodes but

possibly also including patients with smaller tumors and/or fewer positive nodes. A randomized trial comparing the results of mastectomy with breast reconstruction versus mastectomy without breast reconstruction is not feasible, but evidence from retrospective studies shows that expander/implant breast reconstruction does not increase the risk of cancer recurrence or mortality. A retrospective analysis from the SEER registry provided comparison of 46,177 patients treated by mastectomy alone versus 3,620 patients treated by mastectomy and implant reconstruction versus 4,863 treated by mastectomy and tissue-based reconstruction. About 20% of patients in each cohort received post-mastectomy radiation therapy, and at a median follow-up of five years, breast cancer specific mortality was lower in the reconstructed patients. These differences persisted on a multivariate analysis incorporating stage of disease.⁶⁵ Similar results were cited in another study also using SEER data and reporting on 52,249 patients.⁶⁶ A matched cohort study comparison of 300 controls to 300 expander/implant patients observed no differences in local or regional recurrence, and higher rates of distant metastases (27% vs. 20%, respectively) and of breast cancer mortality (23% vs. 17%, respectively) in the control group.⁶⁷ In a comparison of 580 patients with delayed implant reconstruction to 1,158 matched controls, better disease free survival at 10 years (hazard ratio 0.78) and overall survival at 20 years (hazard ratio 0.90) was observed in the reconstructed patients; however, the study concluded that these differences were due to socioeconomic and health factors and not to the performance of breast reconstruction.⁶⁸ In a matched cohort study of 309 women who had mastectomy with immediate tissue expander/implant reconstruction compared to 309 women who had mastectomy alone, similar rates of locoregional recurrence (6.8% vs. 8.1%, respectively) and of time to locoregional recurrence (2.3 yrs vs. 1.9 yrs, respectively) were found, suggesting that reconstruction neither increased the risk nor delayed the diagnosis of locoregional recurrence.⁶⁹ In a comparison of 494 patients who had mastectomy with reconstruction to 427 who had mastectomy alone, similar rates of locoregional recurrence (2.2% vs. 4%, respectively) and time to locoregional recurrence (1.6 yrs vs. 1.6 yrs, respectively) were observed at a median follow-up of 4.5 years, and a lower rate of local and/or distant recurrence in the reconstructed patients (5.9% vs. 11.5%, respectively) was observed. All locoregional recurrences in the reconstructed patients were detected on clinical exam.⁷⁰

Recommendation: Post-mastectomy expander/implant breast reconstruction does not adversely affect oncologic outcomes. The need for post-mastectomy radiation therapy is often, but not always, apparent prior to surgery; accordingly, decisions regarding the sequencing of post-mastectomy breast reconstruction and radiation therapy are best made by a multidisciplinary team including the oncologic surgeon, plastic surgeon, medical oncologist and radiation oncologist.

Level III Evidence

Recommendation Grade: B

Complications Associated with Expander/Implant Breast Reconstruction

Complications, although not limited to, most commonly include the following: infection, hematoma, seroma, wound dehiscence, skin flap necrosis, expander/implant loss, malposition, expander/implant deflation, capsular contracture, hypertrophic or keloid scarring, and venous thromboembolism disease.

Conclusions

Currently in the US, expander/implant reconstruction is the most commonly performed technique for post-mastectomy breast reconstruction.⁷¹ This guideline is designed to promote evidence-based clinical decision-making and to improve the quality of care for breast cancer patients. As a professional society, ASPS aims to ensure that patients are well-informed of all available reconstructive options, including the types of procedures and timing options for post-mastectomy breast reconstruction.

Diagnosis Codes

ICD-9-CM

Scheduled to expire
September 30, 2014

ICD-10-CM

Scheduled to be effective
October 1, 2014. This list of
codes is not all-inclusive

• Malignant neoplasm of female breast	174.0-174.9	C50.01-
• Malignant neoplasm of male breast	175.0-175.9	C50.02-
• Secondary malignant neoplasm of other specified sites; breast	198.81	C79.81
• Carcinoma in situ of breast	233.0	D05.90-
• Capsular contracture of breast implant	611.83	N64.89-
• Unspecified abnormal mammogram	93.80	R92.8-
• Acquired absence of breast	V45.7	Z90.10-
• Encounter for breast reconstruction following mastectomy	V51.	Z42.1
• Personal history of malignant neoplasm of breast	V10.3	Z85.3
• Family history of malignant neoplasm of breast	V16.	Z80.3
• Genetic susceptibility to malignant neoplasm of breast	V84.01	Z15.01

Procedure Codes (CPT Codes)

• Immediate insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction	19340
• Delayed insertion of breast prosthesis following mastopexy, mastectomy or in reconstruction	9342
• Breast reconstruction, immediate or delayed, with tissue expander, including subsequent expansion	19357
• Breast reconstruction with latissimus dorsi flap, without prosthetic implant	19361
• Replacement of tissue expander with permanent prosthesis	11970
• Removal of tissue expander(s) without insertion of prosthesis	11971
• Removal of intact mammary implant	19328
• Removal of intact mammary material	19330
• Nipple/areolar reconstruction	19350
• Open periprosthetic capsulotomy, breast	19370
• Periprosthetic capsulectomy, breast	19371
• Revision of reconstructed breast	19380
• Implantation of biologic implant (e.g., acellular dermal matrix) for soft tissue reinforcement (e.g., breast, trunk) (List separately in addition to code for primary procedure)	15777
• Tissue grafts, other (eg, paratenon, fat, dermis)	20926

HCPS Codes

(Please check payer's policies).

• Implantable breast prosthesis, silicone or equal	L8600
• Prosthesis, breast (implantable) (Saline Implant)	C1789

Appendix A. Summary of Graded Recommendations, Benefits and Harms

Clinical Questions and Recommendations	Supporting Evidence (References and Level of Evidence)	GRADE
<p>PATIENT EDUCATION</p> <p>Clinical Question In patients undergoing surgical treatment for breast cancer, what is the optimal time to discuss breast reconstruction options?</p> <p>Recommendation Although federal law mandates insurance coverage for reconstructive surgery, there are limited mandates that ensure women have the necessary information to make informed decisions about available reconstructive options. Since 2009, New York, New Mexico, and California have enacted laws that address the concerns about patient communication measures. Additionally, in 2012, a bill was introduced in the US House of Representatives that would require the Department of Health and Human Services to plan and implement an education campaign to inform mastectomy patients of breast reconstruction availability, coverage, and relevant options. Overall, patients undergoing post-mastectomy expander/implant breast reconstruction should be given a preoperative referral to a plastic surgeon who can educate the patient about reconstructive options.</p> <ul style="list-style-type: none"> • Benefits: Timely patient education can improve patient satisfaction with the surgical decision-making process and satisfaction with the surgical outcome, without delaying cancer treatment. • Harms: Potential delay in cancer care if coordination of care is not expedited. 	<p>Literature was not critically appraised for this clinical question</p>	<p>D</p>
<p>IMMEDIATE VS. DELAYED RECONSTRUCTION</p> <p>Clinical Questions</p> <ul style="list-style-type: none"> • In patients undergoing mastectomy for the treatment of breast cancer, what is the optimal time for implant-based reconstruction (i.e., immediate versus delayed) when radiation treatment is not required? • In patients undergoing mastectomy for the treatment of breast cancer, what is the optimal time for implant-based reconstruction (i.e., immediate versus delayed) when radiation treatment is required? <p>Recommendation Evidence is varied and conflicting on the association between timing of post-mastectomy expander/implant breast reconstruction and postoperative complications. Additionally, postoperative outcomes are often affected by radiation therapy. Consequently, physicians should evaluate each patient case individually and give priority to patient preference.</p> <ul style="list-style-type: none"> • Benefits: Immediate breast reconstruction may benefit patients' self-esteem and body image by patients not having to live with a mastectomy defect. Immediate reconstruction also limits surgical recovery time. Delayed reconstruction is helpful to those patients who need more time to process their cancer diagnosis and treatment plan or to patients who have preventable surgical risk factors such as nicotine use or obesity. • Harms: Immediate reconstruction may have added risks for post-operative complications if the patient has a risk factor that can be avoided, such as use of nicotine products. Delayed reconstruction may cause added psychosocial stress among those who are distressed by the mastectomy defect. 	<p>12 (R:IV); 13 (T:III); 14 (R:IV); 15 (T:IV); 16 (T:II); 17 (T:IV)</p>	<p>C</p>

Clinical Questions and Recommendations	Supporting Evidence (References and Level of Evidence)	GRADE
<p>RISK FACTORS</p> <p>Clinical Questions</p> <p>In patients undergoing breast reconstruction following mastectomy, what are the risk factors when undergoing immediate implant-based reconstruction?</p> <p>Smoking</p> <p>Recommendation</p> <p>Evidence indicates that smoking is associated with an overall increased risk of complications and reconstructive failure in patients undergoing post-mastectomy expander/implant breast reconstruction. Patients should be informed of complications associated with smoking.</p> <ul style="list-style-type: none"> • Benefits: There is no benefit to smoking and patients should be counseled on smoking cessation. • Harms: Complications associated with nicotine use range from wound complications to implant loss, and smokers are at a 3 to 6 times greater risk of experiencing a postoperative complication compared to non-smokers. <p>Obesity</p> <p>Recommendation</p> <p>Evidence indicates that obesity, defined as body mass index (BMI) greater than 30, increases the risk of postoperative complications in patients undergoing post-mastectomy expander/implant breast reconstruction. Obese patients should be informed of increased surgical risk with expander/implant reconstructions.</p> <ul style="list-style-type: none"> • Benefits: There is no benefit to obesity, and patients should be counseled on practical weight loss solutions. • Harms: Wound infections and expander/implant failures are directly correlated with obesity. This correlation is evident in overweight patients (BMI greater than 25) but is amplified in patients who are obese (BMI greater than 30). Additional complications may include seroma, skin flap necrosis, fat necrosis, hematoma, seroma, wound dehiscence, and infection. <p>Breast Size</p> <p>Recommendation</p> <p>Evidence suggests the breast size, specifically breast cup size C or larger, may be associated with an increased risk of reconstructive failure in patients undergoing post-mastectomy expander/implant breast reconstruction. However, the current evidence does not control for BMI, which is directly associated with both breast size and complication rates. Therefore, physicians should remain flexible with regards to breast size and give priority to patient preference.</p> <ul style="list-style-type: none"> • Benefits: Macromastia may allow for more expander fill volume at the time of surgery or larger implants with direct-to-implant procedures. • Harms: Some evidence suggests that macromastia is associated with higher post-surgical complication rates. <p>Diabetes</p> <p>Recommendation</p> <p>Evidence indicates that diabetes is not a significant independent risk factor for development of postoperative complications and/or reconstruction failure in patients undergoing post-mastectomy expander/implant breast reconstruction. However, for diabetic patients, physicians should aim to practice glycemic control during the peri-operative period.</p> <ul style="list-style-type: none"> • Benefits: Diabetic patients do not require additional preventative measures for expander/implant reconstruction. • Harms: Hyperglycemia can be associated with impaired wound healing and infections. 	<p>14 (R:IV); 16 (T:II); 18 (T:III); 19 (R:II); 20 (T:III); 21 (T:IV); 22 (T:IV); 23 (T:IV); 24 (T:IV)</p> <p>14 (R:IV); 20 (T:III); 21 (T:IV); 22 (T:IV); 24 (T:IV); 25 (T:III); 26 (R:III); 27 (T:III)</p> <p>14 (R:IV); 23 (T:IV); 27 (T:III); 28 (T:III);</p> <p>18 (T:III); 14 (R:IV); 16 (T:II); 21 (T:IV); 26 (R:III)</p>	<p>A</p> <p>A</p> <p>D</p> <p>B</p>

Clinical Questions and Recommendations	Supporting Evidence (References and Level of Evidence)	GRADE
<p>Radiation Therapy</p> <p>Overview</p> <p>Recommendation</p> <p>Evidence indicates that patients undergoing post-mastectomy expander/implant breast reconstruction and receiving radiation therapy experience more postoperative complications than patients who do not require radiation therapy.</p> <ul style="list-style-type: none"> • Benefits: Radiation therapy has been proven to improve local control and overall survival among appropriately selected breast cancer patients. • Harms: Complications associated with reconstruction and radiation therapy include infection, wound dehiscence, necrosis, seroma, hematoma, capsular contracture, extrusion, implant loss, and reconstruction failure. <p>Previous Radiation</p> <p>Recommendation</p> <p>Evidence suggests that post-mastectomy expander/implant breast reconstruction patients are at an increased risk of experiencing postoperative complications if they receive radiation therapy prior to reconstruction. However, these results are inconsistent across the literature and better quality evidence is required.</p> <ul style="list-style-type: none"> • Benefits: Radiation therapy has been proven to improve local control and overall survival among appropriately selected breast cancer patients. • Harms: Complications may include infection and capsular contracture. 	<p>12 (R:IV); 17 (T:IV); 18 (T:III); 26 (R:III); 29 (T:III); 30 (T:III); 31 (T:III); 32 (T:III)</p> <p>14(R:IV); 33 (T:III); 34 (T:IV); 35 (T:III); 36 (T:IV)</p>	<p>B</p> <p>C</p>
<p>Radiation Therapy to Expander</p> <p>Clinical Question</p> <p>In patients undergoing mastectomy and radiation for the treatment of breast cancer, does radiation to the expander affect surgical outcomes?</p> <p>Recommendation</p> <p>Evidence suggests that in patients undergoing post-mastectomy expander/implant breast reconstruction, radiation therapy to the expander leads to higher rates of postoperative complications.</p> <ul style="list-style-type: none"> • Benefits: Radiation therapy has been proven to improve local control and overall survival among appropriately selected breast cancer patients. • Harms: Postoperative complications include infection, skin flap necrosis, seroma, hematoma, implant exposure, and explantation. 	<p>37 (T:III); 38 (T:IV); 39 (T:III)</p>	<p>B</p>
<p>Radiation Therapy to Implant</p> <p>Clinical Question</p> <p>In patients undergoing mastectomy and radiation for the treatment of breast cancer, does radiation to the implant affect surgical outcomes?</p> <p>Recommendation</p> <p>Evidence suggests that in patients undergoing post-mastectomy expander/implant breast reconstruction, radiation therapy to the implant leads to higher rates of postoperative complications.</p> <ul style="list-style-type: none"> • Benefits: Radiation therapy has been proven to improve local control and overall survival among appropriately selected breast cancer patients. • Harms: Complications include capsular contracture and reconstructive failure. 	<p>16 (T:II); 21 (T:IV); 33 (T:III); 34 (T:IV); 40 (T:II); 41 (T:III); 42 (T:III); 44 (T:III); 43 (T:III)</p>	<p>B</p>

Clinical Questions and Recommendations	Supporting Evidence (References and Level of Evidence)	GRADE
<p><i>Optimal Timing of Radiation and Reconstruction</i></p> <p><u>Clinical Question</u> In patients requiring radiation therapy and undergoing immediate breast reconstruction after mastectomy, when is the optimal time for radiation therapy?</p> <p><u>Recommendation</u> Evidence is limited to support optimal timing of radiation therapy for patients undergoing post-mastectomy implant/expander breast reconstruction. However, it is indicated that optimal time for radiation is within eight weeks of the mastectomy</p> <ul style="list-style-type: none"> • Benefits: Radiation therapy has been proven to improve local control and overall survival among appropriately selected breast cancer patients. Decisions about appropriate time for radiation take priority over reconstruction. • Harms: Overall disease-free survival may be compromised if radiation is not provided at the optimal time. Decisions about reconstruction should be optimized in order to reduce the chance for a post-surgical complication that could delay radiation therapy. <p><i>Radiation Therapy</i></p> <p><u>Overall Recommendation</u> Evidence indicates that radiation therapy, regardless of when it is administered, is associated with an increased risk of complications and/or reconstructive failure in patients undergoing post-mastectomy expander/implant breast reconstruction. Patients should be counseled regarding associated complications.</p> <ul style="list-style-type: none"> • Benefits: Radiation therapy has been proven to improve local control and overall survival among appropriately selected breast cancer patients. • Harms: Evidence suggests that radiation is a risk factor for reconstructive surgery, both in regards to complications and aesthetic outcomes. <p><i>Chemotherapy</i></p> <p><u>Recommendation</u> Evidence suggests that chemotherapy does not appear to be a significant risk factor for patients undergoing post-mastectomy expander/implant breast reconstruction. Mostly, the currently available literature does not address postoperative outcomes based on the timing of chemotherapy.</p> <ul style="list-style-type: none"> • Benefits: Chemotherapy can decrease mortality rates in appropriately selected breast cancer patients. • Harms: Currently, there is no persuasive evidence to suggest that chemotherapy impacts reconstruction outcomes. <p><i>Hormonal Therapy</i></p> <p><u>Recommendation</u> Evidence is inconclusive regarding the impact of hormonal therapy on postoperative outcomes for patients undergoing post-mastectomy expander/implant reconstruction. There is a possibility that hormonal therapy may increase risk, however, physicians should evaluate each patient case individually and give priority to patient preference</p> <ul style="list-style-type: none"> • Benefits: Hormonal therapy can decrease mortality rates in appropriately selected breast cancer patients. • Harms: Currently, there is no persuasive evidence to suggest that hormonal therapy impacts reconstruction outcomes. 	<p>18 (T:III); 42 (T:III); 45 (T:III); 46 (T:II); 47 (NR)</p> <p>All literature that was appraised for the above commentary on radiation therapy was considered for this overall recommendation</p> <p>17 (T:IV); 21 (T:IV); 23 (T:IV); 36 (T:IV); 48 (T:II); 49 (T:III); 50 (NR); 51 (NR)</p> <p>16 (T:II); 23 (T:IV)</p>	<p>C</p> <p>B</p> <p>C</p> <p>D</p>

Clinical Questions and Recommendations	Supporting Evidence (References and Level of Evidence)	GRADE
<p>ANTIBIOTIC PROPHYLAXIS</p> <p>Clinical Question In patients undergoing implant-based reconstruction after mastectomy, what is the optimal duration of antibiotic prophylaxis for prevention of postoperative infections?</p> <p>Recommendation SCIP protocol dictates that patients undergoing post-mastectomy expander/implant breast reconstruction should receive preoperative antibiotics in accordance with published guidelines. Documentation of drains in proximity to an implant provides sufficient reason for continuation of intravenous antibiotics beyond the currently advised 24 hour postoperative period. Overall, surgeons should adhere to their specific state and hospital guidelines on antibiotic administration.</p> <ul style="list-style-type: none"> • Benefits: Appropriate antibiotic prophylaxis will decrease the risk of postoperative infections without significantly increasing drug resistant organisms. • Harms: Inappropriate antibiotic prophylaxis may not adequately protect patients against postoperative infections and can increase the incidence of drug resistant organisms. 	Literature was not critically appraised for this clinical question	D
<p>ACELLULAR DERMAL MATRIX</p> <p>Clinical Question In patients undergoing mastectomy and implant-based breast reconstruction, what are the outcomes associated with utilizing Acellular Dermal Matrix during reconstruction?</p> <p>Recommendation Evidence regarding the use of acellular dermal matrix (ADM) in patients undergoing post-mastectomy expander/implant reconstruction is varied and conflicting. Although, the currently available evidence indicates a trend toward increased complications with ADM use, it should be noted that the evidence does not control for selection biases.</p> <ul style="list-style-type: none"> • Benefits: ADM is currently used to increase soft tissue coverage, support the implant pocket, improve contour and reduce pain with expansion. However, evidence to support these improved surgical outcomes are limited. • Harms: Some evidence suggests that use of ADM is associated with increased postoperative complications, specifically related to infection and seroma. 	20 (T:III); 25 (T:III); 56 (NR); 57 (T:III); 58 (T:III); 59 (T:III); 60 (T:III)	C
<p>MONITORING FOR CANCER RECURRENCE</p> <p>Clinical Question In patients undergoing mastectomy and implant-based breast reconstruction, what are the screening recommendations to monitor for cancer recurrence?</p> <p>Recommendation Per clinical expertise, examination is sufficient to detect local recurrence in patients who have undergone post-mastectomy expander/implant breast reconstructions. Diagnostic imaging is indicated if there is any clinical concern for recurrence.</p> <ul style="list-style-type: none"> • Benefits: Breast exams are a highly reliable way to detect a cancer recurrence post-mastectomy. • Harms: There is no evidence to suggest that reconstruction interferes with the detection of a cancer recurrence. 	Literature was not critically appraised for this clinical question	D
<p>IMPLANT-BASED RECONSTRUCTION AND ONCOLOGIC OUTCOMES</p> <p>Clinical Question In patients undergoing breast reconstruction following mastectomy, what are the oncologic outcomes associated with undergoing immediate implant-based reconstruction?</p> <p>Recommendation Evidence indicates that post-mastectomy expander/implant breast reconstruction does not adversely affect oncologic outcomes. Administration of radiation therapy varies per patient and so, decisions regarding sequencing of treatment should be made by a multidisciplinary team.</p> <ul style="list-style-type: none"> • Benefits: Breast reconstruction confers significant quality of life and psychosocial benefits among those that desire to undergo the procedures. • Harms: No evidence to suggest that breast reconstruction negatively impacts cancer surveillance or increases recurrence rates. 	64 (NR); 65 (T:III); 66 (NR); 67 (T:III); 68 (T:III); 69 (T:III); 70 (T:III)	B

Appendix B. Literature Search Process

Literature Search Goal

A literature search was conducted to identify published evidence relevant to several clinical topics in breast reconstruction procedures using tissue expanders and/or implants. Clinical topics to be addressed in an evidence-based guideline were chosen by an expert panel (ASPS Breast Reconstruction Guideline Work Group), and the search and initial screening was performed under a prospective work plan in order to minimize bias.

Literature Search Process

Database(s) Searched

PubMed (including MEDLINE and pre-MEDLINE citations)

Search Terms:

(Mammaplasty[MeSH] AND reconstruction) OR “breast reconstruction”

Limits: English only; Humans; January 1, 2001 to December 31, 2011; NOT publication types case reports, editorial, comment, letter, news, newspaper article, in vitro, legal cases, or legislation

CINAHL (Cumulative Index to Nursing and Allied Health Literature)

Search Terms:

“Breast reconstruction” OR (mammaplasty AND reconstruction)

Limits: English only; January 1, 2001 to December 31, 2011; non-MEDLINE citations

The Cochrane Library

Search Terms:

“Breast reconstruction”

Limits: Cochrane Database of Systematic Reviews (protocols of pending reviews omitted)

Manual reference checks

Search terms: N/A. Bibliographies from accepted studies and recent reviews were reviewed by hand for potentially relevant citations, and compared to the overall yield from the electronic searches.

Study Screening

Inclusion Criteria

Studies published in English from 2001-2011, reporting outcomes of interest for at least 10 women undergoing breast reconstruction using tissue expanders and/or implants. Reconstruction procedures performed after mastectomy for breast cancer, precancerous conditions (e.g. DCIS), or prophylactically (e.g. BRCA carriers, contralateral mastectomy) were eligible. Studies with a mixed population of autologous and implant-based reconstruction were eligible if at least one outcome was separately available for the subgroup of patients with implant-based reconstruction. Outcomes of interest varied by clinical question, but in general, included safety (rates of complication), risk as stratified by patient characteristics, aesthetic outcomes, and patient satisfaction. Single-arm studies were eligible but are a lower tier of evidence than comparative studies; if sufficient higher-tier evidence is available, these studies may not be summarized.

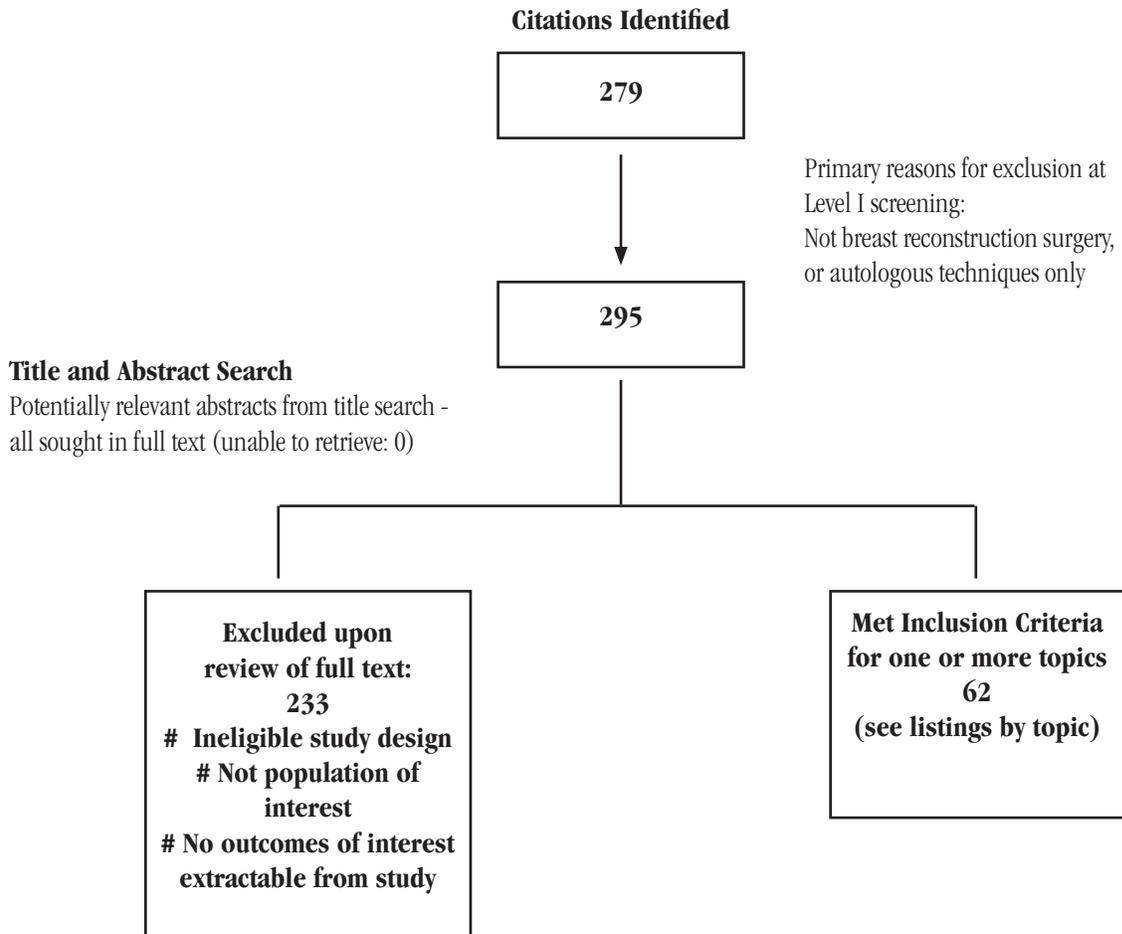
Exclusion Criteria

Languages other than English; Meeting abstracts; Narrative reviews or commentary; Studies with fewer than 10 patients; Studies of autologous techniques only; Breast augmentation with implant (not reconstruction); No outcomes of interest; mixed populations with no separable data.

Primary Search

Databases:

- PubMed (2,731)
- CINAHL (13 non-duplicates)
- Cochrane (0 non-duplicates*)
- Bibliography search (5 non-duplicates)



Appendix C
ASPS Evidence Rating Scales



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Evidence Rating Scale for Therapeutic Studies

Level of Evidence	Qualifying Studies
I	High-quality, multi-centered or single-centered, randomized controlled trial with adequate power; or systematic review of these studies
II	Lesser-quality, randomized controlled trial; prospective cohort or comparative study; or systematic review of these studies
III	Retrospective cohort or comparative study; case-control study; or systematic review of these studies
IV	Case series with pre/post test; or only post test
V	Expert opinion developed via consensus process; case report or clinical example; or evidence based on physiology, bench research or “first principles”

Evidence Rating Scale for Diagnostic Studies

Level of Evidence	Qualifying Studies
I	High-quality, multi-centered or single-centered, cohort study validating a diagnostic test (with “gold” standard as reference) in a series of consecutive patients; or a systematic review of these studies
II	Exploratory cohort study developing diagnostic criteria (with “gold” standard as reference) in a series of consecutive patient; or a systematic review of these studies
III	Diagnostic study in nonconsecutive patients (without consistently applied “gold” standard as reference); or a systematic review of these studies
IV	Case-control study; or any of the above diagnostic studies in the absence of a universally accepted “gold” standard
V	Expert opinion developed via consensus process; case report or clinical example; or evidence based on physiology, bench research or “first principles”

Evidence Rating Scale for Prognostic/Risk Studies

Level of Evidence	Qualifying Studies
I	High-quality, multi-centered or single-centered, prospective cohort or comparative study with adequate power; or a systematic review of these studies
II	Lesser-quality prospective cohort or comparative study; retrospective cohort or comparative study; untreated controls from a randomized controlled trial; or a systematic review of these studies
III	Case-control study; or systematic review of these studies
IV	Case series with pre/post test; or only post test
V	Expert opinion developed via consensus process; case report or clinical example; or evidence based on physiology, bench research or “first principles”

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