SYSTEMATIC REVIEW

European Journal of BREAST HEALTH

DOI: 10.4274/ejbh.galenos.2026.2025-10-1
Eur J Breast Health 2026;22(2):115-125

Evolving Concepts and Contemporary Management of Early-Stage Breast Cancer: An Evidence-Based Approach to Grey Zones from a Comprehensive Breast Unit Part 1: Locoregional Therapy, Pathology, Radiology

Elif Şenocak Taşçı[1], Halil Kara[2], Emir Çapkınoğlu[2], Onur Dülgeroğlu[2], Serra Bayrakçeken[3], Fatma Tokat[2], Serap Yücel[2], Irmak Durur Subaşı[2], Ahmet Yeşilyurt[2], Uğur Özbek[2], Gül Esen İçten[2], Nuran Bese[2], Cihan Uras[2], Yeşim Eralp[2]

[1]Department of Medical Oncology, Acıbadem Mehmet Ali Aydınlar University Atakent Hospital, İstanbul, Türkiye
[2]Acıbadem Research Institute of Senology, Acıbadem Mehmet Ali Aydınlar University, İstanbul, Türkiye
[3]Department of General Surgery, Acıbadem Mehmet Ali Aydınlar University, İstanbul, Türkiye

ABSTRACT

Breast cancer is the most frequently diagnosed malignancy among women worldwide, and significant progress in systemic therapy, surgical techniques, and radiotherapy has contributed to improved clinical outcomes. However, many clinical scenarios encountered in daily practice are not fully addressed by randomized trials, leaving persistent areas of uncertainty in the management of early-stage breast cancer. To meet these challenges, the multidisciplinary panel at Research Institute of Senology, Acıbadem University developed consensus-driven recommendations for clinical scenarios that are encountered in daily practice. Herein, we aim to reflect both current evidence and institutional practice, and to provide practical guidance in areas where uncertainty persists. As breast cancer treatment continues to evolve, updates will be required to integrate emerging data and refine individualized patient care.

Keywords: Breast cancer; early-stage; multidisciplinary; radiation oncology; radiology; pathology; surgery

KEY POINTS

- Early-stage breast cancer management increasingly requires individualized strategies that integrate clinical, radiological, pathological, and molecular data rather than a one-size-fits-all approach.
- Breast-conserving surgery remains oncologically safe for most patients with early-stage breast cancer, provided that adequate surgical margins are achieved and sentinel lymph node biopsy or targeted axillary dissection is performed in accordance with disease stage and treatment response.
- Advances in surgical techniques, such as breast-conserving surgery following neoadjuvant therapy and refined axillary staging, along with hypofractionated radiation schedules, support de-escalation without compromising oncologic safety.

Corresponding Author: Elif Şenocak Taşçı MD;
E-mail: esenocak@gmail.com **ORCID:** orcid.org/0000-0002-1686-1628
Received: 08.10.2025 **Accepted:** 01.01.2026 **Available Online Date:** 24.03.2026
Cite this article as: Şenocak Taşçı E, Kara H, Çapkınoğlu E, Dülgeroğlu O, Bayrakçeken S, Tokat F, et al. Evolving concepts and contemporary management of early-stage breast cancer: an evidence-based approach to grey zones from a comprehensive breast unit part 1: locoregional therapy, pathology, radiology. Eur J Breast Health. 2026;22(2):115-125

Introduction

Breast cancer (BC) is consistently reported as the most frequent cancer in women, with an estimated 2.3 million new cases leading to 670,000 deaths in 2022; its uneven global burden highlights the urgent need for standardized and unrestricted access to comprehensive management strategies (1). Through the exceptional efforts of pre-clinical and clinical researchers worldwide, substantial advances in the understanding of biology and treatment have been achieved, leading to a 2.5% decrease in mortality in some high-income countries (2). Because not all clinical scenarios correspond to clinical trial settings, routine management of BC requires a personalized, evidence-guided approach tailored to each patient's needs.

In this article, we provide practical recommendations for common clinical questions that arise during our weekly multidisciplinary tumor board meetings. The problems addressed here reflect our evolving, personalized approach aligned with emerging data on clinical scenarios encountered in daily practice at the Research Institute of Senology, Acıbadem University (RISA). We acknowledge that some of our statements may not have a strong level of evidence or be generalizable to all patients due to disparities in medical care, patient preferences, or lack of treatment availability. However, we believe the recommendations included in this report will provide guidance on various challenging and controversial issues faced by many physicians involved in BC care nationwide. As RISA, we aim to develop institution-specific standards to guide the evaluation and management of patients with early-stage disease. Our panel comprises general and plastic surgeons, medical oncologists, radiation oncologists, radiologists, clinical geneticists, a pathologist, and supportive medical personnel, including nurses, physiotherapists, nutrition specialists, and a psychologist, working in an academic clinical setting specialized in BC. Initially, each clinical group identified questions of clinical relevance, either because of a lack of robust data, pending data from clinical trials, or unique scenarios not addressed by the available evidence and requiring expert opinion. All these questions were discussed in detail in a separate meeting, and if a consensus on an issue was not reached, alternative opinions were put to a vote to determine the best approach reflecting the recommendations of the experts on the panel.

Because treatment for BC rapidly evolving, the statements reported as RISA opinions may be challenged by emerging data from ongoing clinical trials. Therefore, this work will be updated every two years.

Clinical and Research Consequences

1. Radiology

1.1. What is the Optimal Screening for Women?

Mammographic screening and early detection of disease decrease BC mortality (3). In our country, cancer early diagnosis, screening, and education centers offer biannual mammographic screening to women over the age of 40. However, the sojourn time for BC is shorter in younger women. The risk of advanced-stage disease is 21–28% higher with biannual screening than with annual screening, and the reduction in mortality is smaller when the screening interval exceeds 1 year in young women (4). It has been documented that more than 1/3 of BC patients in our country are younger than 50 years of age (5). Therefore, we recommend annual screening for all women aged 40–49. For women over the age of 50, screening intervals should be determined by individual risk factors and breast composition.

Breast density reduces cancer detection rates (CDR) and significantly increases interval cancer risk by masking small cancers; it is an independent risk factor, conferring a 2.9–6-fold higher BC incidence than in fatty breasts (6, 7). Accordingly, women with dense breasts benefit from supplemental screening. The main supplemental screening methods are digital breast tomosynthesis (DBT), ultrasound (US), and contrast-enhanced modalities, such as magnetic resonance imaging (MRI) and contrast-enhanced mammography (CEM) (8). DBT detects lesions similar to those detected by mammography (MMG), may miss more aggressive, benign-appearing tumors, and does not reduce the interval cancer rate. US increases the CDR more than DBT does (by an additional 2.5–4/1,000), particularly for invasive tumors, and reduces interval cancers; however, it is operator-dependent and time-consuming. Because performance is highly user-dependent and benign and malignant features can overlap, US can prompt unnecessary biopsies and short-interval follow-up recommendations for BI-RADS 3 lesions. Automated breast US, designed to mitigate these limitations, yields a similar or slightly lower CDR, but a higher recall rate. Contrast-enhanced modalities (MRI, MMG) provide functional and morphologic information with markedly higher sensitivity, yielding large CDR gains (≈14–16 per 1,000), but require intravenous contrast and are relatively expensive and less accessible (8).

Today, instead of a "one-size-fits-all" approach, risk-based screening is preferred in many centers (9), and we also believe that we can best serve our patients by applying personalized screening. Current guidelines recommend annual MRI screening in addition to MMG/DBT for high-risk patients (those with high-

risk gene mutations, those who have received mediastinal radiotherapy (RT) at a young age, and those with a lifetime risk higher than 20%) (3). It has been demonstrated that patients at intermediate risk for BC (patients who have dense breasts, who have had a diagnosis of an atypical lesion in previous biopsies, who have a history of BC, or who have a lifetime risk of 15–20%) also benefit from supplemental screening (9, 10). We recommend annual US and MMG/DBT screening for these women. Moreover, based on studies showing increased CDR with MRI screening in women with dense breasts (11, 12), we recommend that contrast-enhanced studies (MRI or CEM) replace US every 2–4 years. Screening with MMG or DBT is sufficient for women who do not have any of the above risk factors. We anticipate that artificial intelligence and machine learning programs that can evaluate the complexity of breast tissue will play a role in identifying those patients at increased risk who might benefit from MRI screening (13).

1.2. What is the Optimal Radiologic Modality for Preoperative Staging and Response Evaluation?

Breast MRI is the most sensitive modality for delineating the extent of disease in patients with newly diagnosed BC (14, 15). Preoperative MRI is recommended for patients with dense breasts who are candidates for breast-conserving surgery (BCS), particularly those younger than 50 years. It is also appropriate for patients with invasive lobular carcinoma (ILC) or ductal carcinoma *in situ* (DCIS), for those with suspected multifocal disease, and for those with discordant conventional imaging findings. CEM is an acceptable alternative when MRI is unavailable (16). This strategy may reduce re-excision rates and local recurrence (17, 18). However, any suspicious finding on contrast-enhanced imaging that could alter the treatment plan should be confirmed histologically before surgery.

In patients receiving neoadjuvant chemotherapy, MRI is the most accurate modality for evaluating treatment response (19, 20). Baseline and post-treatment MRIs should be obtained to determine treatment response, and when an interim assessment is required, an MRI can objectively measure early response and support timely modification of the therapeutic plan. For candidates for BCS, the primary tumor should be marked with a clip before systemic therapy. When axillary disease is limited (≤2 biopsy-proven metastatic nodes), the involved nodes should be marked prior to therapy to enable targeted axillary dissection (TAD) (21).

1.3. What is the Optimal Post-Treatment Radiological Modality During Routine Follow-up?

Regardless of age, annual MMG, with or without DBT, is recommended for all women who have undergone BCS (10). The first imaging follow-up should be performed 6 months after completion of therapy. Routine semiannual US surveillance is not indicated. We recommend annual supplemental US for patients after BCS and screening MRI every 2 years for those at increased risk; in years when MRI is performed, supplemental US may be omitted. Patients considered at increased risk include:

- <40 years at diagnosis
- carriers of *BRCA1/BRCA2* pathogenic variants
- patients <50 years at diagnosis with dense breasts
- whose tumor was detected only by MRI at diagnosis
- tumor >5 cm at diagnosis
- multicentric or multifocal tumors treated with BCS
- patients who did not receive RT after BCS
- triple-negative tumors
- ILC
- interval cancers.

Patients not considered at increased risk should return to the population-based screening program 10 years after treatment, and screening should continue as long as they remain in good health.

Although some evidence supports screening after nipple- or skin-sparing mastectomy with reconstruction, current guidelines do not recommend routine radiologic follow-up (20). However, any residual breast tissue—particularly after nipple-sparing procedures—should be evaluated with MMG or MRI 6–12 months after therapy. If substantial residual tissue is present, follow-up should use the same protocol as for patients treated with BCS. If no significant tissue remains, perform a physical examination every 6 months and/or an annual US; MRI may be added every 3–4 years or as clinically indicated. In our experience, US and MRI can detect residual or recurrent breast tumors in these patients earlier than by physical examination.

In patients who have undergone simple mastectomy, physical examination alone is sufficient to evaluate the chest wall and no imaging follow-up is required (22).

2. Pathology

2.1. What is the Optimal Method to Evaluate Ki-67?

Ki-67 is a nuclear proliferation marker expressed in all active cell-cycle phases and has diagnostic and prognostic utility across cancers, including BC, where it is an independent predictor of disease-free survival; for example, five-year disease-free survival was 86.7% with Ki-67 ≤15% versus 75.8% with Ki-67 >45%

(23, 24). By immunohistochemistry (IHC), any brown nuclear staining is considered indicative of Ki-67 positivity in tumor cells; cytoplasmic staining alone is not counted. Only invasive tumor nuclei should be scored, excluding the typically smaller, scattered lymphocytes (often Ki-67–positive) and spindle-shaped stromal cells surrounding tumor nests. Several methodologies have been developed for the estimation of Ki-67–positive cells, including visual estimation, manual counting, and automated digital image analysis. While visual estimation is the fastest and least costly method (typically <1 minute), it suffers from poor reproducibility and limited reliability. Manual counting is a cost-effective alternative, but is time-consuming, requiring approximately 5–6 minutes per case. This method is impractical for routine use due to its low reproducibility (25). Furthermore, inter-observer variability is a known challenge in Ki-67 scoring, and threshold values may vary considerably across institutions (26). Therefore, automated analysis has been developed to minimize such variability and improve reproducibility (27).

Digital image analysis involves identifying hotspots and calculating the mean percentage of brown-stained pixels among all stained pixels. The Ki-67 index is calculated automatically as the number of positively stained tumor nuclei divided by the total number of tumor nuclei × 100.

2.2. What is the Optimal Method for HER2 Evaluation?

HER2 is overexpressed in about 15% of BC cases, due to gene amplification, and is routinely assessed by IHC to determine eligibility for anti-HER2 therapy. IHC scoring per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) evaluate at least 10% of invasive tumor cells and is based on membrane staining completeness and intensity: 0 (null) if <1% of cells stain; 0 (ultralow) if ≥1% stain but without sufficient completeness or intensity; 1+ if ≥10% show weak, incomplete staining (negative/low); 2+ if ≥10% show weak-moderate complete or incomplete staining or if <10% show strong staining (equivocal); and 3+ if ≥10% show strong, complete membranous staining (positive). For IHC 2+ tumors, fluorescence *in situ* hybridization/*in situ* hybridization is required to quantify *HER2* gene amplification using both the HER2/CEP17 ratio and mean HER2 copy number; the results are classified into the five ASCO/CAP-defined interpretive groups. Ambiguous genomic profiles (e.g., Groups 2 and 4) necessitate integration with IHC findings and morphological features to establish a final HER2 status. This combined stepwise evaluation minimizes analytical discrepancies, improves diagnostic precision, and ensures accurate identification of patients most likely to benefit from HER2-targeted therapies (28).

To reduce interobserver variability, digital pathology workflows use automated pipelines comprising slide digitization, tumor-region detection (with optional manual annotation), parameter calibration, cell segmentation, quantitative assessment of membrane completeness and intensity, cell-level classification, and generation of a final HER2 score according to ASCO/CAP criteria (29-31).

In our daily practice;

• Ki-67 and HER2 samples are first digitized using high-resolution slide scanners such as Leica, Hamamatsu, and 3DHİSTECH.

• Once the digital slides are available on the ViraSight platform, superusers can initiate Ki-67 and HER2 analyses directly on the whole slide images.

• Importantly, the algorithms are compatible with all major slide formats, ensuring smooth performance regardless of the scanner vendor (27, 30).

• Upon completion of the analysis, the system automatically sends notifications to the relevant pathologists. The pathologists then review the analyses through the platform.

• The pathologist interprets the ViraSight-generated output and determines their final score or index based on the diagnostic context.

• This workflow not only enhances diagnostic accuracy but also accelerates and standardizes the evaluation process through digital and artificial intelligence-assisted integration.

3. Controversial Issues in Breast Cancer Surgery

3.1. What are the Optimal Surgical Margins for Invasive and In-situ Breast Cancer?

Achieving negative surgical margins in BCS is essential to minimize the risk of local recurrence. After excision, histopathological assessment of the margins is required to confirm adequacy. For patients with invasive breast carcinoma, with or without an associated DCIS component, the “no ink on tumor” criterion (absence of invasive or *in situ* carcinoma at the inked margin) is considered sufficient (32). In contrast, for patients with pure DCIS or DCIS with microinvasion, a wider surgical margin of at least 2 mm is generally recommended to lower the risk of ipsilateral breast tumor recurrence (33). Moreover, when partial breast irradiation (PBI) is planned, margins of ≥2 mm are advised to ensure optimal local control (34, 35).

3.2. What is the Gold Standard Surgical Approach for Invasive Breast Cancer?

With advances in surgical techniques over recent decades, the operative management of BC has become considerably less invasive. BCS followed by RT has been shown to provide overall survival (OS) outcomes comparable to mastectomy, while offering additional benefits such as faster postoperative recovery, fewer

complications, and superior cosmetic results (36, 37). Discussions at the 2025 St Gallen International Breast Cancer Conference delivered one of the clearest messages to date, emphasizing the need to avoid mastectomies that are not clinically indicated and are often driven by misperceived risk or misunderstanding of treatment outcomes (38). Absolute indications for mastectomy include pregnancy during the first trimester, diffuse pleomorphic microcalcifications, or extensive disease that prevents achieving negative margins with an acceptable cosmetic outcome. Relative contraindications to BCS include a prior history of RT to the breast or chest wall, active connective tissue disorders (e.g., scleroderma), persistently positive margins despite re-excision, and known or suspected hereditary BC syndromes (32, 39). We carefully evaluate patients and, when mastectomy is not strictly indicated, discuss the potential benefits of breast-conserving approaches with patients as part of our daily routine.

3.3. When Can Sentinel Lymph Node Biopsy be Omitted in Primary Breast Cancer Undergoing Upfront Surgery?

Axillary staging has long been a standard component of surgical management for BC, with a positive sentinel lymph node biopsy (SLNB) traditionally leading to axillary lymph node dissection (ALND). However, recent studies have increasingly emphasized de-escalation of axillary surgery to reduce morbidity without compromising oncologic outcomes (40, 41). Current consensus guidelines support omission of SLNB in carefully selected patients with early-stage BC undergoing breast-conserving therapy, such as those aged over 70 years with clinical T1N0M0 invasive ductal carcinoma (IDC), grade 1, hormone receptor (+) and HER2(-) disease, and in settings where axillary nodal status is unlikely to alter prognosis or influence adjuvant treatment decisions (42). In our practice, we proceed in accordance with established guidelines. Although evidence supports omitting SLNB in patients older than 50 years, our institutional practice uses a 60-year threshold.

3.4. What is the Optimal Surgical Approach Following Neoadjuvant Therapy in Breast Cancer?

For patients whose BC management begins with neoadjuvant treatment (NAT), BCS is recommended when there are no contraindications or known genetic predispositions are present. Data indicate that BCS is oncologically safe in this setting, with local recurrence rates comparable to or lower than those observed after mastectomy (43, 44). Accurate localization of the primary tumor prior to therapy initiation is critical for surgical planning, particularly in cases where a significant radiologic or pathologic response is anticipated. MRI is strongly recommended both before and after NAT to assess the extent of response and guide surgical decision-making. In patients undergoing BCS after NAT, if a pathologic complete response (pCR) is not achieved, the tumor bed should be marked intraoperatively with at least four surgical clips to facilitate adjuvant therapy and long-term surveillance (45, 46). Although the role of less invasive approaches is expanding in the post-neoadjuvant setting, current evidence does not yet support the complete omission of surgical intervention. Consistent with international guidelines and the current body of evidence, our clinical practice is to prefer BCS as the primary surgical option following neoadjuvant systemic therapyin the absence of contraindications such as multicentric disease, a persistent large tumor burden not amenable to clear margin control, high-risk genetic mutations (e.g., *BRCA1/2*), or other patient-specific factors.

3.5. What is the Optimal Use of Targeted Axillary Dissection and SLNB in Axillary Management Following Neoadjuvant Therapy?

Axillary surgical management following NAT remains the subject of ongoing debate. With the increasing adoption of NAT, strategies for axillary staging and intervention have evolved to reduce the morbidity associated with ALND. Minimally invasive approaches, such as SLNB, may be appropriate depending on both the initial clinical nodal status and the response to therapy (47). Nodal staging can be broadly categorized as follows: clinically node-negative (cN0) before and after NAT; clinically node-positive (cN+) at baseline and pathologically node-negative (ypN0) after NAT; and persistently node-positive (cN+/ypN+) following therapy. In patients who remain cN0 after NAT, SLNB is generally sufficient. In those who convert from cN+ to ypN0, TAD—defined as SLNB combined with removal of previously clipped metastatic nodes—or SLNB with retrieval of at least three sentinel nodes are recommended (48, 49). For optimal post-treatment assessment, we recommend placement of clips in two biopsy-proven positive nodes prior to systemic therapy. If three or more positive nodes are initially identified, clipping may not be required, as adequate sampling at surgery is expected. In contrast, if residual nodal disease persists following NAT, ALND remains the standard of care (47-49).

3.6. How Should the Axillary Management be in Patients with DCIS?

Axillary lymph node involvement remains an important prognostic factor in BC management, and the role of SLNB in DCIS continues to be debated. According to the ASCO, SLNB may be considered in patients with DCIS undergoing mastectomy, in cases with extensive lesions (≥50 mm), or when clinical or radiologic findings suggest a possible invasive component (50). For patients scheduled for BCS, SLNB is recommended in the presence of high-risk features such as grade 3 DCIS, comedo-type necrosis, or a palpable mass, all of which may indicate an increased likelihood of occult invasion (51, 52). These recommendations are supported by the current literature and are consistent with our institutional practice.

3.7. Is Breast-Conserving Surgery a Feasible Option for Patients with Connective Tissue Disorders or Multifocal/ Multicentric Breast Cancer?

Current clinical guidelines identify active connective tissue disorders—such as scleroderma or systemic lupus erythematosus—as relative contraindications to BCS, primarily due to the heightened risk of radiation-induced toxicity (34, 53, 54). However, in patients whose disease is in remission under appropriate medical management, BCS may be considered feasible following careful multidisciplinary evaluation.

The role of BCS in the management of multifocal and multicentric BC also remains a subject of clinical debate, particularly regarding local recurrence and long-term oncologic safety. Results from the American College of Surgeons Oncology Group (ACOSOG) Z11102 (alliance) trial (55) demonstrated that BCS in this setting is associated with acceptable rates of local recurrence. Consistent with these findings, a recent meta-analysis concluded that BCS may represent a viable treatment option for carefully selected patients with multifocal or multicentric disease (54). Accordingly, BCS can be considered in patients who fulfill the criteria outlined by the St Gallen International Expert Consensus Conference (2017), which include the achievement of negative surgical margins, the delivery of adjuvant RT, and the preservation of satisfactory cosmetic outcomes (34). In our clinical practice, when disease remission is achieved with systemic medical management, BCS may be considered a feasible option following a comprehensive multidisciplinary evaluation. BCS also appears to be an appropriate option for carefully selected patients with multifocal or multicentric BC, as modern surgical and adjuvant approaches have helped narrow the gap in local recurrence risk. Meta-analyses demonstrate that local recurrence, DFS, and OS outcomes following BCS are comparable to those observed after mastectomy in this population (54). In our clinical practice, when clear surgical margins and satisfactory aesthetic outcomes can be achieved, we routinely prefer BCS using oncoplastic techniques after thoroughly discussing the expected outcomes with the patient.

3.8. What is the Optimal Localization Method for Non-Palpable Breast Lesions?

Non-palpable breast lesions can be localized using several techniques, including wire-guided localization (WGL), radio-guided occult lesion localization (ROLL), radioactive seed localization, and more recently developed methods such as SAVI SCOUT and magnetic seed localization. WGL was the first widely adopted method and remained the standard approach for many years; however, it carries several limitations, including the risk of wire dislodgement, migration, fracture, patient discomfort, and logistical challenges—particularly the requirement for same-day placement prior to surgery. These drawbacks have been associated with suboptimal cosmetic outcomes and higher rates of non-radical excision (56, 57). ROLL has emerged as a superior alternative, offering improved surgical precision and patient experience. Clinical studies have demonstrated lower rates of positive resection margins, reduced need for re-excision, better cosmetic results, and higher patient satisfaction (56-59). In light of this evidence, we prefer ROLL over WGL owing to its technical advantages and favorable oncologic and aesthetic outcomes.

3.9. What are the Preferred Incision Types in Nipple-Sparing Mastectomy?

Multiple incision types have been described for nipple-sparing mastectomy (NSM); the most commonly used approaches are radial, periareolar, and inframammary fold incisions. None of these techniques has been demonstrated to be definitively superior; therefore, choice of incision should be individualized according to patient-specific anatomical and oncologic considerations. The radial incision remains the most frequently employed, largely due to its compatibility with immediate implant-based reconstruction and its ability to provide adequate access to the axillary fossa without requiring an additional incision.

In recent consensus recommendations, a lateralized parabolic multiplanar incision described by Sağır et al. (59) has been endorsed. This incision begins approximately 4 cm lateral to the nipple-areola complex (NAC) in small breasts and approximately 5 cm lateral to the NAC in larger breasts, extending in a parabolic trajectory toward the mid-axillary line without crossing it, and has a total length ranging from 8 to 13 cm. Compared with the traditional radial approach, this lateral placement reduces the risk of NAC ischemia and necrosis by avoiding disruption of the periareolar vascular supply. It also minimizes lateral displacement of the NAC due to scar contracture, thereby preserving its circular shape and symmetry. In patients with larger breasts, or when NAC excision is anticipated, this technique further supports a more symmetric postoperative breast contour (60).

The inframammary fold incision provides favorable cosmetic results, as the scar is concealed within the natural crease. It is most appropriate for patients with medium-sized breasts and mild ptosis in whom adequate access and reshaping can be achieved safely. However, in patients with larger or more ptotic breasts, this approach may limit surgical exposure and make it more challenging to perform precise tumor resection and optimal glandular remodeling (60). Periareolar incisions provide wide exposure of the breast parenchyma, but are associated with a higher risk of NAC ischemia and necrosis compared with alternative techniques. Where pre-existing surgical scars are present, these can often be incorporated into the planned

incision to minimize additional scarring. In cases requiring skin excision or concurrent reduction mammoplasty, oncoplastic approaches, such as the Wise pattern, may be preferred.

In light of the available evidence and consensus recommendations, our clinical practice has increasingly adopted the lateralized parabolic multiplanar incision as the preferred approach for NSM (59). This technique provides an optimal balance between oncologic safety and aesthetic outcomes, while reducing the risks of nipple-areola complex ischemia and asymmetry. Nonetheless, incision type is ultimately individualized according to each patient's anatomical characteristics and oncologic considerations, with inframammary and oncoplastic approaches reserved for carefully selected cases. This tailored strategy underscores our commitment to optimizing both surgical safety and cosmetic outcomes.

3.10. Who are the Candidates for Nipple-Sparing Mastectomy?

Historically, oncologic eligibility criteria for NSM have included a tumor-to-nipple distance of at least 2 cm, absence of skin involvement, and no clinical or radiologic evidence of Paget's disease or inflammatory BC (61). However, emerging evidence indicates that NSM can be safely performed in carefully selected patients with tumors located close to the nipple without compromising oncologic outcomes (62). Based on evolving data, our consensus group recommends avoiding NSM in patients who have a tumor-to-nipple distance of less than 5 mm, in those with suspicious microcalcifications beneath the nipple-areola complex, or when radiologic findings demonstrate focal contrast enhancement involving the NAC.

4. Controversial Topics in Breast Radiation

The role of RT in BC management continues to evolve, with several aspects remaining the focus of ongoing debate. Key issues include the definition of adequate surgical margins, the extent of axillary treatment, the application of RT following primary systemic therapy (PST), and the selection of optimal fractionation schedules.

In patients with invasive carcinoma undergoing BCS, a negative surgical margin is defined as "no ink on tumor", as previously mentioned, a standard supported by multiple randomized trials demonstrating excellent local control when followed by whole-breast irradiation (WBI) (63). However, for patients treated with PBI, a more conservative margin of at least 2 mm is generally recommended to minimize the risk of recurrence. Surgical margins require special attention after skin-sparing or NSM, as an anterior margin of less than 1 mm has been associated with increased recurrence risk, warranting strong consideration of adjuvant RT. For DCIS, current guidelines recommend margins of at least 2 mm. When narrower margins are reported, evaluation of residual calcifications by specimen radiography and postoperative MMG is essential to guide the need for re-excision. If re-excision is not feasible, whole-breast RT with a tumor-bed boost is advised (64). We recommend moderate hypofractionation (40 Gy in 15 fractions or 42.5 Gy in 16 fractions), which has demonstrated equivalent efficacy, greater convenience and lower toxicity, and is the preferred regimen for the whole breast, chest wall (with or without reconstruction), regional nodes, and after.

Axillary management has undergone a paradigm shift with increasing evidence supporting the omission of ALND in selected patients. The ACOSOG Z0011 and AMAROS trials (65, 66) demonstrated that patients with early-stage, cN0 disease and one or two positive sentinel lymph nodes may safely avoid ALND, provided that appropriate regional nodal irradiation is delivered. These findings have been reinforced by the SENOMAC and SINODAR-ONE trials (67, 68). In contrast, patients with a higher nodal burden or additional high-risk features may still require ALND followed by RT.

The role of RT after PST requires a tailored approach that integrates pretreatment clinical stage, the degree of clinical and pathological response, and the surgical approach. RT is routinely indicated following BCS, regardless of the systemic response. Patients with locally advanced disease, including cT4 tumors or cN2–3 nodal involvement, should receive postmastectomy RT (PMRT) and regional nodal irradiation irrespective of pathological downstaging (69). Conversely, patients with cT1–2N0 disease who achieve a pCR may be spared PMRT. For patients with cT3 tumors or those with triple-negative BC, treatment decisions remain complex and should be individualized within a multidisciplinary tumor board (70).

Special populations also require careful consideration. In women aged 70 years or older with small, estrogen receptor (ER) (+), node-negative tumors who are receiving endocrine therapy, omission of RT after BCS has been shown to be safe in randomized trials, particularly when life expectancy is limited by comorbidity (71, 72). In such cases, PBI or ultra-hypofractionated WBI may be effective alternatives (73, 74). Appropriate candidates for PBI typically include women aged 50 years or older with IDC, stage T1N0 disease, grade 1–2 histology, ER positivity, and margins ≥2 mm (75). Reconstruction strategies must also be considered, as autologous techniques are generally more compatible with PMRT than implant-based approaches, although institutional expertise and patient preference are key determinants.

Fractionation schedules are another area of active refinement. Conventional fractionation with 50 Gy in 25 fractions over five weeks has largely been replaced by moderate hypofractionation (40 Gy in 15 fractions over three weeks), which has demonstrated equivalent efficacy, lower toxicity, and greater convenience (76, 77). More recently, the FAST-Forward trial (74) confirmed the

safety and efficacy of ultra-hypofractionated regimens (26 Gy in 5 fractions over one week) for appropriately selected patients with early-stage disease. The use of a tumor-bed boost remains an important component of local therapy for patients with high-risk features, including young age, grade 3 histology, extensive intraductal components, or triple-negative and HER2(+) subtypes.

Conclusion

In summary, decision-making in breast radiation oncology is increasingly individualized, guided by tumor biology, disease extent, systemic therapy response, patient age, comorbidities, and reconstructive considerations. While consensus exists regarding key principles—such as the margin definition for invasive carcinoma and the adoption of hypofractionated schedules—controversies persist around RT omission in older patients, management of the axilla following systemic therapy, and indications for PMRT in select subgroups. WBI after BCS is standard for early BC. PBI is an option for selected low-risk early-stage patients. Patients with ≥50 years with invazive ductal biology, T1N0, grade 1 or 2, ≥2 mm surgical margins, ER+ tumors are candidates for PBI (75). Patients presenting with cT4 or cN2-N3 generally require PMRT and regional nodal irradiation regardless of pathological response. Ongoing trials and long-term follow-up data are expected to further refine these practices and enhance the personalization of RT in BC care.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Ş.T., H.K., E.Ç., O.D., S.B., F.T., S.Y., I.D.S., G.E.İ., N.B., C.U., Y.E.; Concept: A.Y., U.Ö., G.E.İ., N.B., C.U., Y.E.; Design: N.B., C.U., Y.E.; Data Collection or Processing: E.Ş.T., H.K., E.Ç., O.D., S.B., F.T., S.Y., I.D.S.; Analysis or Interpretation: N.B., C.U., Y.E.; Literature Search: E.Ş.T., H.K., E.Ç., O.D., S.B., F.T., S.Y., I.D.S.; Writing: E.Ş.T., H.K., E.Ç., O.D., S.B., F.T., S.Y., I.D.S., A.Y., U.Ö., G.E.İ., N.B., C.U., Y.E.

Conflict of Interest: No conflict of interest declared by the authors.

Financial Disclosure: The authors declare that this study received no financial disclosure.

References

1. World Health Organization. Breast cancer – WHO Fact Sheet. WHO; 2025. [Crossref]
2. Kim J, Harper A, McCormack V, Sung H, Houssami N, Morgan E, et al. Global patterns and trends in breast cancer incidence and mortality across 185 countries. Nat Med. 2025; 31: 1154-1162. (PMID: 39994475) [Crossref]
3. Sardanelli F, Aase HS, Álvarez M, Azavedo E, Baarslag HJ, Balleyguier C, et al. Position paper on screening for breast cancer by the European Society of Breast Imaging (EUSOBI) and 30 national breast radiology bodies from Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Israel, Lithuania, Moldova, The Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Spain, Sweden, Switzerland and Turkey. Eur Radiol. 2017; 27: 2737-2743. (PMID: 27807699) [Crossref]
4. Eby PR. Evidence to support screening women annually. Radiol Clin North Am. 2017; 55: 441-456. (PMID: 28411672) [Crossref]
5. Ozkan Gurdal S, Ozaydın AN, Aribal E, Ozcinar B, Cabioglu N, Sahin C, et al. Bahcesehir long-term population-based screening compared to National Breast Cancer Registry Data: effectiveness of screening in an emerging country. Diagn Interv Radiol. 2021; 27: 157-163. (PMID: 33599208) [Crossref]
6. Wanders JOP, van Gils CH, Karssemeijer N, Holland K, Kallenberg M, Peeters PHM, et al. The combined effect of mammographic texture and density on breast cancer risk: a cohort study. Breast Cancer Res. 2018; 20: 36. (PMID: 29720220) [Crossref]
7. Freer PE. Mammographic breast density: impact on breast cancer risk and implications for screening. Radiographics. 2015; 35: 302-315. (PMID: 25763718) [Crossref]
8. Mann RM, Athanasiou A, Baltzer PAT, Camps-Herrero J, Clauser P, Fallenberg EM, et al; European Society of Breast Imaging (EUSOBI). Breast cancer screening in women with extremely dense breasts recommendations of the European Society of Breast Imaging (EUSOBI). Eur Radiol. 2022; 32: 4036-4045. (PMID: 35258677) [Crossref]
9. Allweis TM, Hermann N, Berenstein-Molho R, Guindy M. Personalized screening for breast cancer: rationale, present practices, and future directions. Ann Surg Oncol. 2021; 28: 4306-4317. (PMID: 33398646) [Crossref]
10. Monticciolo DL, Newell MS, Moy L, Lee CS, Destounis SV. Breast cancer screening for women at higher-than-average risk: updated recommendations from the ACR. J Am Coll Radiol. 2023; 20: 902-914. (PMID: 37150275) [Crossref]
11. Bakker MF, de Lange SV, Pijnappel RM, Mann RM, Peeters PHM, Monninkhof EM, et al; DENSE Trial Study Group. Supplemental MRI screening for women with extremely dense breast tissue. N Engl J Med. 2019; 381: 2091-2102. (PMID: 31774954) [Crossref]
12. Veenhuizen SGA, de Lange SV, Bakker MF, Pijnappel RM, Mann RM, Monninkhof EM, et al; DENSE Trial Study Group. Supplemental breast MRI for women with extremely dense breasts: results of the second screening round of the DENSE trial. Radiology. 2021; 299: 278-286. (PMID: 33724062) [Crossref]
13. Salim M, Liu Y, Sorkhei M, Ntoula D, Foukakis T, Fredriksson I, et al. AI-based selection of individuals for supplemental MRI in population-based breast cancer screening: the randomized ScreenTrustMRI trial. Nat Med. 2024; 30: 2623-2630. (PMID: 38977914) [Crossref]
14. Ray KM, Hayward JH, Joe BN. Role of MR imaging for the locoregional staging of breast cancer. Magn Reson Imaging Clin N Am. 2018; 26: 191-205. (PMID: 29622125) [Crossref]
15. Houssami N, Turner RM, Morrow M. Meta-analysis of pre-operative magnetic resonance imaging (MRI) and surgical treatment for breast cancer. Breast Cancer Res Treat. 2017; 165: 273-283. (PMID: 28589366) [Crossref]
16. Liu J, Xiao R, Yin H, Hu Y, Zhen S, Zhou S, et al. Meta-analysis and systematic review of the diagnostic value of contrast-enhanced spectral mammography for the detection of breast cancer. BMJ Open. 2024; 14: e069788. (PMID: 39231551) [Crossref]
17. Cozzi A, Di Leo G, Houssami N, Gilbert FJ, Helbich TH, Álvarez Benito M, et al. Preoperative breast MRI for invasive ductal carcinoma with or without a DCIS component at needle biopsy: influence on surgical outcomes in the MIPA study. Eur Radiol. 2025; 35: 6433-6443. (PMID: 40272491) [Crossref]

18. Cozzi A, Di Leo G, Houssami N, Gilbert FJ, Helbich TH, Álvarez Benito M, et al. Preoperative breast MRI reduces reoperations for unilateral invasive lobular carcinoma: a patient-matched analysis from the MIPA study. Eur Radiol. 2025; 35: 3990-4000. (PMID: 40016317) [Crossref]

19. Janssen LM, den Dekker BM, Gilhuijs KGA, van Diest PJ, van der Wall E, Elias SG. MRI to assess response after neoadjuvant chemotherapy in breast cancer subtypes: a systematic review and meta-analysis. NPJ Breast Cancer. 2022; 8: 107. (PMID: 36123365) [Crossref]

20. Kim J, Han BK, Ko EY, Ko ES, Choi JS, Park KW. Prediction of pathologic complete response on MRI in patients with breast cancer receiving neoadjuvant chemotherapy according to molecular subtypes. Eur Radiol. 2022; 32: 4056-4066. (PMID: 34989844) [Crossref]

21. Boughey JC, Yu H, Dugan CL, Piltin MA, Postlewait L, Son JD, et al. Changes in surgical management of the axilla over 11 years - report on more than 1500 breast cancer patients treated with neoadjuvant chemotherapy on the prospective I-SPY2 trial. Ann Surg Oncol. 2023; 30: 6401-6410. (PMID: 37380911) [Crossref]

22. Expert Panel on Breast Imaging; Heller SL, Lourenco AP, Niell BL, Ajkay N, Brown A, Dibble EH, et al. ACR appropriateness criteria® imaging after mastectomy and breast reconstruction. J Am Coll Radiol. 2020; 17: S403-S414. (PMID: 33153553) [Crossref]

23. Kinra P, Malik A. Ki 67: are we counting it right? Indian J Pathol Microbiol. 2020; 63: 98-99. (PMID: 32031132) [Crossref]

24. Inwald EC, Klinkhammer-Schalke M, Hofstädter F, Zeman F, Koller M, Gerstenhauer M, et al. Ki-67 is a prognostic parameter in breast cancer patients: results of a large population-based cohort of a cancer registry. Breast Cancer Res Treat. 2013; 139: 539-552. (PMID: 23674192) [Crossref]

25. Kroneman TN, Voss JS, Lohse CM, Wu TT, Smyrk TC, Zhang L. Comparison of three ki-67 index quantification methods and clinical significance in pancreatic neuroendocrine tumors. Endocr Pathol. 2015; 26: 255-262. (PMID: 26072124) [Crossref]

26. Catteau X, Zindy E, Bouri S, Noël JC, Salmon I, Decaestecker C. Comparison between manual and automated assessment of ki-67 in breast carcinoma: test of a simple method in daily practice. Technol Cancer Res Treat. 2023; 22: 15330338231169603. (PMID: 37559526) [Crossref]

27. Solmaz-Yilmaz G, Gumuskaya B, Tokat F, Soylemez-Akkurt T, Dirilenoglu F, Koy Y, et al. Validation of algorithmic ki-67 scoring in breast cancer using four different whole slide image formats. Laboratory Investigation. 2024; 104(Suppl 1): S1623. Abstract #1295. Presented at: United States & Canadian Academy of Pathology (USCAP) 113th Annual Meeting; March 23-28, 2024; Baltimore, Maryland. [Crossref]

28. Ohlschlegel C, Kradolfer D, Hell M, Jochum W. Comparison of automated and manual FISH for evaluation of HER2 gene status on breast carcinoma core biopsies. BMC Clin Pathol. 2013; 13: 13. (PMID: 23601823) [Crossref]

29. Dobson L, Conway C, Hanley A, Johnson A, Costello S, O'Grady A, et al. Image analysis as an adjunct to manual HER-2 immunohistochemical review: a diagnostic tool to standardize interpretation. Histopathology. 2010; 57: 27-38. (PMID: 20584089) [Crossref]

30. Uzel B, Gumuskaya B, Solmaz Yilmaz G, Cayir S, Tekin E, Ozsoy G, et al. Digital analysis of breast cancer Ki-67 scores in different whole slide image formats. Journal of Pathology Informatics. 2023; 14(Suppl): Abstract. Presented at: Digital Pathology Association / Pathology Visions 2023; October 29-31, 2023; Orlando, Florida. [Crossref]

31. Li Z, Uzel B, Kellough D, Solmaz-Yilmaz G, Parwani A. 194 computational algorithm-assisted reclassification of HER2 immunohistochemistry (0) breast carcinomas: enhancing detection of subtle HER2 expression. Laboratory Investigation, 2025; 105: 102418. [Crossref]

32. Gradishar WJ, Moran MS, Abraham J, Aft R, Agnese D, Allison KH, et al. Breast cancer, version 3.2022, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2022; 20: 691-722. (PMID: 35714673) [Crossref]

33. Morrow M, Van Zee KJ, Solin LJ, Houssami N, Chavez-MacGregor M, Harris JR, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. Ann Surg Oncol. 2016; 23: 3801-3810. (PMID: 27527714) [Crossref]

34. Curigliano G, Burstein HJ, Winer EP, Gnant M, Dubsky P, Loibl S, et al. De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017. Ann Oncol. 2017; 28: 1700-1712. Erratum in: Ann Oncol. 2018; 29: 2153. Erratum in: Ann Oncol. 2019; 30: 1181. (PMID: 28838210) [Crossref]

35. Strnad V, Ott OJ, Hildebrandt G, Kauer-Dorner D, Knauerhase H, Major T, et al; Groupe Européen de Curiethérapie of European Society for Radiotherapy and Oncology (GEC-ESTRO). 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. Lancet. 2016; 387: 229-238. (PMID: 26494415) [Crossref]

36. Gu J, Groot G, Boden C, Busch A, Holtslander L, Lim H. Review of factors influencing women's choice of mastectomy versus breast conserving therapy in early stage breast cancer: a systematic review. Clin Breast Cancer. 2018; 18: e539-e554. (PMID: 29396079) [Crossref]

37. De la Cruz Ku G, Karamchandani M, Chambergo-Michilot D, Narvaez-Rojas AR, Jonczyk M, Príncipe-Meneses FS, et al. Does breast-conserving surgery with radiotherapy have a better survival than mastectomy? A meta-analysis of more than 1,500,000 patients. Ann Surg Oncol. 2022; 29: 6163-6188. (PMID: 35876923) [Crossref]

38. Ditsch N, Gnant M, Thomssen C, Harbeck N. St. Gallen/Vienna 2025 summary of key messages on therapy in early breast cancer from the 2025 St. Gallen International Breast Cancer Conference. Breast Care (Basel). 2025: 1-10. Erratum in: Breast Care (Basel). 2025. (PMID: 40546709) [Crossref]

39. Loibl S, André F, Bachelot T, Barrios CH, Bergh J, Burstein HJ, et al; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2024; 35: 159-182. (PMID: 38101773) [Crossref]

40. Gentilini OD, Botteri E, Sangalli C, Galimberti V, Porpiglia M, Agresti R, et al; SOUND Trial Group. Sentinel lymph node biopsy vs no axillary surgery in patients with small breast cancer and negative results on ultrasonography of axillary lymph nodes: the SOUND randomized clinical trial. JAMA Oncol. 2023; 9: 1557-1564. (PMID: 37733364) [Crossref]

41. Reimer T, Stachs A, Veselinovic K, Kühn T, Heil J, Polata S, et al. Axillary surgery in breast cancer - primary results of the INSEMA trial. N Engl J Med. 2025; 392: 1051-1064. (PMID: 39665649) [Crossref]

42. Brackstone M, Baldassarre FG, Perera FE, Cil T, Chavez Mac Gregor M, Dayes IS, et al. Management of the axilla in early-stage breast cancer: ontario health (Cancer Care Ontario) and ASCO guideline. J Clin Oncol. 2021; 39: 3056-3082. (PMID: 34279999) [Crossref]

43. Tinterri C, Barbieri E, Sagona A, Bottini A, Canavese G, Gentile D. De-escalation surgery in cT3-4 breast cancer patients after neoadjuvant therapy: predictors of breast conservation and comparison of long-term oncological outcomes with mastectomy. Cancers (Basel). 2024; 16: 1169. (PMID: 38539504) [Crossref]

44. Zhou X, Li Y. Local recurrence after breast-conserving surgery and mastectomy following neoadjuvant chemotherapy for locally advanced breast cancer - a meta-analysis. Breast Care (Basel). 2016; 11: 345-351. (PMID: 27920628) [Crossref]

45. Minella C, Villasco A, D'Alonzo M, Cellini L, Accomasso F, Actis S, et al. Surgery after neoadjuvant chemotherapy: a clip-based technique to improve surgical outcomes, a single-center experience. Cancers (Basel). 2022; 14: 2229. (PMID: 35565357) [Crossref]

46. Conti M, Morciano F, Bufi E, D'Angelo A, Panico C, Di Paola V, et al. Surgical planning after neoadjuvant treatment in breast cancer: a multimodality imaging-based approach focused on MRI. Cancers (Basel). 2023; 15: 1439. (PMID: 36900231) [Crossref]

47. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, et al; Alliance for Clinical Trials in Oncology. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. JAMA. 2013; 310: 1455-1461. (PMID: 24101169) [Crossref]

48. Pfob A, Heil J. Breast and axillary surgery after neoadjuvant systemic treatment - a review of clinical routine recommendations and the latest clinical research. Breast. 2022; 62(Suppl 1): S7-S11. (PMID: 35135710) [Crossref]

49. Almahariq MF, Levitin R, Quinn TJ, Chen PY, Dekhne N, Kiran S, et al. Omission of axillary lymph node dissection is associated with inferior survival in breast cancer patients with residual N1 nodal disease following neoadjuvant chemotherapy. Ann Surg Oncol. 2021; 28: 930-940. (PMID: 32712895) [Crossref]

50. Lyman GH, Somerfield MR, Bosserman LD, Perkins CL, Weaver DL, Giuliano AE. Sentinel lymph node biopsy for patients with early-stage breast cancer: american society of clinical oncology clinical practice guideline update. J Clin Oncol. 2017; 35: 561-564. (PMID: 27937089) [Crossref]

51. Davey MG, O'Flaherty C, Cleere EF, Nohilly A, Phelan J, Ronane E, et al. Sentinel lymph node biopsy in patients with ductal carcinoma in situ: systematic review and meta-analysis. BJS Open. 2022; 6: zrac022. (PMID: 35380620) [Crossref]

52. Li X, Zhou C, Xu T, Ren Y, Li M, Shang J. Meta-analysis on axillary lymph node metastasis rate in ductal carcinoma in situ with microinvasion. Cancer Med. 2024; 13: e7413. (PMID: 38925621) [Crossref]

53. Purswani JM, Oh C, Jaros B, Sandigursky S, Xiao J, Gerber NK. Breast conservation in women with autoimmune disease: the role of active autoimmune disease and hypofractionation on acute and late toxicity in a case-controlled series. Int J Radiat Oncol Biol Phys. 2021; 110: 783-791. (PMID: 33545303) [Crossref]

54. Sun Y, Gao L, Zhou X, Wang Z, Li Y, Sun Q. Local recurrence and survival outcomes of multifocal/multicentric breast cancer after breast conserving therapy: a systematic review and meta-analysis. Clin Breast Cancer. 2025; 25: e229-e239.e9. (PMID: 39542811) [Crossref]

55. Boughey JC, Rosenkranz KM, Ballman KV, McCall L, Haffty BG, Cuttino LW, et al. Local recurrence after breast-conserving therapy in patients with multiple ipsilateral breast cancer: results from ACOSOG Z11102 (alliance). J Clin Oncol. 2023; 41: 3184-3193. (PMID: 36977292) [Crossref]

56. Garzotto F, Comoretto RI, Michieletto S, Franzoso G, Lo Mele M, Gregori D, et al. Preoperative non-palpable breast lesion localization, innovative techniques and clinical outcomes in surgical practice: a systematic review and meta-analysis. Breast. 2021; 58: 93-105. (PMID: 33991806) [Crossref]

57. Moreira IC, Ventura SR, Ramos I, Fougo JL, Rodrigues PP. Preoperative localisation techniques in breast conservative surgery: a systematic review and meta-analysis. Surg Oncol. 2020; 35: 351-373. (PMID: 33002840) [Crossref]

58. Sarı A, Hot S, Bender Ö, Ertürk A, Yüney E, Günay S. Total excision accompanied by roll in non-palpable breast lesion. Eur J Breast Health. 2013; 9: 151-155. [Crossref]

59. Sağır M, Güven E, Saylik O, Dülgeroğlu O, Uras C. A new convenient incision model of the nipple-sparing mastectomy: lateralized parabolic multiplanar incision. Aesthetic Plast Surg. 2024; 48: 4965-4972. (PMID: 38769149) [Crossref]

60. Park S, Yoon C, Bae SJ, Cha C, Kim D, Lee J, et al. Comparison of complications according to incision types in nipple-sparing mastectomy and immediate reconstruction. Breast. 2020; 53: 85-91. (PMID: 32653836) [Crossref]

61. Weber WP, Haug M, Kurzeder C, Bjelic-Radisic V, Koller R, Reitsamer R, et al. Oncoplastic breast consortium consensus conference on nipple-sparing mastectomy. Breast Cancer Res Treat. 2018; 172: 523-537. (PMID: 30182349) [Crossref]

62. Balci FL, Kara H, Dulgeroglu O, Uras C. Oncologic safety of nipple-sparing mastectomy in patients with short tumor-nipple distance. Breast J. 2019; 25(4): 612-618. (PMID: 31087467) [Crossref]

63. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al; Society of Surgical Oncology; American Society for Radiation Oncology. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. J Clin Oncol. 2014; 32: 1507-1515. (PMID: 24516019) [Crossref]

64. Early Breast Cancer Trialists' Collaborative Group (EBCTCG); Darby S, McGale P, Correa C, Taylor C, Arriagada R, Clarke M, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet. 2011; 378: 1707-1716. (PMID: 22019144) [Crossref]

65. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA. 2011; 305: 569-575. (PMID: 21304082) [Crossref]

66. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. 2014; 15: 1303-1310. (PMID: 25439688) [Crossref]

67. de Boniface J, Frisell J, Andersson Y, Bergkvist L, Ahlgren J, Rydén L, et al; SENOMAC Trialists' Group. Survival and axillary recurrence following sentinel node-positive breast cancer without completion axillary lymph node dissection: the randomized controlled SENOMAC trial. BMC Cancer. 2017; 17: 379. (PMID: 28549453) [Crossref]

68. Tinterri C, Gentile D, Gatzemeier W, Sagona A, Barbieri E, Testori A, et al; SINODAR-ONE Collaborative Group. Preservation of axillary lymph nodes compared with complete dissection in T1-2 breast cancer patients presenting one or two metastatic sentinel lymph nodes: the SINODAR-ONE multicenter randomized clinical trial. Ann Surg Oncol. 2022; 29: 5732-5744. (PMID: 35552930) [Crossref]

69. EBCTCG (Early Breast Cancer Trialists' Collaborative Group); McGale P, Taylor C, Correa C, Cutter D, Duane F, Ewertz M, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet. 2014; 383: 2127-2135. Erratum in: Lancet. 2014; 384: 1848. (PMID: 24656685) [Crossref]

70. Banys-Paluchowski M, Gasparri ML, de Boniface J, Gentilini O, Stickeler E, Hartmann S, et al. Surgical management of the axilla in clinically node-positive breast cancer patients converting to clinical node negativity through neoadjuvant chemotherapy: current status, knowledge gaps, and rationale for the EUBREAST-03 AXSANA study. Cancers (Basel). 2021; 13: 1565. (PMID: 33805367) [Crossref]

71. Hughes KS, Schnaper LA, Berry D, Cirrincione C, McCormick B, Shank B, et al; Cancer and leukemia group B; radiation therapy oncology group; eastern cooperative oncology group. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. N Engl J Med. 2004; 351: 971-977. (PMID: 15342805) [Crossref]

72. Kunkler IH, Williams LJ, Jack WJ, Cameron DA, Dixon JM; PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. Lancet Oncol. 2015; 16: 266-273. Erratum in: Lancet Oncol. 2015; 16: e105. (PMID: 25637340) [Crossref]

73. Whelan TJ, Pignol JP, Levine MN, Julian JA, MacKenzie R, Parpia S, et al. Long-term results of hypofractionated radiation therapy for breast cancer. N Engl J Med. 2010; 362: 513-520. (PMID: 20147717) [Crossref]

74. Murray Brunt A, Haviland JS, Wheatley DA, Sydenham MA, Alhasso A, Bloomfield DJ, et al; FAST-Forward Trial Management Group. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. Lancet. 2020; 395: 1613-1626. (PMID: 32580883) [Crossref]

75. Meattini I, Marrazzo L, Saieva C, Desideri I, Scotti V, Simontacchi G, et al. Accelerated partial-breast irradiation compared with whole-breast irradiation for early breast cancer: long-term results of the randomized phase III APBI-IMRT-florence trial. J Clin Oncol. 2020; 38: 4175-4183. (PMID: 32840419) [Crossref]

76. START Trialists' Group; Bentzen SM, Agrawal RK, Aird EG, Barrett JM, Barrett-Lee PJ, Bliss JM, et al. The UK standardisation of breast radiotherapy (START) trial A of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet Oncol. 2008; 9: 331-341. (PMID: 18356109) [Crossref]

77. START Trialists' Group; Bentzen SM, Agrawal RK, Aird EG, Barrett JM, Barrett-Lee PJ, Bentzen SM, et al. The UK standardisation of breast radiotherapy (START) trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet. 2008; 371: 1098-1107. (PMID: 18355913) [Crossref]