Taipei Veterans General Hospital Practices Guidelines Oncology

Breast Cancer

Version 2022
Proofing at RO Guideline Meeting on 2022/6/15

Summary of Guidelines Updates in RT vs 2021

Presented in RO Guideline Meeting on 2022/06/15

- Lumpectomy changed to breast-conserving surgery (BCS)
- In Abbreviated Guidelines for post-BCS RT, for 1-3 positive axilla nodes, criteria modified for consistency with NCCN guideline.
- IORT is not listed nor discussed in the 2022 NCCN guideline and should be restricted to patients who meet the “suitable criteria” of 2016 ASTRO APBI consensus and 2020 ESTRO IORT Task Force/ACROP recommendations.
- References are updated.

Abbreviated Guidelines For Post-Operative Radiotherapy

- **Post- breast conserving surgery (BCS)**
  - Usually indicated for all BCS cases,
  - 40-42.5Gy in15-16 fractions (**preferred for no regional nodal irradiation**) or 45-50.4Gy to whole breast in 1.8~2 Gy per fraction
  - Conventional fractionation may be preferred when treating breast cancer with rare histologies
  - With or without **10~16Gy** boost to the tumor bed in **2~2.5 Gy** per fraction
    A boost to the tumor bed is recommended in higher risk patients (age ≤ 50, age 51-70 with high grade, positive axillary nodes, lymphovascular invasion, or positive or close margins).
  - **Simultaneous integrated boost (SIB)** to CTV_H with fraction size up to 2.2 Gy to shorten RT treatment time by one week
  - **Optional** for patient age ≥ 70 with **T1**N0, hormone receptor positive disease of low to intermediate grade and adequate (**≥ 2mm**) surgical margin
  - ~~**Optional:** For~~ patients with ~~N1 (~~1-3 positive axillary nodes~~)~~ disease who
    (1) meet **ALL** ACOSOG Z0011 criteria (cT1-2N0M0, underwent lumpectomy with planned whole breast radiation, 1-2 positive SLN, ~~no ENE~~, negative margin, no preoperative chemotherapy), regional nodal irradiation (RNI) with or without intentional inclusion of axilla is at the discretion of radiation oncologist
    (2) do not meet ALL ACOSOG Z0011 criteria, inclusion of any portion of undissected axilla at risk
- **Post-mastectomy**
  - Indications:
    - pN2 or pN3 (≥ 4 positive nodes or positive IMN)
    - pT3 (>5cm) or pT4
    - Positive margins
    - Strongly recommended for pT2N1a, and pT1N1a with ENE (extranodal extension), pT1-2N1 with triple negative breast cancer, pT1-2N1 with 3 positive LNs
    - Optional for pT1N1 without ENE
    - Optional for pT1-2N0-1 with close margin < 1mm
  - 50-54Gy in 25-30 fractions (1.8~2Gy per fraction)
  - Optional focal boost for positive margins or residual tumor
- **Post neoadjuvant RT**
  - Indications for post-operative RT and target volume delineation are usually based on the maximal disease stage at diagnosis and pathology results after neoadjuvant chemotherapy.
- **Irradiation of Internal Mammary Node (IMN)**
  - If IMN are clinically or pathologically positive, RT should be given to the IMN, otherwise the treatment to

Principles of Radiation Therapy

- **Post-BCS Radiation Therapy**
  - **Hypofractionated whole breast irradiation (HF-WBI) is preferred for invasive breast cancer without covering reginal lymph nodes, and DCIS**
    - 45 Gy in 20 fractions or 40~42.5 Gy in 15~16 fractions for DCIS if margin ≥ 2mm
    - 40~42.5 Gy in 15~16 fractions for IDC if margin ≥ 2 mm
    - For age ≤50, or high grade, positive or margin < 2mm, tumor bed boost should be given after HF-WBI
  - **Simultaneous Integrated Boost (SIB) to CTV_H with fraction size up to 2.2 cGy could be used to shorten RT treatment time by one week**
    - 55 Gy & 45 Gy in 25 fractions to primary tumor surgical bed and whole breast, respectively,
      - For DCIS with margin < 2 mm
      - For IDC with margins **>** 1mm
    - 60.2 Gy & 50.4 Gy in 28 fractions to primary tumor surgical bed and whole breast, respectively, for IDC with margins ≤ 1 mm
  - **Accelerated Partial Breast Irradiation (APBI)**
    - **Brachytherapy (interstitial or intracavitary)**
    - **EBRT: 3DCRT or IMRT**
    - **Intra-Operative Radiation Therapy (IORT)**
- **Post-mastectomy Radiation Therapy**
- **Irradiation of IMN**

Post-BCS Radiotherapy

- **Surgical Margin Status**
  - Patients with a positive margin should generally undergo either a re-excision or a mastectomy to achieve a negative margin.
  - It may be reasonable to treat selected BCS cases with a microscopically focally positive margin in the absence of an extensive intraductal component. For these patients, the use of a higher radiation boost dose to the tumor bed should be considered.
- **Clinical Target Volume (CTV)**
  - CTV_H: Tumor bed, marked by surgical clips or post-operative seroma, with optional 5~10mm margin
  - CTV_M:
    - N0 diseases: Whole Breast Only
    - N0i+: Whole Breast +/- Supraclavicular Fossa (including level III axillary fossa)
    - pN1: Whole Breast +/- Supraclavicular Fossa (including level III axillary fossa). Patients who meet **ALL ACOSOG Z0011** criteria (cT1-2N0M0, underwent lumpectomy with planned whole breast radiation, 1-2 positive SLN, ~~no ENE~~, negative margin, no preoperative chemotherapy), RNI is at the discretion of radiation oncologist; if not ALL criteria are met, inclusion of any portion of undissected axilla at risk
    - pN2 or more: Whole Breast and Supraclavicular Fossa (including level III axillary fossa)
  - See Internal Mammary Node Irradiation for the inclusion criteria of IMN in CTV
- **Planning Target Volume (PTV)**
  - Dual Respiration Phase CT Simulation or 4D CT Simulation
    - 5mm around ITV (Internal Target Volume) with flash out of skin in tangential fields
  - Conventional CT Simulation (If dual phase CT simulation is not feasible)
    - 1cm around CTV with flash out of skin in tangential field
- **Radiation Dose**
  - CTV_M:
    - 45-50.4Gy in 25-28 fractions (1.8~2Gy per fraction)
    - 40-42.5 Gy in 15-16 fractions
  - CTV_H:
    - Negative margin:
      10 Gy boost in 4-5 fractions
    - Focally positive margin
      14-16 Gy in 7-8 fractions or 12.5 Gy in 5 fractions
  - See Internal Mammary Node Irradiation for the dose to IMN
- **Radiation Technique**
  - CT Simulation with 3D-CRT/IMRT* treatment planning
    *Breath-hold or other measure should be used to reduce target motion during IMRT
  - Whole Breast Irradiation
    - 3D Split-beam tangential fields or IMRT*
  - Supraclavicular Irradiation
    - Anterior split-beam for junction matching of 3D split-beam tangential field, or IMRT*
  - Boost to CTV_H
    - 3D coplanar or non-coplanar boost
    - Appositional Electron Beam Boost
    - Brachytherapy Boost
    - Simultaneous Integrated Boost (SIB) with fraction size up to 220cGy could be used to shorten RT treatment time by one week
- **Timing of Radiation Therapy**

  Within 6 weeks after the BCS or after the last course of adjuvant chemotherapy

Post-mastectomy Radiotherapy

- **Indications**
  - pN2 or pN3 (≥ 4 positive nodes or positive IMN)
  - pT3 (>5cm) or pT4
  - Positive margins
  - Strongly recommended for pT2N1a, and pT1N1a with ENE (extranodal extension), pT1-2N1 with triple negative breast cancer, pT1-2N1 with 3 positive LNs
  - Optional for pT1N1 without ENE
  - Optional for pT1-2N0-1 with close margin < 1mm
- **Clinical Target Volume (CTV)**
  - CTV_H:
    - Chest Wall and Supraclavicular Fossa (Including level III axillary fossa) for most cases
    - Chest Wall only, optional for cases with pT3N0 or N0+positive margin
- **Planning Target Volume (PTV)**
  - Dual Respiration Phase CT Simulation or 4D CT Simulation
    - 5mm around ITV (Internal Target Volume) with flash out of skin in tangential fields
  - Convention CT Simulation (If dual phase CT simulation is not feasible)
    - 1cm around CTV with flash out of skin in tangential field
- **Radiation Dose**
  - CTV_H:
    - 50-54Gy in 25-30 fractions (1.8~2Gy per fraction)
    - Optional focal boost to scar
    - Focal boost if positive margins or residual tumor
  - See Internal Mammary Node Irradiation for the dose to IMN
- **Radiation Technique**
  - CT Simulation with 3D-CRT/IMRT* treatment planning
    *Breath-hold or other measure should be used to reduce target motion during IMRT
  - Chest Wall Irradiation
    - 3D Split-beam tangential fields or 3D appositional electron beam field or IMRT*
    - Optimal application of bolus material to achieve adequate skin dose
  - Supraclavicular Irradiation
    - Anterior split-beam for junction matching of 3D split-beam tangential field or IMRT*
- **Timing of Radiation Therapy**

  Within 6 weeks after the mastectomy or after the last course of adjuvant chemotherapy.

Irradiation of Internal Mammary Node (IMN)

- **If IMN are clinically or pathologically positive, radiation therapy should be given to the internal mammary nodes, otherwise the treatment to the IMN is at the discretion of the treating radiation oncologist.**
- **If IMN irradiation should be planned as part of the post-operative radiotherapy after lumpectomy or after mastectomy, the dose to the additional target volume of IMN depends the extent of surgery.**
- **Clinical Target Volume (CTV)**
  - CTV_H_IMN: GTV of residual IMN
  - CTV_M_IMN: Post IMN Resection CTV to the cranial of border of 4th rib
- **Planning Target Volume (PTV)**
  - Dual Respiration Phase CT Simulation or 4D CT Simulation
    - A 5mm around ITV (Internal Target Volume)
  - Convention CT Simulation (If dual phase CT simulation is not feasible)
    - 1cm around CTV with flash out of skin in tangential field
- **Radiation Dose**
  - CTV_H_IMN:
    60~70Gy in 30~35 fractions
  - CTV_M_IMN:
    45~50.4Gy in 25~28 fractions
- **Radiation Technique**
  - 3-D conformal radiation or IMRT*.

Accelerated Partial Breast Irradiation (APBI)

- **Per NCCN guideline 2022, APBI is encouraged to be performed in clinical trial.**

- **APBI could be considered in selected low-risk patients after lumpectomy, per the "suitable criteria" of the 2016 American Society for Radiation Oncology (ASTRO) consensus, if:**
  - Tumor size: Invasive ≤2cm; DCIS ≤ 2.5cm
  - ER+, preferably luminal A, age ≥50
  - Unifocal primary tumor
  - N0, no lymph node metastases
  - DCIS with Nottingham grade 1-2
  - No BRCA mutation (if tested)
  - Invasive cancer, without EIC and LCIS
  - Adequate surgical margin
    - Invasive≥2mm, DCIS≥3mm,

- **Clinical Target Volume (CTV)**
  - CTV_H: Tumor bed plus 1 cm margin.
- **Planning Target Volume (PTV)**
  - Dual respiration phase CT simulation or 4D CT simulation
    - A 5mm around ITV (Internal Target Volume) when using photon radiation
  - Convention CT Simulation (If dual phase CT simulation is not feasible)
    - 1cm around CTV with flash out of skin in tangential field
- **Radiation Dose**
  - CTV_H:
    - **34 Gy in 10 fractions** delivered twice per day with brachytherapy
    - **38.5 Gy in 10 fractions** delivered twice per day with photon radiation
- **Radiation Technique**
  - Brachytherapy or 3-D external beam conformal radiation or IMRT.
- **Timing of Radiation Therapy**

  Within 6 weeks after the BCS or after the last course of adjuvant chemotherapy.

Intra-Operative Radiation Therapy (IORT) in BCS

- IORT is an extreme form of APBI, and should be performed only as part of a prospective trial.
- If not trial eligible, per the "**suitable criteria**" of the consensus statement of the ASTRO, IORT should be reserved for patients with negative surgical margin and a low risk of recurrence, should be avoided in patients with **diagnosis of invasive lobular carcinoma, positive margin, EIC and/or LCIS.**
  - 14% of Target-A requiring additional post-Op EBRT
- One of the most important differences of IORT from APBI is that the permanent pathology report of BCS is not available, and hence there is chance that IORT is applied to unsuitable cases with false negative frozen report of positive margin and/or positive sentinel node.
- If permanent pathology report shows adverse features, additional local treatment, either surgery or further external beam RT, is indicated. The patient should be well informed of the increased complication associated in this circumstance.

- **IORT is not currently endorsed or discussed in NCCN 2022 Breast Cancer Treatment Guideline.**
  - Update results of TARGIT trial, the 5-year IBTR **3.3% in IORT vs. 1.3 % in WBI** (**p=0.042**)
- **Clinical Target Volume (CTV)**
  - Surface of surgical cavity.
- **Planning Target Volume (PTV)**
  - No PTV with IORT
- **Radiation Dose**
  - CTV_H:
    - 20Gy single fraction per TARGIT-A trial
- **Radiation Technique**
  - Brachytherapy with suitable radiation source
- **Timing of Radiation Therapy**

  During BCS with frozen section report confirming negative margin, negative sentinel node, and other criteria listed in "suitable criteria" of 2016 ASTRO APBI consensus statement.

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