INTRODUCTION:

Breast cancer is the second most commonly diagnosed cancer among women, after skin cancer, and it accounts for nearly 25% of cancer diagnoses in US women. In 2010, approximately 207,090 new cases of invasive breast cancer were expected to be diagnosed among US women. Approximately 39,840 women were expected to die from breast cancer in 2009; only lung cancer accounts for more cancer deaths in women.

After a breast cancer diagnosis is made, it is followed by a staging evaluation to determine extent of disease (local, regional, or metastatic) and prognostic findings. Importance is placed on tumor size, lymph node involvement (sentinel node), the histopathological interpretation, margins of resection, and hormonal and growth-factor receptor status. Treatment for breast cancer may consist of one of several mastectomy options or breast-conserving surgery and radiation therapy.

Radiation therapy is used to treat the breast and lymph node bearing areas after partial mastectomy or lumpectomy. Since breast cancers are relatively responsive to moderate doses of radiation therapy following tumor excision, treatment for cure may be achieved by external beam techniques or by partial breast irradiation techniques. The latter is a relatively new approach that builds on many years of experience with breast brachytherapy in conjunction with earlier diagnosis, surgical technical improvements, and invention of new high dose rate (HDR) brachytherapy devices.

The methods suitable for delivering breast radiation therapy have been established through clinical trials providing strong evidence in support of radiation therapy as an effective breast cancer treatment. The traditional approach utilizes tangential radiation fields to the breast and chest wall; based on the clinical and pathological factors, this may be followed by an electron beam boost to the site of excision (tumor bed). The axilla and supra-clavicular regions also may be included in a separate field based on analysis of prognostic risk factors. Improvements in technology, the observation that local tumor recurrence is most frequently observed near the site of excision, and the desire to limit the extent of radiation have led to restriction of the radiation to the tumor bed (partial breast irradiation) for selected cases.

GOAL OF THE GUIDELINE:

This guideline outlines several methods suitable for the employment of radiation therapy in conjunction with breast cancer treatment. These include the use of three-dimensional conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), image guided radiation therapy (IGRT) and internal radiation (brachytherapy). IMRT is not
indicated as a standard treatment option for breast cancer but may be indicated for selected cases of breast cancer with close proximity to critical structures. Most external beam treatments are delivered using a high energy linear accelerator. Brachytherapy is generally delivered using temporary HDR sources such as 192-Iridium (192-Ir) or Cesium-137 (137-Cs). Fortunately, these advances in treatment offer a range of regimens and the goal of this program is to guide diagnosis and treatment to the most efficient, comparatively effective and treatment pathway. With the unusual exception of extreme palliative circumstances, radiation treatment is performed, in all cases, in conjunction with surgical intervention from lumpectomy to mastectomy.

GENERAL CONSIDERATIONS

- Radiation therapy appropriate for patients with early stage breast cancer following mastectomy
  o Positive axillary lymph node
  o Primary tumor > 5 cm in size
- Radiation therapy appropriate for patients with early stage breast cancer following breast-conserving surgery
- Radiation therapy to the breast, chest wall, or regional lymphatics is appropriate for palliation for some patients with metastatic breast cancer.
- Re-irradiation following local or regional recurrence after prior mastectomy and prior breast or chest wall radiation may be appropriate.

MEDICALLY NECESSARY INDICATIONS FOR RADIATION THERAPY AND TREATMENT OPTIONS:

**Whole Breast Radiation**
Three-dimensional conformal radiation therapy (3D-CRT) is the appropriate technique for treatment of the whole breast following breast conserving surgery. Electron beam or photon beam are the most commonly used techniques for delivering boost radiotherapy.

- **DCIS after wide local excision with negative margins**
  - Whole breast radiation (45-50.4 Gy) with or without a partial breast boost, (Total combined dose with boost 59-66.4 Gy)
  - Whole breast hypo-fractionated radiation (42.5Gy at 2.66Gy per fraction in 16 fractions) with or without a partial breast boost

- **Invasive carcinoma after wide local excision with negative margins (Stage T1-2N0)**
  - Whole breast radiation (45-50.4 Gy) with or without a partial breast boost. (Total combined dose with boost 59-66.4 Gy)
  - Whole breast hypo-fractionated radiation with or without a partial breast boost (42.5Gy at 2.66Gy per fraction in 16 fractions)

- **Invasive carcinoma after wide local excision with negative margins (Stage T3 N0, T1-3N1 with adequate axillary dissection and no adverse nodal features)**
  - Whole breast radiation (45-50.4 Gy) with or without a partial breast boost(Total combined dose with boost 59-66.4 Gy) with or without regional nodal treatment
Partial Breast Irradiation

Accelerated partial breast irradiation (APBI) may be considered as the sole form of radiation therapy, in lieu of whole breast radiation following lumpectomy for selected cases. Patients with a small tumor, clear surgical margins after lumpectomy, and no lymph nodes containing cancer are typically eligible for APBI. APBI is considered unsuitable for patients who meet any of the following criteria:

- Less than 50 years of age
- Use of adjuvant chemotherapy
- Any positive lymph nodes
- Positive margins
- Tumor size of more than 3 cm (including ductal carcinoma in situ)
- Clinically or microscopically multifocal
- Presence of BRCA in 1/2 mutation, if applicable

Appropriate fractionation schemes for APBI are 34 Gy in 10 fractions delivered twice per day with brachytherapy or 38.5 Gy in 10 fractions twice per day with external beam photon therapy

Chest Wall Radiation

Three-dimensional conformal radiation therapy (3D-CRT) is the appropriate technique for treatment of the chest wall following mastectomy. Electron beam or photon beam are the most commonly used techniques for delivering boost radiotherapy.

- Invasive carcinoma after mastectomy
  - For T3-4N0, TanyN2-3 lesions, chest wall radiation with or without nodal radiation with or without a partial chest wall boost
  - T2 N0, chest wall radiation with nodal radiation with or without a partial chest wall boost
  - If close margins are the only indication for radiation, radiation to the chest wall with or without a partial chest wall boost
  - If N1 is the only indication for radiation in a patient with an adequate axillary dissection and no adverse nodal features, radiation to the chest wall and regional nodes with or without a partial chest wall boost
  - For local or regional chest wall recurrence, chest wall radiation with nodal radiation with or without a partial chest wall boost
- **Inflammatory breast cancer**
  For inflammatory breast cancer, whole breast or chest wall radiation, consider nodal radiation with or without chest wall boost.

### Dosage Guidelines
45-50.4 Gy with boost 59.4-66.4Gy

*Unless otherwise indicated standard radiation fractionation consists of 1.8 Gy to 2.0 Gy per day*

### TREATMENT OPTIONS REQUIRING ADDITIONAL CLINICAL REVIEW:

#### Intensity modulated radiation therapy (IMRT)
IMRT is not indicated as a standard treatment option and should not be used routinely for the delivery of radiation therapy for breast cancer. IMRT is strictly defined by the utilization of inverse planning modulation techniques. IMRT may be appropriate for limited circumstances in which radiation therapy is indicated and 3D conformal radiation therapy (3D-CRT) techniques cannot adequately deliver the radiation prescription without exceeding normal tissue radiation tolerance, the delivery is anticipated to contribute to potential late toxicity or tumor volume dose heterogeneity is such that unacceptable hot or cold spots are created. If IMRT is utilized, techniques to account for respiratory motion should be performed.

Clinical rationale and documentation for performing IMRT rather than 2D or 3D-CRT treatment planning and delivery will need to:

- Demonstrate how 3D-CRT isodose planning cannot produce a satisfactory treatment plan (as stated above) via the use of a patient specific dose volume histograms and isodose plans. 3D-CRT techniques such as step-and-shoot or field-in-field should be considered for the comparison.

- Confirm the IMRT requested will be inversely planned (forward plans or ‘field-in-field' plans are not considered IMRT).

- Provide tissue constraints for both the target and affected critical structures.

#### Brachytherapy
Interstitial brachytherapy boost treatment requires a peer review and documentation that improvement in dose delivery to the boost target cannot be delivered with external beam therapy. Other emerging techniques such as intraoperative radiotherapy (IORT) and Non invasive Image Guided Breast Brachytherapy (NIIGBB) techniques are being investigated and are not considered a medically necessary treatment option for the treatment of breast cancer.

#### Proton Beam Radiation Therapy
Proton beam is not an approved treatment option for breast cancer. There are limited clinical studies comparing proton beam therapy to 3-D conformal radiation or IMRT.
Overall, studies have not shown clinical outcomes to be superior to conventional radiation therapy.
REFERENCES:


Marks LB, Zeng J, Prosnitz LR. One to three versus four or more positive nodes and postmastectomy radiotherapy: Time to end the debate. *J Clin Oncol* 2008; 26(13):2075-2077.


Overgaard M, Nielsen HM, Overgaard J. Is the benefit of postmastectomy irradiation limited to patients with four or more positive nodes, as recommended in international consensus reports? A subgroup analysis of the DBCG 82 b&c randomized trials. *Radiother Oncol* 2007; 82:247-253.


