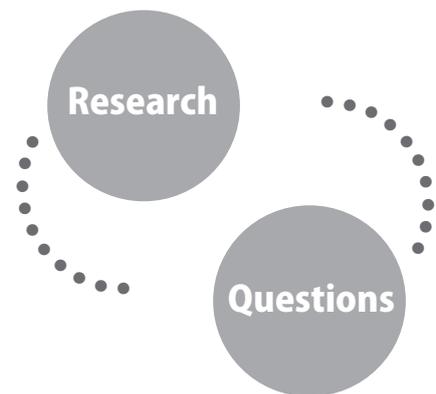


## "Practice Guidelines for Breast Cancer"

~ A Comparison between U.S. and Japan ~

(U.S.: as of 2007, Japan: according to "Practice Guideline for Breast Cancer"(2005) published by the Japanese Breast Cancer Society)

# 2. Radiotherapy



National Comprehensive Cancer Network (NCCN)

Nonprofit Organization Japan Comprehensive Cancer Network, Breast (JCCNB)

Workshop on Clinical Cancer Research Project organized by  
The Ministry of Health, Labour and Welfare, Japan

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### NCCN Categories of Consensus

<Category 1> There is uniform NCCN consensus, based on high-level evidence, that the recommendation is appropriate.

<Category 2A> There is uniform NCCN consensus, based on lower-level evidence including clinical experience, that the recommendation is appropriate.

<Category 2B> There is nonuniform NCCN consensus, (but no major disagreement), based on lower-level evidence including clinical experience, that the recommendation is appropriate.

<Category 3> There is major NCCN disagreement that the recommendation is appropriate

# Breast-conserving therapy plus radiotherapy in early invasive breast cancer

## 1 Is radiation of breast necessary after breast-conserving surgery of early breast cancer?

 Japan < Recommended Grade : **A** >

Radiation of breast is recommended for early breast cancer (Stage I/II).

 U.S. < Recommended Grade : **A** >

Radiation of breast is recommended for early breast cancer (Stage I/II), but may be omitted in favorable tumors in women >70 years of age.

## 2 What is the appropriate radiation regimen after breast-conserving surgery?

### 2-a Is radiation of entire breast recommendable?

 Japan < Recommended Grade : **A** >

Radiation of entire breast is recommended.

 U.S. < Recommended Grade : **A** >

Radiation of the entire breast is recommended.

### 2-b What is the adequate dose/fractionation of radiation?

 Japan < Recommended Grade : **B** >

A dose of 1.8-2.0Gy and a total of 45-50.4Gy during 4.5-5.5 weeks are recommended for entire breast.

 U.S. < Recommended Grade : **B** >

45-50.4 Gy in 4.5-5.5 weeks at 1.8-2.0 Gy is recommended to the entire breast. Alternatively, the Canadian fractionation of 40-42.5 Gy in 3 weeks, followed by a boost of 12.5 Gy could be considered in older women.

### 2-c Is boost radiation of tumor bed useful?

 Japan < Recommended Grade : **B** >

Boost radiation of tumor bed is useful, as frequency of intramammary occurrence is reduced.

 U.S. < Recommended Grade : **B** >

Boost radiation should be considered for most women unless there is a very wide margin in patients without lymphovascular invasion, extensive DCIS, or positive nodes. The minimum tumor bed dose should be >50 Gy.

## 3 Is radiation of lymph node region useful after breast-conserving surgery of early breast cancer?

### 3-a Can radiation of axillary lymph node region replace axillary dissection?

 Japan < Recommended Grade : **C** >

Axillary dissection and axillary radiation are comparable in terms of survival rate. However, axillary dissection is superior in axillary control, and therefore, axillary radiation cannot be aggressively recommended as replacement of axillary dissection.

 U.S. < Recommended Grade : **C** >

Axillary surgery provides prognostic information and controls the axilla. Axillary radiation could be considered in a clinically negative axilla if prognostic information is not useful.

### 3-b Is radiation of axillary lymph node region after axillary dissection useful?

 Japan < Recommended Grade : **D** >

Postoperative axillary radiation must not be performed in patients whose axillary lymph node was sufficiently dissected.

 U.S. < Recommended Grade : **C** >

Axillary radiation should be given in patients with an inadequate dissection, matted axillary nodes, or gross Extranodal extension.

### 3-c Is prophylactic radiation of supraclavicular node useful?

 Japan < Recommended Grade : **C** >

Radiation of supraclavicular node is possibly useful in patients who test positive for 4 or more metastases in axillary lymph nodes, but there is no sufficient evidence for recommendation.

 U.S. < Recommended Grade : **B** >

Radiation of the supraclavicular lymph nodes is indicated in patients with 4 or more positive axillary nodes.

### 3-d Is prophylactic radiation of the parasternal lymph node region useful?

 Japan < Recommended Grade : **C** >

No supporting evidence is available, since recurrence is rare in the parasternal lymph node region of patients who underwent breast-conserving therapy.

 U.S. < Recommended Grade : **C** >

Internal mammary node radiation could be considered in patients at extremely high risk of nodal involvement; however its effect on survival is likely small and it complicates radiation treatment.

## 4 What is the timing of chemotherapy and radiation after breast-conserving surgery?

### 4-a What is the optimal order of radiation and chemotherapy ?

 Japan < Recommended Grade : **B** >

Prognosis is not affected, whichever comes first, radiation or chemotherapy.

 U.S. < Recommended Grade : **B** >

Prognosis is not affected, whichever comes first- radiation or chemotherapy.

### 4-b When should radiation be started?

 Japan < Recommended Grade : **C** >

Sufficient evidence is not available for the time of starting radiation, regardless of postoperative chemotherapy.

 U.S. < Recommended Grade : **C** >

Radiation therapy should start within 3-8 weeks of surgery if no chemotherapy is planned for invasive carcinoma and 12 weeks for DCIS. It should start within 3-6 weeks of chemotherapy. Little data exists regarding exact timing.

## Radiotherapy after breast-conserving surgery of DCIS

### 5 Is radiation necessary after breast-conserving surgery of DCIS?

 Japan < Recommended Grade : **A** >

Radiation is required after breast-conserving surgery of DCIS.

 U.S. < Recommended Grade : **A** >

Most patients benefit from breast irradiation after breast-conserving surgery for DCIS in regards to local control, but not survival. There may be a subgroup of patients with very small low grade DCIS that is widely excised for whom radiation could be omitted.

### 6 In which DCIS cases can radiation be omitted after breast-conserving therapy?

 Japan < Recommended Grade : **C** >

Sufficient information is not available concerning the DCIS cases for which radiation after breast-conserving surgery can be omitted.

 U.S. < Recommended Grade : **B** >

Most patients benefit from breast irradiation after breast-conserving surgery for DCIS in regards to local control, but not survival. There may be a subgroup of patients with very small low grade DCIS that is widely excised for whom radiation could be omitted.

### 7 What are the risk factors for local recurrence after breast-conserving therapy of DCIS?

 Japan < Recommended Grade : **B** >

Histopathological factors for local recurrence include comedo type, advanced nuclear atypicality or low differentiation, and positive resection stump, while young age is the patient' s factor.

 U.S. < Recommended Grade : **B** >

Histopathological factors for local recurrence include high grade, comedo-type, close or positive margins, and tumor size.

### 8 What is the form of local recurrence after breast-conserving therapy of DCIS?

 Japan < Recommended Grade : **B** >

Invasive cancer accounts for about half of recurrences after breast-conserving therapy of DCIS.

 U.S. < Recommended Grade : **B** >

Invasive cancer accounts for about half of recurrences after breast-conserving therapy in DCIS.

## Radiotherapy after breast-conserving therapy- others

### 9 In which cases is radiation contraindicated after breast-conserving therapy?

 Japan < Recommended Grade : **D** >

Absolute contraindication : Pregnant women and the patients whose affected breast/chest wall was previously radiated.  
Relative contraindication : Patients who cannot raise the affected arm in dorsal position

 U.S. < Recommended Grade : **B** >

Absolute contraindication: Pregnancy, prior radiation to the same area. Scleroderma. Relative contraindication: Systemic lupus, BRCA1-2 carrier

### 10 Will radiation cosmetically affect the patients after breast-conserving therapy?

 Japan < Recommended Grade : **C** >

Cosmetic effect of radiation of entire breast is minimal. While boost radiation may have a short-term adverse cosmetic effect, there is no long-term effect.

 U.S. < Recommended Grade : **C** >

Cosmesis is related to: extent of surgery, breast size, dose homogeneity, use of boost radiation, and dose fraction size. Fibrosis and telangiectasia can occur late.

## Radiotherapy after mastectomy in advanced breast cancer

### 11 Is radiation recommended after mastectomy?

#### 11-a Will radiotherapy improve the control rate of chest wall?

 Japan < Recommended Grade : **A** >

Radiation after mastectomy improves the control rate of chest wall in patients with 4 or more metastases in axillary lymph nodes.

 U.S. < Recommended Grade : **A** >

Postmastectomy radiation improves locoregional control in patients with 4 or more positive axillary nodes, T3-4 cancers, positive margins, and possibly in patients with 1-3 positive nodes with a high ratio of positive to dissected nodes or extensive lymphovascular invasion.

#### 11-b Will it improve survival rate?

 Japan < Recommended Grade : **B** >

Radiation after mastectomy on top of adequate systemic treatment can improve the survival rate of patients with 4 or more metastases in axillary lymph nodes, as they have high risks of recurrence in chest wall.

 U.S. < Recommended Grade : **B** >

Postmastectomy radiation improves locoregional control in patients with 4 or more positive axillary nodes, and T3-4 cancers, and possibly in patients with 1-3 positive nodes.

#### 11-c What is the indication?

 Japan < Recommended Grade : - >

Radiation after mastectomy is recommended for patients with 4 or more metastases in axillary lymph nodes.

 U.S. < Recommended Grade : **B** >

4 or more positive axillary nodes T3-4 primary cancers  
1-3 positive nodes with >25% involvement and possibly with extensive lymphovascular invasion.

### 12 What is the appropriate radiotherapy regimen after mastectomy?

#### 12-a What is the appropriate radiation field?

 Japan

< Recommended Grade : **A** > Inclusion of chest wall is highly recommended.

< Recommended Grade : **B** > Inclusion of supraclavicular fossa is highly recommended.

< Recommended Grade : **C** > Parasternal lymph nodes are frequently included, but there is no sufficient evidence for recommendation.

 U.S.

< Recommended Grade : **A** > Chest wall

< Recommended Grade : **B** > Supraclavicular nodes for patients with positive nodes

< Recommended Grade : **C** > Internal mammary nodes for patients with medially located tumors with positive nodes.

## 12-b What is the right dose/fractionation?

 Japan < Recommended Grade : **C** >

Sufficient information is not available concerning total dose or a single dose.

 U.S. < Recommended Grade : **C** >

Fractionation similar to breast conserving surgery should be considered.

## 13 Is postoperative radiation useful in patients who received preoperative chemotherapy?

 Japan < Recommended Grade : **B** >

Postoperative radiation is recommended in a majority of locally advanced tumor patients who received preoperative chemotherapy.

 U.S. < Recommended Grade : **A** >

All patients who received neoadjuvant breast cancer for documented locally advanced cancers should receive postoperative radiation, despite any response.

## 14 What is the right order of chemotherapy and radiotherapy after mastectomy?

 Japan < Recommended Grade : **C** >

Sufficient information is not available concerning which should be performed first, systemic therapy or radiation after mastectomy.

 U.S. < Recommended Grade : **B** >

Postmastectomy radiation should be given after chemotherapy to assure adequate doses of chemotherapy.

## 15 Is breast reconstruction plus postoperative radiation safe after mastectomy?

### 15-a What is the right order of breast reconstruction and postoperative radiation after mastectomy?

 Japan < Recommended Grade : **C** >

Sufficient information is not available concerning the right order of breast reconstruction and postoperative radiation.

 U.S. < Recommended Grade : **C** >

No level I evidence exists regarding timing. Institutional preference suggests that TRAM flaps be delayed until after radiation.

### 15-b Is it safe, even if prosthesis is included in the radiation field?

 Japan < Recommended Grade : **C** >

It is unknown whether radiation is safe with prosthesis included in the radiation field.

 U.S. < Recommended Grade : **B** >

No level I evidence exists regarding timing. Institutional preference suggests that TRAM flaps be delayed until after radiation.

## Adverse events

## 16 Will the incidence of secondary or contralateral cancer increase due to radiation after surgery of breast cancer?

 Japan < Recommended Grade : **A** >

Although the incidence of secondary or contralateral cancer increases after radiation, the absolute number of such cases is extremely small, and usefulness of radiation after surgery of breast cancer remains unchanged.

 U.S. < Recommended Grade : **A** >

Although the incidence of secondary or contralateral cancer increases after radiation, the absolute number of such cases is extremely small, and usefulness of radiation after surgery of breast cancer remains

## 17 Are the adverse events of radiation after breast cancer surgery acceptable?

 Japan < Recommended Grade : **C** >

Almost all patients have mild dermatitis due to radiation after breast cancer surgery, but the frequency of other adverse events is low and acceptable.

 U.S. < Recommended Grade : **A** >

Adverse events include dermatitis, breast edema and fibrosis, pectoralis muscle fibrosis, rib fracture, pneumonitis, myocardial infarction, and second malignancies. Only the first 2 listed events are common and are usually mild and self-limited. The others are rare or asymptomatic.

## Radiotherapy for metastasis

### 18 Is radiotherapy useful for metastasis of cancer from breast to bone?

 Japan

< Recommended Grade : **A** > Radiotherapy is useful in alleviating pain of bone metastasis.

< Recommended Grade : **C** > Total dosage or fractionation method has not fully been established.

 U.S.

< Recommended Grade : **A** > Radiation therapy for bone metastases is very effective to alleviate pain.

< Recommended Grade : **A** > Limited or extended fractionation schemes are equally effective to alleviate pain.

### 19 Is radiotherapy useful for metastasis of cancer from breast to brain?

 Japan < Recommended Grade : **B** >

Radiotherapy is useful for metastasis of cancer from breast to brain.

 U.S. < Recommended Grade : **A** >

Symptoms from brain metastasis from breast cancer are palliated with whole or partial brain radiation therapy.