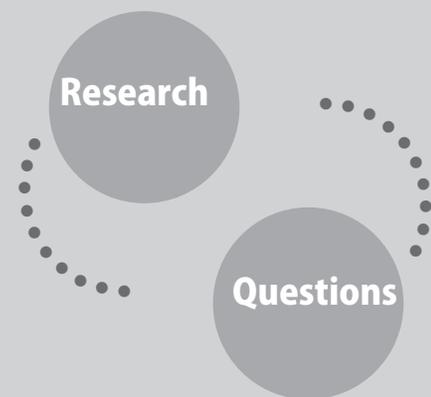


"Practice Guidelines of Surgical Therapy and Radiotherapy for Breast Cancer"

~ 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)



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

Surgical Therapy -List of Questions-

Ductal carcinoma in situ (DCIS)

- Q1 Can breast-conserving therapy replace mastectomy in DCIS?
- Q2 Is breast-conserving therapy recommended for DCIS?
- Q3 Is axillary dissection recommended in DCIS?

Invasive breast cancer

- Q4 Is pectoral muscle-conserving mastectomy a standard mastectomy?
- Q5 Is there any difference in survival rate between breast-conserving therapy and mastectomy as local therapy in Stage I/II invasive breast cancer?
- Q6 Can breast-conserving therapy become a local therapy for Stage I/II invasive breast cancer?
- Q7 Is axillary lymph node dissection therapeutically meaningful?
- Q8 Is parasternal lymph node dissection therapeutically meaningful?
- Q9 Is it possible to spare breast skin and papilla/areola in mastectomy?
- Q10 Is it acceptable in NO breast cancer patients to omit axillary lymph node dissection after sentinel-node biopsy?
- Q11 Is it desirable to use both dye and isotope for identifying sentinel lymph node?
- Q12 Is omission of axillary lymph node dissection after sentinel-node biopsy effective in reducing the incidence of postoperative lymphatic edema in an affected limb?
- Q13 Does breast reconstruction cause a delay in diagnosis of local recurrence?

Advanced/recurrent breast cancer

- Q14 Is it possible to treat locally advanced breast cancer only with surgery?
- Q15 Is it possible to treat inflammatory breast cancer only with surgery?
- Q16 What is the extent of axillary dissection before or during surgery in patients who are clearly positive for axillary lymph node metastasis?
- Q17 Is the breast-conserving therapy acceptable in breast cancer that has been shrunken with preoperative chemotherapy?
- Q18 Is axillary dissection based on the sentinel node biopsy result acceptable after preoperative chemotherapy?
- Q19 Is a repeated breast-conserving therapy recommended in intramammary recurrence after the first breast-conserving therapy?
- Q20 Is chest wall resection & reconstruction acceptable in the cases of extensive chest wall recurrence?

Others

- Q21 Can breast cancer be operated during pregnancy/lactation?
- Q22 Will pregnancy after breast cancer treatment affect prognosis?
- Q23 Will biopsy (puncture aspiration cytologic examination, needle biopsy, Manmottom™ biopsy, incision biopsy) affect prognosis?
- Q24 Is it effective to prophylactically administer an antibiotic drug during breast cancer surgery? If effective, what is the recommended regimen?
- Q25 Can prophylactic mastectomy be recommended for healthy women experiencing familial occurrence of breast cancer?

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

Ductal carcinoma in situ (DCIS)

1 Can breast-conserving therapy replace mastectomy in DCIS?

 Japan < Recommended Grade : **B** >

Breast-conserving therapy can replace mastectomy in DCIS, if the right patients are selected.

 U.S. < NCCN Categories of Consensus : **2A** >

Clear data demonstrating equivalent long term survival in women treated with BCT (excision + radiation)

2 Is breast-conserving therapy recommended for DCIS?

 Japan < Recommended Grade : **B** >

Breast-conserving therapy can be indicated in the following DCIS patients: the DCIS site < 3cm, cosmetically acceptable post-surgery appearance of breasts, histologically negative margin and low or intermediate nuclear atypicity.

 U.S. < NCCN Categories of Consensus : **2A** >

NCCN Guidelines do not use grade for defining the appropriateness of breast conserving therapy. There is no need to restrict breast conserving therapy to DCIS low or intermediate grade. For breast conserving therapy for DCIS over 5 mm in size, and of high grade, radiation to the whole breast is required (Category 1 Evidence).NCCN guidelines provide for breast conserving therapy with NO radiation for low grade DCIS less than 5 mm in size.

3 Is axillary dissection recommended in DCIS?

 Japan < Recommended Grade : **C** >

There is no supporting evidence for recommending axillary dissection.

 U.S. < NCCN Categories of Consensus : **2A** >

There are no data to support the use of axillary dissection or sentinel node biopsy with DCIS.NCCN Guidelines allow the use of sentinel node biopsy in situations when the surgery will make a subsequent SNB impossible at a second operation for those cases where the tumor proves invasive on excision. These situations include any time mastectomy is used to treat DCIS, or when a large excision of breast tissue is needed in the upper outer quadrant.

Invasive breast cancer

4 Is pectoral muscle-conserving mastectomy a standard mastectomy?

 Japan < Recommended Grade : **A** >

As the survival rate and local inhibition rate of pectoral muscle-conserving mastectomy can be comparable to those of radical mastectomy, pectoral muscle-conserving mastectomy is recommended as standard mastectomy.

 U.S. < NCCN Categories of Consensus : **1** >

There is no benefit to removing the pectoral muscles (e.g. radical mastectomy). This is demonstrated by a major randomized clinical trial done (NSABP B-04).Note that the use of radical mastectomy is not even addressed in the NCCN Guidelines as its use was abandoned 20 years before the NCCN guidelines were first developed.

5 Is there any difference in survival rate between breast-conserving therapy and mastectomy as local therapy in Stage I/II invasive breast cancer?

 Japan < Recommended Grade : **C** >

There is no difference in survival rate between breast-conserving therapy and mastectomy as local therapy in Stage I/II invasive breast cancer.

 U.S. < NCCN Categories of Consensus : **1** >

The equivalence in long term survival between mastectomy and breast conserving therapy is clearly demonstrated in randomized clinical trials.

6 Can breast-conserving therapy become a local therapy for Stage I/II invasive breast cancer?

 Japan < Recommended Grade : **B** >

Breast-conserving therapy can basically be recommended as local therapy for Stage I/II invasive breast cancer. However, (1) extensive growth of breast cancer and (2) evident multiple cancer should be excluded. Refer to the explanation for tumor size.

 U.S. < NCCN Categories of Consensus : **1** >

BCT is appropriate for Stage I and II breast cancer, and this has been proven in randomized clinical trials. Mastectomy is still used in some circumstances. Contraindications to BCT include

- Multicentric cancer (synchronous cancers in more than one quadrant of the breast)
- BCT is appropriate for Stage I and II breast cancer, and this has been proven in randomized clinical trials. Mastectomy is still used in some circumstances. Contraindications to BCT include
- Multicentric cancer (synchronous cancers in more than one quadrant of the breast)
 - Widespread disease that cannot be incorporated into excision to achieve negative margins.
 - Diffuse suspicious calcifications
 - Prior radiation to the involved (e.g. prior breast cancer)
 - Large tumor in relation to the size of the breast that precludes appropriate breast conservation

7 Is axillary lymph node dissection therapeutically meaningful?

 Japan < Recommended Grade : **C** >

Except for sentinel-node biopsy in breast cancer patients with negative lymph node metastasis, axillary lymph node dissection is meaningful for the purpose of local inhibition. However, no evidence is available concerning improvement of survival rate with axillary lymph node dissection.

 U.S. < NCCN Categories of Consensus : **1** >

The best evidence from randomized trials is that axillary dissection does not affect survival. Axillary dissection provides information for staging the cancer, and axillary dissection controls local disease in the axilla. One major clinical trial is ongoing to determine if axillary dissection affects survival in women who have a negative sentinel node biopsy (NSABP B-32 study).

8 Is parasternal lymph node dissection therapeutically meaningful?

 Japan < Recommended Grade : **C** >

Parasternal lymph node dissection does not have any therapeutic significance, and no evidence is available for recommending this method.

 U.S. < Not addressed in NCCN guideline >

Parasternal lymph node dissection does not have therapeutic significance

9 Is it possible to spare breast skin and papilla/areola in mastectomy?

 Japan

< Recommended Grade : **B** >

If the right mastectomy patient is selected, skin-sparing mastectomy can safely be performed. Skin-sparing mastectomy is indicated in patients with tumors or multiple cancer <5cm or DCIS, though nipple/areola are basically removed.

< Recommended Grade : **C** >

While nipple-sparing mastectomy is possible only in limited cases, no evidence exists for recommendation.

 U.S.

< NCCN Categories of Consensus - Skin sparing : **2A** >

Skin sparing appropriate in cases where :

- Skin not involved
- No prior surgical biopsy
- Reconstruction planned

< Not addressed in NCCN - Papilla / areola sparing >

Papilla/areola sparing:

- Minimal data
- Not included in US guidelines
- A few surgeons are doing this operation, but its use is not supported by sufficient data to allow its use in general practice

10 Is it acceptable in NO breast cancer patients to omit axillary lymph node dissection after sentinel-node biopsy?

 Japan < Recommended Grade : **B** >

When sentinel-node biopsy by a competent physician tests negative for metastasis, omission of dissection can be justified in NO breast cancer.

 U.S. < NCCN Categories of Consensus : **2A** >

There is a large body of evidence that SNB:

- Provides accurate information on lymph node staging
- The rate of recurrence in the axilla in women with a negative sentinel node.
- To date, there are no data from large clinical trials to demonstrate survival equivalence with SNB. However, it has become the standard care in US

11 Is it desirable to use both dye and isotope for identifying sentinel lymph node?

 Japan < Recommended Grade : **B** >

There is evidence for supporting the use of both dye and isotope in identifying sentinel lymph node.

 U.S. < Not addressed in NCCN guidelines >

NCCN guidelines do not address the technique of SNB. The guidelines require that SNB be performed by an experienced surgeon and team of physicians. Many US surgeons use only radioactive material due to risk of allergies, and skin staining from blue dye. Others use both isotope and dye.

12 Is omission of axillary lymph node dissection after sentinel-node biopsy effective in reducing the incidence of postoperative lymphatic edema in an affected limb?

 Japan < Recommended Grade : **A** >

Evidence suggests that omission of axillary lymph node dissection after sentinel-node biopsy reduces postoperative lymphatic edema in an affected limb, compared with the cases treated with axillary lymph node dissection.

 U.S. < Not addressed in NCCN guidelines >

There is clear evidence from both large non-randomized series and from randomized studies that the risk of postoperative lymphedema is much lower in women treated with sentinel node biopsy and breast conserving therapy. There are limited data on the risk of lymphedema with sentinel node biopsy with mastectomy, but most surgeons report this is reduced.

13 Does breast reconstruction cause a delay in diagnosis of local recurrence?

 Japan < Recommended Grade : **B** >

There is hardly any evidence that suggests that breast reconstruction (implant, autogenous tissue) causes a delay in diagnosis.

 U.S. < Not addressed in NCCN guidelines >

Most evidence shows that reconstruction does NOT delay the diagnosis of local recurrence, and does not impact on the outcome or survival in women who have this recurrence.

Advanced/recurrent breast cancer

14 Is it possible to treat locally advanced breast cancer only with surgery?

 Japan < Recommended Grade : **D** >

Locally advanced cancer should not be treated only with surgery.

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

It is not appropriate to treat locally advanced breast cancer with surgery alone. Locally advanced cancer requires multidisciplinary treatment, most often with surgery, radiation, chemotherapy, and hormonal therapy is ER positive.

15 Is it possible to treat inflammatory breast cancer only with surgery?

 Japan < Recommended Grade : **D** >

Inflammatory breast cancer should not be treated only with surgery.

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

Inflammatory cancer should not be treated with surgery alone.

16 What is the extent of axillary dissection before or during surgery in patients who are clearly positive for axillary lymph node metastasis?

 Japan < Recommended Grade : **B** >

Axillary lymph node dissection should desirably include Level III.

 U.S. < NCCN Categories of Consensus : **2A** >

NCCN guidelines call for Level I and II dissection. In general US surgeons perform Level I and II dissection unless there is gross disease in Level II, in which case Level III dissection is performed.

17 Is the breast-conserving therapy acceptable in breast cancer that has been shrunken with preoperative chemotherapy?

 Japan < Recommended Grade : **B** >

Breast-conserving therapy is acceptable in limited cases where breast cancer has been shrunken with preoperative chemotherapy.

 U.S. < NCCN Categories of Consensus : **2A** >

Clinical trial data demonstrate that this is an appropriate when breast conserving therapy is possible.

18 Is axillary dissection based on the sentinel node biopsy result acceptable after preoperative chemotherapy?

 Japan < Recommended Grade : **C** >

No evidence is available that supports omission of dissection based on the sentinel node biopsy result after preoperative chemotherapy.

 U.S. < NCCN Categories of Consensus : **2A** >

There are limited data on the accuracy of SNB performed either before or after preoperative chemotherapy. NCCN guidelines recommend that sentinel node biopsy be performed before preoperative chemotherapy

19 Is a repeated breast-conserving therapy recommended in intramammary recurrence after the first breast-conserving therapy?

 Japan < Recommended Grade : **C** >

No evidence exists that recommends repetition of breast conservation in intramammary recurrence after breast-conserving therapy.

 U.S. < Not accepted >

NCCN guidelines call for mastectomy with an intramammary recurrence after breast conserving therapy.

20 Is chest wall resection & reconstruction acceptable in the cases of extensive chest wall recurrence?

 Japan < Recommended Grade : **C** >

Chest wall resection & reconstruction can safely be performed. While this procedure may contribute to QOL improvement, it is not expected to improve prognosis, and therefore, there is no rationale for recommendation.

 U.S. < Not addressed in NCCN guidelines >

Chest wall resection is only rarely indicated for the purpose of providing local control to improve QOL

Others

21 Can breast cancer be operated during pregnancy/lactation?

 Japan < Recommended Grade : **B** >

Breast cancer surgery may be undertaken during pregnancy/lactation.

 U.S. < Not graded >

Yes. Surgery should be performed during pregnancy. Can do breast conserving therapy as long as radiation is administered after delivery of the child.

22 Will pregnancy after breast cancer treatment affect prognosis?

 Japan < Recommended Grade : **C** >

There is not sufficient evidence suggesting that pregnancy following breast cancer treatment may affect prognosis.

 U.S. < Not graded by NCCN >

All available evidence shows that pregnancy after breast cancer does not affect prognosis

23 Will biopsy (puncture aspiration cytologic examination, needle biopsy, Manmotom™ biopsy, incision biopsy) affect prognosis?

 Japan < Recommended Grade : **C** >

No evidence exists that suggests that biopsy (puncture aspiration cytologic examination, needle biopsy, Manmotom™ biopsy, incision biopsy) may affect prognosis.

 U.S. < NCCN Categories of Consensus : **2A** >

There are no data that needle biopsy adversely affects prognosis. Needle biopsy is preferred over surgical biopsy.

24 Is it effective to prophylactically administer an antibiotic drug during breast cancer surgery? If effective, what is the recommended regimen?

 Japan < Recommended Grade : **B** >

Effectiveness is observed in administering a prophylactic antibiotic drug during breast cancer surgery, and prophylactic administration is acceptable. However, instead of administering the drug in every patient, administration in the patients at risk is

 U.S. < Not addressed by NCCN guidelines >

Yes - there are randomized data that the use of a single dose of antibiotic reduces infection rates. Most US surgeons provide a single dose of a first generation cephalosporin. It is unclear what might constitute a "patient at risk" to make decisions about antibiotics.

25 Can prophylactic mastectomy be recommended for healthy women experiencing familial occurrence of breast cancer?

 Japan < Recommended Grade : **C** >

Prophylactic bilateral mastectomy reduces morbidity rate of breast cancer and death rate in women with pathogenic factor of breast cancer, but there is not yet evidence available in Japan that supports prophylactic mastectomy.

 U.S. < NCCN Categories of Consensus : **2A** >

Prophylactic mastectomy reduces the risk of subsequent breast cancer. There are NO data showing an impact on survival. Generally should be done only after careful counseling regarding cancer risk.

Radiotherapy -List of Questions-

Breast-conserving therapy plus radiotherapy in early invasive breast cancer

- Q1 Is radiation of breast necessary after breast-conserving surgery of early breast cancer?
- Q2 What is the appropriate radiation regimen after breast-conserving surgery?
- Is radiation of entire breast recommendable?
 - What is the adequate dose/fractionation of radiation?
 - Is boost radiation of tumor bed useful?
- Q3 Is radiation of lymph node region useful after breast-conserving surgery of early breast cancer?
- Can radiation of axillary lymph node region replace axillary dissection?
 - Is radiation of axillary lymph node region after axillary dissection useful?
 - Is prophylactic radiation of supraclavicular node useful?
 - Is prophylactic radiation of the parasternal lymph node region useful?
- Q4 What is the timing of chemotherapy and radiation after breast-conserving surgery?
- What is the optimal order of radiation and chemotherapy ?
 - When should radiation be started?

Radiotherapy after breast-conserving surgery of DCIS

- Q5 Is radiation necessary after breast-conserving surgery of DCIS?
- Q6 In which DCIS cases can radiation be omitted after breast-conserving therapy?
- Q7 What are the risk factors for local recurrence after breast-conserving therapy of DCIS?
- Q8 What is the form of local recurrence after breast-conserving therapy of DCIS?

Radiotherapy after breast-conserving therapy- others

- Q9 In which cases is radiation contraindicated after breast-conserving therapy?
- Q10 Will radiation cosmetically affect the patients after breast-conserving therapy?

Radiotherapy after mastectomy in advanced breast cancer

- Q11 Is radiation recommended after mastectomy?
- Will radiotherapy improve the control rate of chest wall?
 - Will it improve survival rate?
 - What is the indication?
- Q12 What is the appropriate radiotherapy regimen after mastectomy?
- What is the appropriate radiation field?
 - What is the right dose/fractionation?
- Q13 Is postoperative radiation useful in patients who received preoperative chemotherapy?
- Q14 What is the right order of chemotherapy and radiotherapy after mastectomy?
- Q15 Is breast reconstruction plus postoperative radiation safe after mastectomy?
- What is the right order of breast reconstruction and postoperative radiation after mastectomy?
 - Is it safe, even if prosthesis is included in the radiation field?

Adverse events

- Q16 Will the incidence of secondary or contralateral cancer increase due to radiation after surgery of breast cancer?
- Q17 Are the adverse events of radiation after breast cancer surgery acceptable?

Radiotherapy for metastasis

- Q18 Is radiotherapy useful for metastasis of cancer from breast to bone?
- Q19 Is radiotherapy useful for metastasis of cancer from breast to brain?

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 atypicity 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.