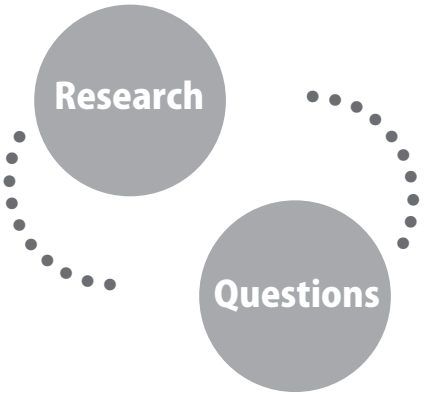
"Practice Guidelines for Breast Cancer"

～ 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)

1. Surgical Therapy



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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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 consenus, 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 atypicality.

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

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- 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 addressediin 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 advance 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, ManmotomTM biopsy, incision biopsy) affect prognosis?

Japan ＜ Recommended Grade : **C** ＞

No evidence exists that suggests that biopsy (puncture aspiration cytologic examination, needle biopsy, ManmotomTM 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 guideilines ＞

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.