UCCH Pathway

UCCH Guideline
Early Breast Cancer

2.03.01 Anlage 07

Version April 2023

Hubertus Wald Tumorzentrum
Universitäres Cancer Center Hamburg
Ein Kompetenznetzwerk des UKE

Guideline Early Breast Cancer

Version 12, April 2023

according to TNM classification 8th edition

Early breast cancer board members
Metastatic breast cancer board members
E. Burandt (Pathology) e.burandt@uke.de
S. Nilsson (Med. Oncology) s.nilsson@uke.de
E. Gökkurt (external cooperation partner) goekkurt@onkologie-eppendorf.de
L. Well (Radiology) l.well@uke.de
A. Krüll (Radiooncology) kruell@uke.de
V. Müller (Gynecology) v.mueller@uke.de
C. Petersen (Radiooncology) cor.petersen@uke.de
U. Göbel (patient representative UCCH) u.goebel@uke.de
B. Schmalfeldt (Gynecology) b.schmalfeldt@uke.de
L. Steinhilper (Gynecology) l.steinhilper@uke.de
E. Laakmann (Gynecology) e.laakmann@uke.de

Responsible authors	L. Steinhilper, V. Müller (Gynecology)
Implemented	Apr/2008
Revised	2012, 2013, Nov/2015, May 2017, June 2018, April 2020, April 2023
Next planned review	May 2024

Legend of Colours

= Therapeutic procedure

= Clinical or diagnostical condition

= Diagnostic procedure

= Clinical trial

= Supportive measure

= Referral

TB

= Tumorboard (including post tumorboard interaction with patient that follows the principles of shared decision-making)

Pathway: Early Breast Cancer

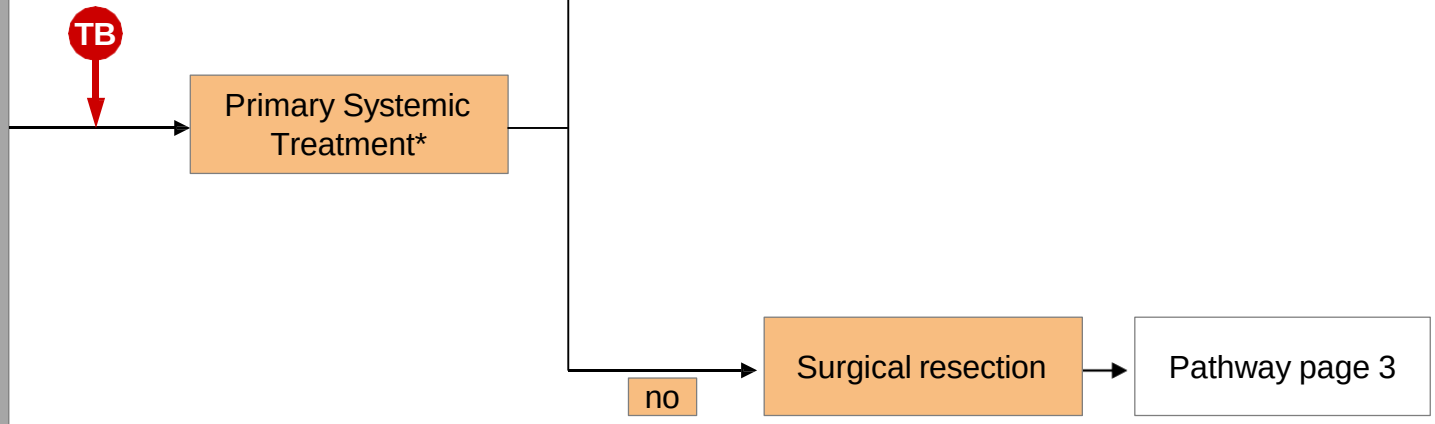
Work up

Baseline:
- Medical history
- Physical examination
- Biopsy of the suspicious lesion
- Mammography and ultrasound of both breasts, in case of unclear results MRI of the breasts

In case of malignant finding:
- Laboratory work-up

In case of clinical suspected and / or pathologic confirmed involvement of axillary lymph nodes, in case of primary systemic treatment or in case of recurrent disease:
- Staging (CT scan of the thorax and the abdomen, abdominal ultrasound and chest X-ray if CT scan is not feasible, bone scintigraphy)

Supportive:
Offer contact to patient group
Offer psychooncological support
Offer social services
Offer fertility counseling (for pat. <40 years)
Offer genetic counseling in case of fulfilled criteria (GC-HBOC)



* based on general indication for chemotherapy, in addition improvement of surgical outcome expected

Pathway page 2: Primary systemic chemotherapy (PST)

Primary systemic chemotherapy (PST)

Primary systemic chemotherapy

Treatment regimens

- TNBC → EC x 4 q2w followed by Pac/carboplatin x 12 qw; Addition of pembrolizumab in case of <cT2 and cN+ (CNB recommended) and/or ≥ cT2, then start with Pac/carboplatin followed by EC q3w
- **HER2-positive eBC** → 6 x docetaxel + carboplatin q3w + trastuzumab + pertuzumab OR 4x EC followed by Pac with trastuzumab + pertuzumab neoadjuvant; post-neoadjuvant therapy depending on tumor response (non-pCR → switch to T-DM1 for 14 cycles; pCR → cN0: trastuzumab for a total duration of 1 year, cN+ trastuzumab + pertuzumab for a total duration of 1 year

- **HR+ HER2- eBC** → EC x 4 q2w followed by PAC x 12 qw (preferred)

- **Axillary surgery after PST:**
- cN0: SLNB
- cN+ → ycN0: TAD in case of initially max 3 suspicious nodes, ALND in case of ≥ 4 suspicious nodes

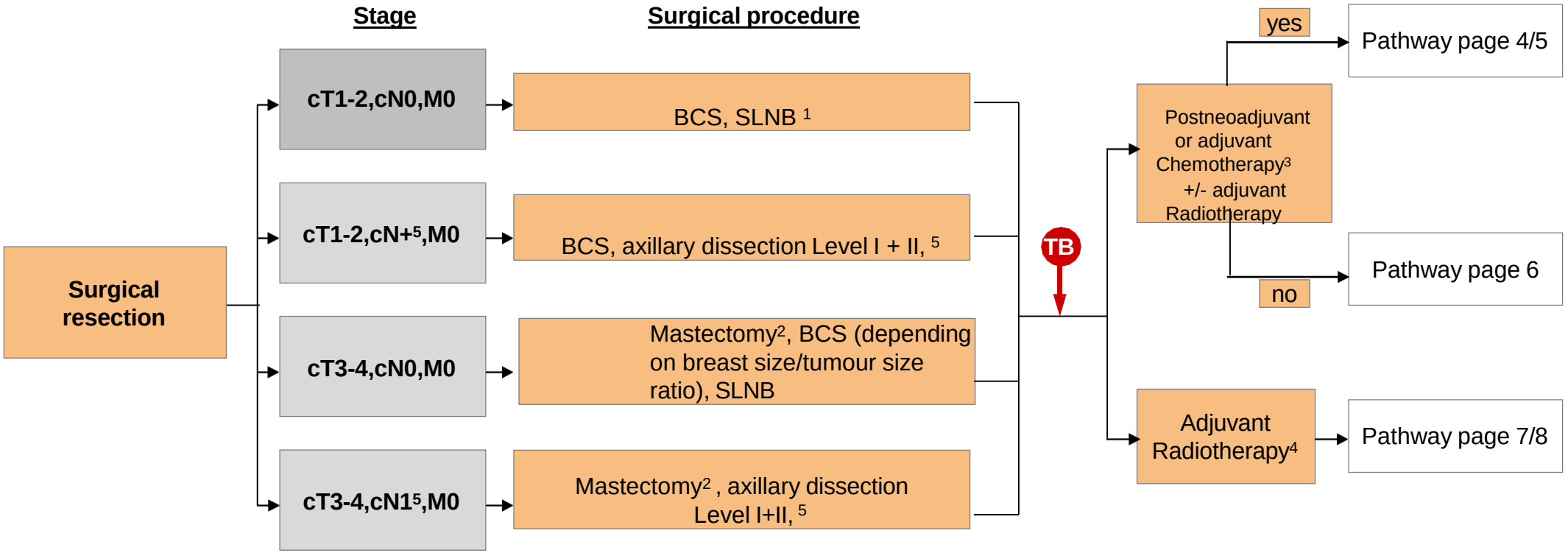
- If possible, confirm suspicious nodes using minimally-invasive biopsy before start of PST; marking of biopsied nodes with a clip/coil or a probe-detectable marker recommended

- **Assessment of tumor response:** clinical and sonographic examination every 6-8 weeks

Pathway page 3

TNBC= Triple negative Breast Cancer,
CNB= core needle biopsy,
EC=Epirubicin/Cyclophosphamide,
Pac=Paclitaxel,
pCR= pathological complete remission,
TAD= Targeted axillary dissection

Pathway page 3: Surgical resection



BCS Breast Conserving Surgery / SLNB Sentinel lymph node biopsy / TAD Targeted axillary dissection / PST primary systemic chemotherapy

1 Patients are offered to omit complete axillary dissection in case of BCS and consecutive radiotherapy including a tangential field if only 1 or 2 SLN are tumor involved (without gross extracapsular extension ECE)

2 The patient should be counseled about reconstructive options and their advantages and disadvantages (immediate vs. delayed reconstruction, implant/tissue expander vs. autologous reconstruction vs. combination).
Depending on individual situation and patient based on our own SOP and AGO guidelines for risk stratification for node negative and pN1a breast cancer.

3 Risk prediction is based on clinic-pathologic factors. If these factors do not allow a recommendation concerning the use of chemotherapy a multigene test can be performed, e.g. Oncotype DX or Endopredict.
Radiation therapy of breast or thoracic wall commonly follows chemotherapy when chemotherapy is indicated
After primary systemic chemotherapy tumor resection is done in new margins.
5 Nodal status should be confirmed by core needle biopsy in case of suspected involved axillary lymph nodes.TAD/SNL possible when initally pN+ converting to ycN0 after PST.

Pathway page 4: Adjuvant treatment

Adjuvant Chemotherapy

- Depending on AGO guidelines and no previous neoadjuvant chemotherapy
- Consider additional test in HR+ HER2- eBC for prognostic information (Oncotype DX or Endopredict based on availability)

Nodal +

- All age groups EC x 4q2w followed by 12xPac weekly
- For patients HER-2 positive, 6x Docetaxel/Carboplatin q3w (or 4xEC + 12xPac) with Trastuzumab and Pertuzumab administered for one year.
- For patients not tolerating 18 or 20 weeks of chemotherapy, 12 weeks of Paclitaxel or 4 cycles of TC (Docetaxel/Cyclophosphamid) is an option. Add Trastuzumab in HER2 positive an additional Pertuzumab in high-risk patients

Nodal –

- N0 or 1-3 involved lymph nodes with good prognostic factors (HR pos., HER2 neg., G1 or G2, Ki67 <20%,) no adjuvant chemotherapie (differences between pre- and postmenopausal women)
- In N0 patients with additional risk factors (e.g. <35 years, triple negative, Recurrence Score >25) treatment as for N+ is recommended.
- In HER-2/neu positive patients 6x Docetaxel/Carboplatin q3w with Trastuzumab or 4xEC +12x Pac with Trastuzumab. For patients with cT1 N0 offer Paclitaxel 12x weekly plus trastuzumab. Trastuzumab should be administered for one year.

HR positive

Endocrine treatment according to

Pathway page 5

HR hormone receptor

Pathway page 5: Postneoadjuvant treatment

Primary systemic chemotherapy

pCR

- For patients with TNBC (without neoadjuvant Pemrolizumab) and HR+/HER2- tumors no postneoadjuvant treatment is recommended
- For patients with TNBC with neoadjuvant Pembrolizumab additional 9 cycles of Pembrolizumab recommended
- For patients with HER2 positive, initally N+: completion with trastuzumab and pertuzumab for 1 year
- For patients with HER2 positive tumors, initally N0: completion with trastuzumab mono for 1 year

non-pCR

- For patients with TNBC with neoadjuvant pembrolizumab, additional 9 cycles of Pembrolizumab. Consider 6-8 cycles of capecitabine additionally.
- For patients with TNBC without indication for pembrolizumab, offer 6-8 cycles of capecitabine
- In case of BRCA1/2 mutation and any TNBC oder HR+/HER2- with CPS-EG Score >=3, offer olaparib for 1 year
- In HER2 positive patients switch to T-DM1 for 14 cycles in total. Consider neratinib for 1 year in case of HR+.
- In patients HR+/HER2-negative with initially >= 4 lymph nodes involved or 1-3 lymph nodes involved with pT3 tumor an/or G3 offer therapy with Abemaciclib for 2 years in addition to ET

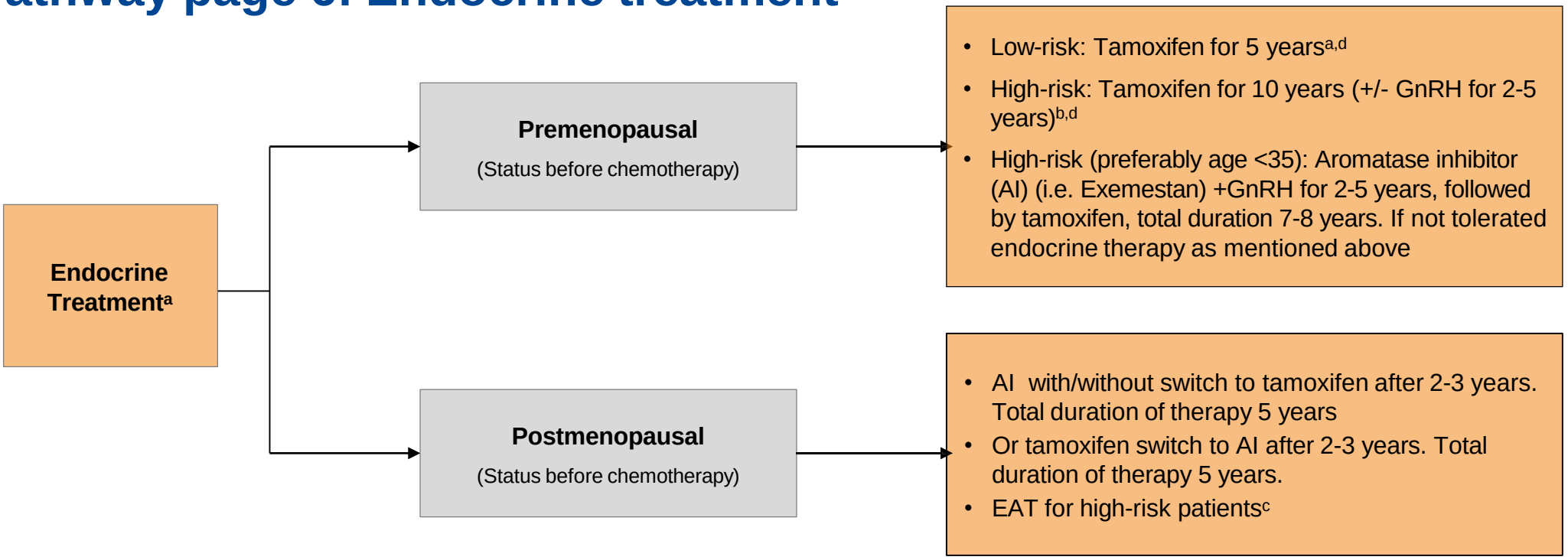
HR-positive

Endocrine treatment according to

Pathway page 6

pCR = pathologic complete response

Pathway page 6: Endocrine treatment



[a] ER positive and also patients with questionable response to endocrine therapy (1-9% positive cells) should be considered positive. For premenopausal patients with contraindications to tamoxifen, GnRH analogues for 5 years could be administered.

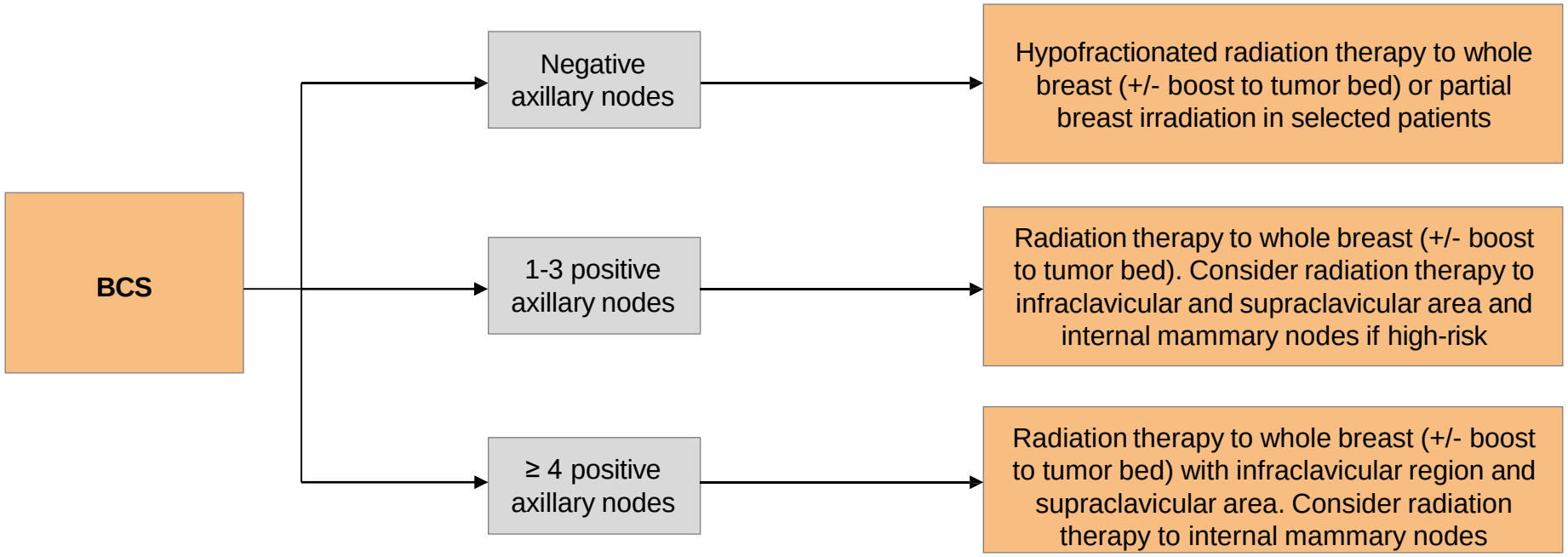
[b] In young patients (<45 years) and ovarian recovery with high risk of recurrence (node positive and/or indication for chemotherapy) addition of GnRH-Analogue should be offered. In very young patients (< 35 years) with high risk of recurrence the combination of Exemestan and GnRH analogue should be offered. However, these therapies can have more side effects and patients can switch to tamoxifen if these options are not tolerated.

[c] Duration of therapy more than 5 years of benefit in several studies. Patients should be informed about this fact and discuss this after completing of 5 years therapy with their physicians. Longer duration recommended for patients with higher risk of recurrence after 5 years (N pos and/or indication of chemotherapy). Patients should be informed about study results demonstrating benefit of zoledronic acid for postmenopausal patients administered q6mon for at least 2 years. High risk patients should be offered to receive zoledronic acid, also after chemotherapy.

[D] switch from Tam to AI after 2-3 years possibe if patient is postmenopausal

EAT= extended adjuvant treatment

Pathway page 7: Radiotherapy after breast conserving therapy



BCS Breast Conserving Surgery

Pathway page 8: Radiotherapy after mastectomy