中山醫學大學附設醫院

乳癌診療指引

本臨床指引參考台灣國家衛生研究院、與美國NCCN版本、台灣乳房醫學會

乳癌多專科醫療團隊編修

乳癌治療指引制訂日期

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癌症委員會主任委員	癌症委員會執行長	癌症防治中心主任	團隊負責人

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第 6 頁	Tamoxifen 10 years for ER(+)(Level 2B) Physical examination every 6 months Mammography and/or Ultrasonography every 6 months for 2 years then every 12 months	修訂： Hormone therapy 5-10 years (Level 2B) Physical examination every 6 months Mammography and/or Ultrasonography every 6-12 months for 2 years then every 12 months
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第 9 頁	Ultrasonography of liver/Abd CT(optional)	刪除
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第 11 頁	IORT Patient selection criteria (皆符合): Age ≧50、Unicentric only、Clinical size ≤3cm、Negative surgical margin、pN0 (Sentinel lymph node evaluation or Axillary lymph node dissection)	修訂:Unicentric only、Clinical size ≤3cm、Negative surgical margin、pN0 (Sentinel lymph node evaluation or Axillary lymph node dissection)
第 18 頁	NA	新增：Caboplantin 6mg Q3W.
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一、何謂乳癌

乳癌是由乳房乳腺管細胞或是腺泡細胞經由不正常分裂、繁殖所形成之惡性腫瘤。
這些惡性腫瘤除了侵犯局部器官 (乳房)，更可能轉移到遠處器官如骨骼、肺、肝、腦等，而破壞身體重要器官的功能，造成身體健康之損害，甚至危害生命。

二、乳癌的診斷

乳癌最重要的臨床表徵是可觸摸到的乳房腫塊。自我檢查時，若腫塊甚硬、形狀不規則、邊緣不清楚、乳頭凹陷或有不正常分泌物等現象，均應懷疑是乳癌。

自我檢查除注意乳房變化外，也應檢查是否有腋下、鎖骨上及頸部淋巴結腫塊。然而上述變化出現，往往已非早期乳癌，因此摸到任何乳房腫塊，即應先由專科醫師理學檢查外，必要時安排進一步檢查，包括乳房超音波、乳房 X 光攝影及細針抽吸細胞學檢查。

影像檢查若懷疑是乳癌，即應以細胞學檢查或組織切片檢查確定診斷。細針抽吸細胞學檢查，方便易做，不需麻醉，以空針及細針頭，刺入腫塊，做多次抽吸，取得細胞檢查。細針抽吸細胞學檢查的診斷率相當高，但仍有偽陰性 (應是乳癌，卻診斷為良性) 及偽陽性 (良性腫塊，卻診斷為乳癌) 的可能。由於無法完全避免偽陽性，因此以細胞學檢查做為整個乳房切除的診斷根據必須慎重。

而臨床上疑似乳癌，而細胞檢查是陰性時，應做組織切片檢查。另外，細胞檢查無法區別侵犯性癌或零期原位癌，若治療方式會因病理結果而有不同考量，應有組織切片結果為依據。

病理組織切片檢查可以藉手術切片或以粗針穿刺取檢體做組織病理學診斷，這是乳癌診斷的黃金標準。

組織切片除了確定病理診斷，另一重要目的為檢測乳癌預後因子，如荷爾蒙接受體以及 HER-2/neu 過度表現，以做為治療參考。粗針穿刺切片術由於操作簡單，在門診即可進行，已被廣泛採用。手術切片取得的檢體可立即做冷凍切片，或以福馬林固定，做石蠟切片。前者約 30 分鐘可知結果，後者需至少一天。冷凍切片發生偽陽性及偽陰性的機會，可說微乎其微，然而仍有一些情況不宜以冷凍切片做為診斷依據，例如乳突瘤或經細針定位切除之觸摸不到的小腫塊 (小於 1 公分) 等。評估乳房保留手術的腫瘤安全切除範圍及原位癌是否有顯微侵犯，最好以石蠟切片再估。

三、乳癌的篩檢

隨著生活型態、飲食習慣的日漸西化，台灣的乳癌越來越多。但多數乳癌病人太晚就醫，顯見婦女自我乳房檢查率太低；且因醫學知識偏差或個性保守，摸到乳房腫塊後，不願就醫。因此每位婦女應於月經結束後一星期，自我檢查乳房，摸到任何腫塊，即刻就醫。

由於乳房自我檢查對早期乳癌的發現幫助有限，必須藉助其他方式，如乳房 X 光攝影及乳房超音波，偵測出觸診無法發現的零期或第一期乳癌，以進一步降低死亡率。相較於歐美，台灣雖屬乳癌低發生率地區，但罹病年齡層偏低且婦女乳房較緻密，因此如何建議婦女做乳癌篩檢，尚待研究。

基本上，若有危險因子的婦女，35 歲起應接受醫師檢查，必要時安排超音波檢查或乳房 X 光攝影。一般 40 歲做第一次乳房 X 光攝影，而後以超音波及 X 光攝影交替檢查，50 歲後篩檢則以乳房 X 光攝影為主。若乳房 X 光攝影或超音波出現密集的顯微鈣化點或不規則邊緣腫塊、或其他疑似乳癌變化時，則應以立體定位做大範圍切除，並送病理組織石蠟切片檢查。

乳癌的危險因子如下：

A.高危險群 (致癌相對機率大於 4 倍)：

- ♦ 一側乳房得過乳癌
- ♦ 特殊家族史 (停經前得過兩側乳癌)
- ♦ 乳房切片有不正常細胞增生現象

B. 次高危險群 (致癌相對機率 2～4 倍)：

- ♦ 母親或姐妹得過乳癌
- ♦ 卵巢癌及大腸癌患者

C. 略高危險群 (致癌相對機率 1.1～1.9 倍)：

- ♦第一胎生育在三十歲以後
- ♦ 子宮內膜癌患者
- ♦ 未曾生育者
- ♦ 停經後肥胖
- ♦ 胸部放射線治療
- ♦ 過量飲酒
- ♦ 初經在 12 歲以前
- ♦ 停經在 55 歲以後
- ♦ 長期口服避孕藥
- ♦ 長期補充女性荷爾蒙

四、乳癌的分期

乳癌分期的主要目的在確立治療方式的選擇，評估預後及比較不同治療方式的結果。目前乳癌的分期是依據腫瘤大小(T)、腋下淋巴腺轉移與否 (N)、遠處是否轉移 (M) 等 TNM 系統來分為：(依據 UICC，AJCC 2002 分期)

A. 零期乳癌：即原位癌，為最早期乳癌，癌細胞仍在乳腺管基底層內。

B. 第一期乳癌：腫瘤小於 2 公分以下的浸潤癌且腋下淋巴結無癌轉移。

C. 第二期乳癌：腫瘤在 2 公分至 5 公分之間的浸潤癌；或腫瘤小於 2 公分但腋下淋巴結 1～3 顆有癌轉移。

D. 第三期乳癌：局部廣泛性乳癌，腫瘤大於 5 公分的浸潤癌且腋下淋巴結有任何癌轉移或有胸壁皮膚的浸潤乳癌。或鎖骨上淋巴結轉移，或腋下淋巴結 4 顆以上有轉移。

E. 第四期乳癌：轉移性乳癌，已有遠處器官轉移 (如肝、肺、骨) 等。

五、乳癌的治療

(一)乳癌的外科治療 (外科手術是治療乳癌最重要的一環)

A. 改良型乳房根除手術：適用於任何沒有胸大肌侵犯或非第四期轉移性乳癌的患者，為目前最常使用的手術。術式包含腋下淋巴結廓清術。

B. 乳房保留手術：適用於乳房腫瘤小於 3 公分，非於乳頭或乳暈下方，而且無多發病灶的第一、二期乳癌患者。術式包含部分乳房組織切除術及腋下淋巴結廓清術，通常術後需放射線治療。

C. 單純性全乳房切除手術：適用於乳房腺管原位癌乳癌患者，術式不包含腋下淋巴結廓清術。

D. 部分乳房組織切除術：可用於小而非粉刺型的乳房腺管原位癌。粉刺型原位癌若採用此手術，宜加放射線治療。

E. 腋下淋巴結廓清術：腋下淋巴結被癌細胞侵犯的狀況，為乳癌預後最重要的指標之一，因此腋下淋巴結廓清術兼具有診斷及治療的目的(註：目前前哨淋巴結摘除術可取代部分腋下淋巴結廓清術，但此項手術之安全性及可靠性仍在臨床研究中)。

F. 前哨淋巴結摘除術：傳統侵襲性乳癌患者的手術治療，除了全乳房或部分乳房切除外，皆必須接受例行之同側腋窩淋巴清除術。這樣做，不但可減少腋窩再發率，也是乳癌分期的重要根據。估計在早期乳癌約有 20% 至 30% 的患者會有淋巴轉移。對這些患者而言，淋巴切除是必須的；但反而言之，則有約 70% 的患者接受了不必要的淋巴切

除，而淋巴切除術本身會帶給病人相當程度的手術後遺症，約有 10～20% 不等的病人會因此產生淋巴水腫，而深受困擾。

(二)乳癌的輔助藥物治療

A. 零期乳癌 (原位癌)：

乳房保留手術加上輔助性放射線治療或單純性全乳房切除手術。原位癌發生腋下淋巴結癌細胞轉移的機會很小 (0～ 3%) ，故不必做腋下淋巴結廓清術。術後不需輔助性化學治療，但需定期追蹤檢查。

B. 第一、二期乳癌：腋下淋巴結無癌細胞轉移者：

(a) 低危險群：術後可不加輔助性化學治療，但可給抗荷爾蒙治療，並需定期追蹤檢查。

- ♦ 乳癌小於 2 公分、細胞分化良好且荷爾蒙接受體陽性者。
- ♦ 組織學形態良好 (如乳突狀癌、管狀癌、黏液性癌) 且小於 2 公分者。術後不需輔助性化療，但需定期追蹤檢查。

(b) 高危險群：包括 35 歲以下，乳癌大於 2 公分、細胞核分化不良或荷爾蒙接受體陰性。上述任一狀況，術後予以輔助性化學治療。若荷爾蒙接受體為陽性，則加上抗癌荷爾蒙治療。

腋下淋巴結有癌細胞轉移者：

化學治療應依病人狀況考量因乳癌的預後與腋下淋巴結轉移數目皆大不相同，依其預後所需要的化學治療也不一樣。是以化學治療應由腫瘤內科醫師及其他專科醫師來執行或參與，方能收到最好的效果。

C. 局部廣泛性乳癌：

因乳癌的腫塊太大時，不易切除乾淨，而導致癌細胞的擴散。先給予手術前的化學治療可能降低遠處復發率，且往往可縮小腫瘤，而可能接受乳房保留手術。

D. 轉移乳癌：

乳癌細胞常經淋巴及血液系統轉移至骨骼、肺、肋膜以及其它內臟器官。此時治癒機會微小，但經荷爾蒙及化學抗癌藥物之治療再輔以適當的手術或放射治療，可緩解病情的急速惡化，生命得以延長，且生活品質也可維持不錯的水準。

(三)乳癌的荷爾蒙治療

荷爾蒙療法之先決條件是腫瘤細胞有雌性激素受體(Estrogen Receptor，以下簡稱 ER) 或是黃體素受體 (Progesterone Receptor，以下簡稱 PR) 之表現，而且這些受體會在雌性激素之調節後刺激腫瘤生長。若一位患者之

腫瘤細胞同時有 ER 及 PR 之表現 (ER+PR+)，則其使用荷爾蒙治療得到緩解之機率約為 75～80%；若只有 ER 表現沒有 PR 表現 (ER+PR-)，則緩解率約為 25～30%；若只有 PR 表現沒有 ER 表現 (ER-PR+)，則約為 40～45%；即使兩者均無表現 (ER-PR-)，仍有小於 10% 之病人可達到緩解。

內分泌治療條件為：停經前、Stage IV，consider bilateral oophorectomy.

而根據兩項不同之研究顯示，大約有四分之三的患者其腫瘤細胞有表 ER 或 PR，因此絕大部分之患者均有機會接受荷爾蒙療法。

(四)乳癌的放射線治療

何種情況乳癌患者需接受手術後放射治療：

(a) 乳房保存療法：

(b) 乳房切除術後需輔助放射治療的情形：

- ♦ 原來乳房腫瘤大於 5 公分或在術前已經出現皮膚侵犯現象。
- ♦ 手術邊緣有殘存癌細胞或癌細胞靠近手術切口。
- ♦ 癌細胞轉移到三個以上的腋窩下淋巴。上述情況追加輔助性

放射治療確實可減少病患局部腫瘤復發的可能性。

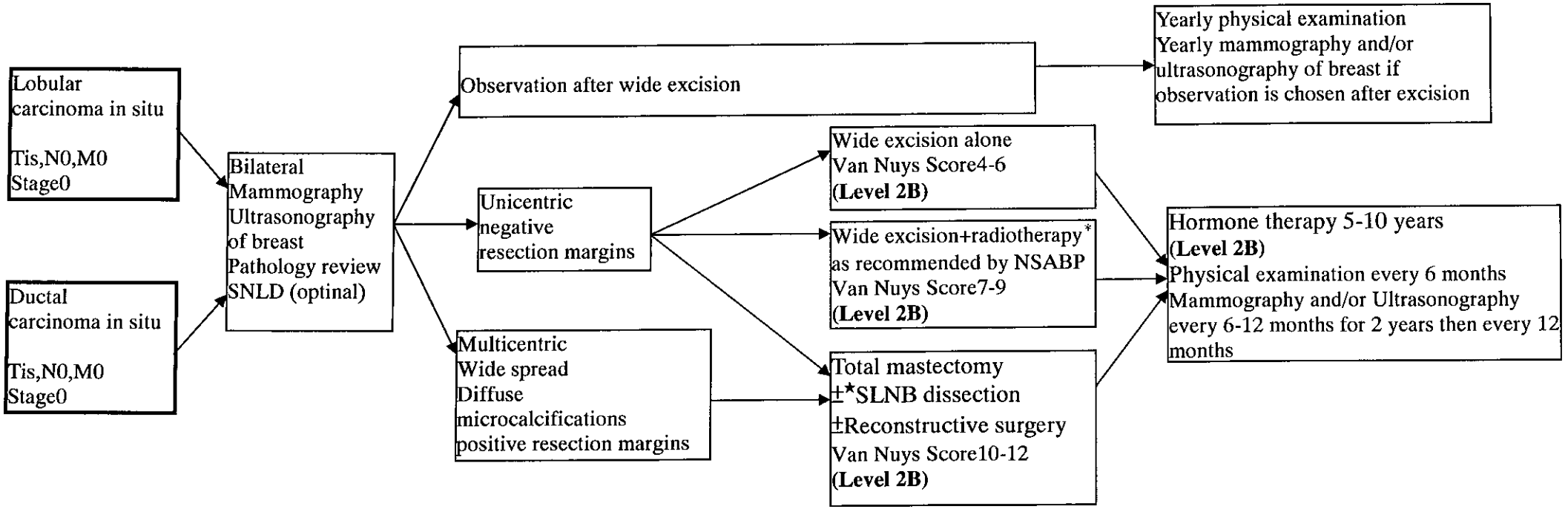
Neoadjuvant Regimens 的病患條件

1. Stage Ⅱ、Stage Ⅲ and Fulfills criteria for breast conserving surgery.
2. Locally advanced and inflammatory breast cancer.
3. Triple negative、luminal B、Her-2 type early breast cancer

乳房檢查之條件：

1. 乳房攝影：≧45 歲
2. 乳房超音波：≦45 歲

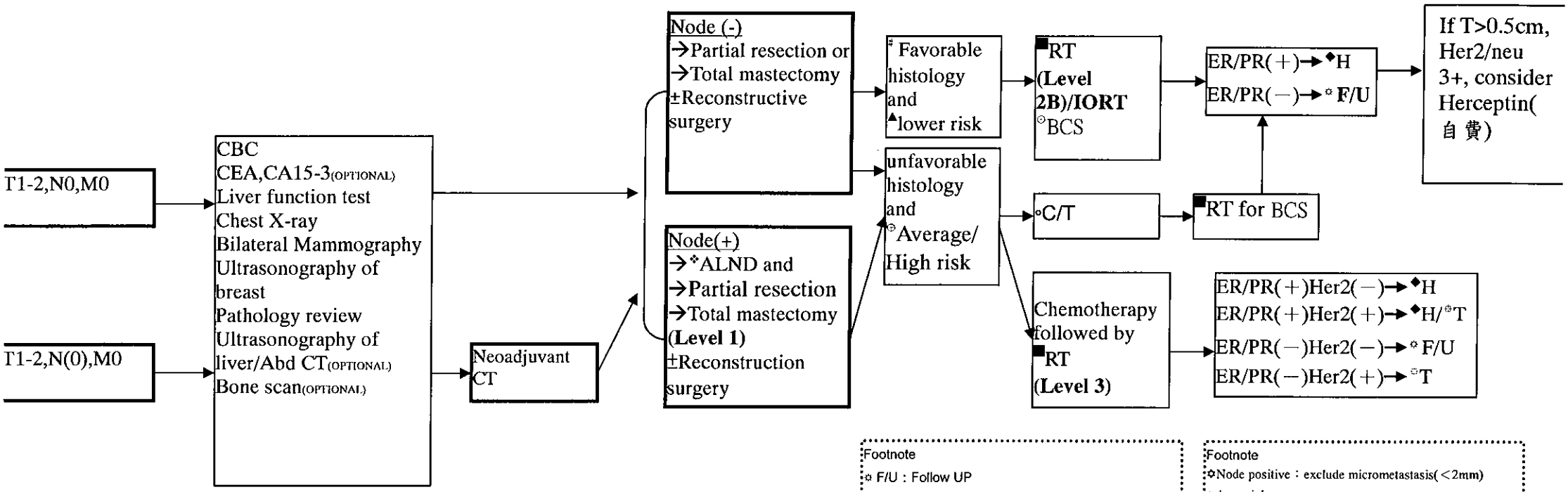
DIAGNOSIS	WORK-UP	PRIMARY TREATMENT	FOLLOW-UP



New Van Nuys Prognostic Index Scoring System			
Score	1	2	3
Size	≦15mm	16-40mm	≧40mm
Margin	≧10mm	1-9mm	<1mm
Pathologic Classification	Non-high grade w/o necrosis	Non-high grade with necrosis	High grade with or w/o necrosis
Age	>60	40-60	<40

Pathologic status of ER、PR、Herb-2 Score please see page 7
*refer to page： principle of radiation therapy

DIAGNOSIS	WORK-UP	PRIMARY TREATMENT	ADJUVANT THERAPY	FOLLOW-UP



Footnote
- ● SLN : Sentinel Lymph Node
- ▲SLND : Sentinel Lymph Node dissection
- ★SLNB : Sentinel Lymph Node Biopsy
- ❖ALND : Axillary Lymph Node Dissection
- ■RT : Radiotherapy
- ⊙BCS : Breast conserring surgery
- ◆H : Hormone Therapy
- ⊕T : Target Therapy
- ◘CT : Chemotherapy

Footnote
- ✡ F/U : Follow UP

Physical examination :
every 3 months for 2 years,every 6 months for 3 years,then every 12 months.
Mammography and/or ultrasonography of breast, and chest x-ray every 12 months
CBC,blood cheristries,CEA and/or CA15-3every 3-6months for 3 years ,then every 6-12 months.
Bone scan (Optional)n
Abdominal Ultrasound(Optional)
Women on tamoxifen : GYN examination every 12 months.

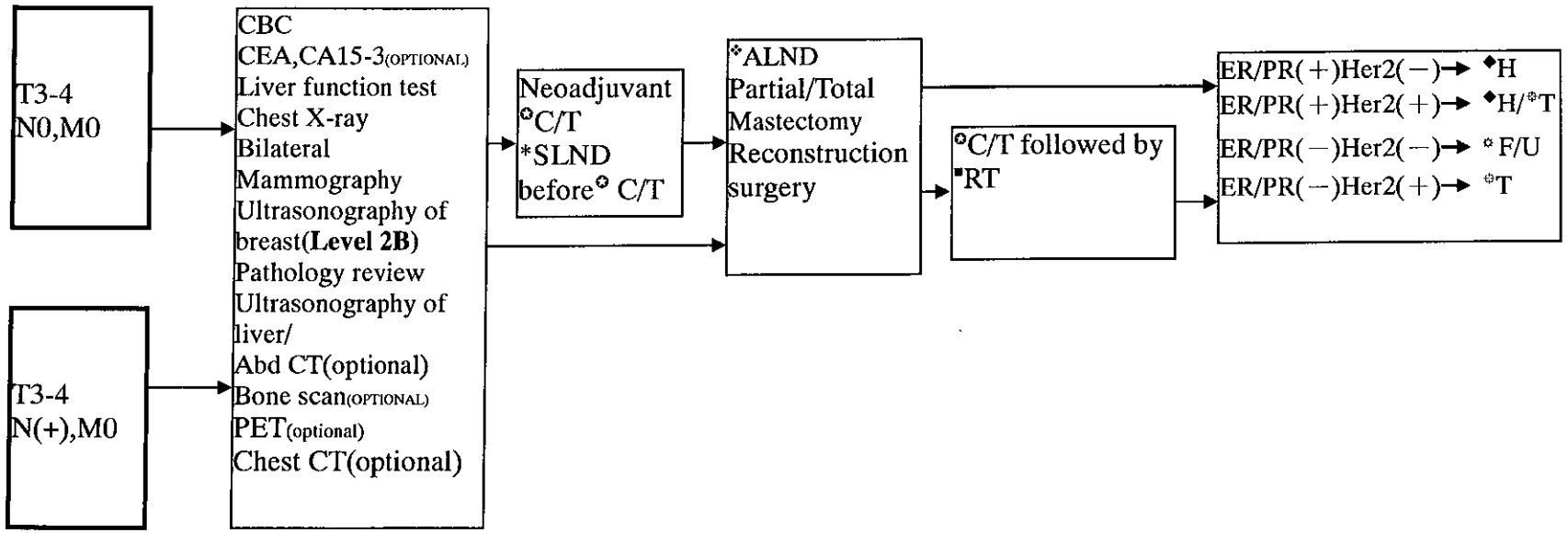
Footnote
- ✡Node positive : exclude micrometastasis(＜2mm)
- ▲ Low risk :

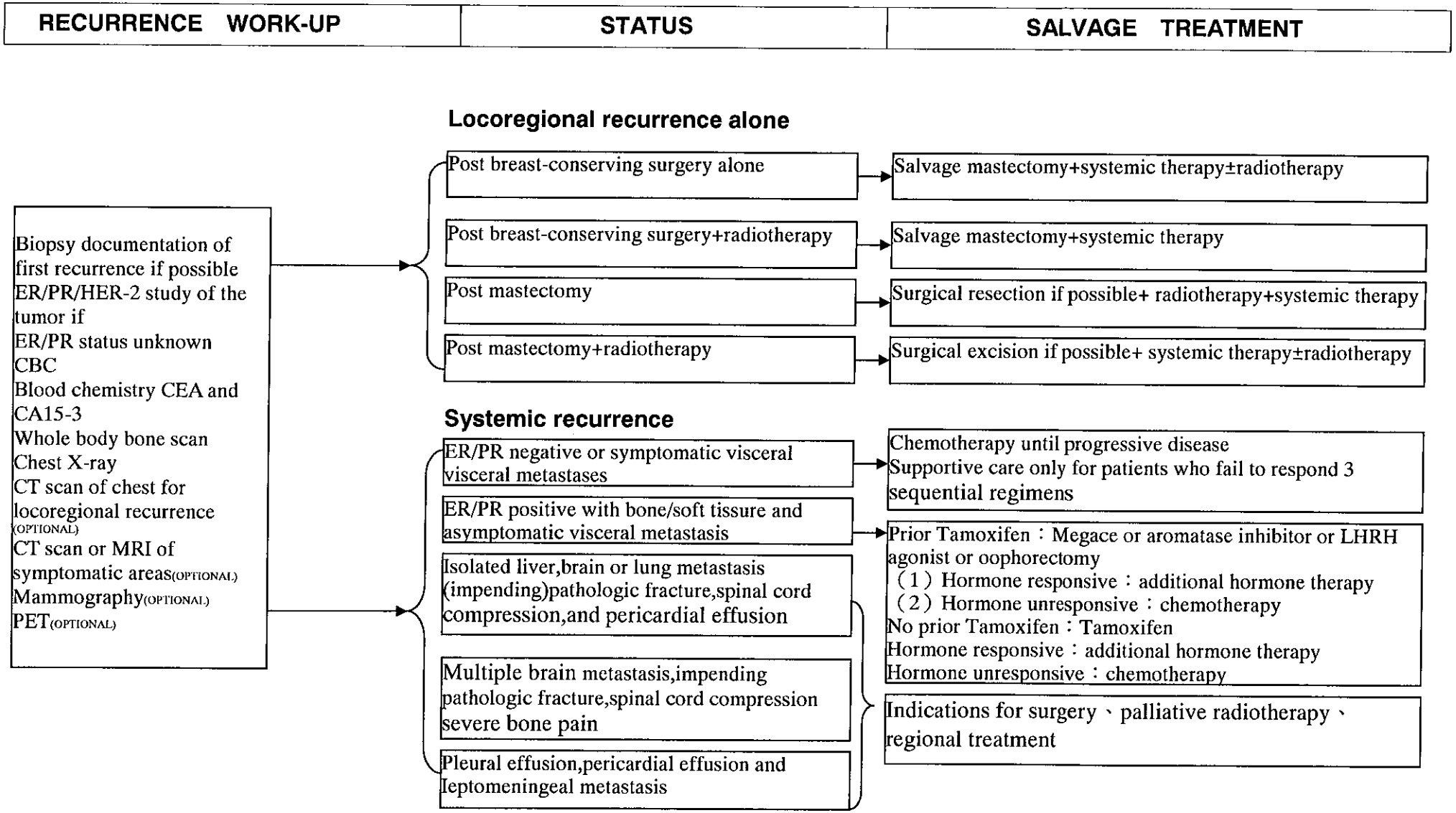
ER and/or PR (+) and Her-2(-) and all of the following features : Gradel ,and pT size≦ 2cm, LVI(-) and age≧ 35
- ✡ Favorable histology :

medullary,mucinous,papillary,tubular carcinoma
- ⊕ Average/high risk :

ER and/or PR (+) and at least one of the following feature : Grade II-III, or pT size > 2cm or age < 35
ER and PR (-), Her2/neu 3+

DIAGNOSIS	WORK-UP	PRIMARY TREATMENT	ADJUVANT THERAPY	FOLLOW-UP




RECURRENCE WORK-UP
STATUS
SALVAGE TREATMENT
Biopsy documentation of first recurrence if possible
ER/PR/HER-2 study of the tumor if
ER/PR status unknown
CBC
Blood chemistry CEA and CA15-3
Whole body bone scan
Chest X-ray
CT scan of chest for locoregional recurrence (OPTIONAL)
CT scan or MRI of symptomatic areas(OPTIONAL)
Mammography(OPTIONAL)
PET(OPTIONAL)
Locoregional recurrence alone
Post breast-conserving surgery alone
Salvage mastectomy+systemic therapy±radiotherapy
Post breast-conserving surgery+radiotherapy
Salvage mastectomy+systemic therapy
Post mastectomy
Surgical resection if possible+ radiotherapy+systemic therapy
Post mastectomy+radiotherapy
Surgical excision if possible+ systemic therapy±radiotherapy
Systemic recurrence
ER/PR negative or symptomatic visceral visceral metastases
Chemotherapy until progressive disease
Supportive care only for patients who fail to respond 3 sequential regimens
ER/PR positive with bone/soft tissure and asymptomatic visceral metastasis
Prior Tamoxifen：Megace or aromatase inhibitor or LHRH agonist or oophorectomy
（1）Hormone responsive：additional hormone therapy
（2）Hormone unresponsive：chemotherapy
No prior Tamoxifen：Tamoxifen
Hormone responsive：additional hormone therapy
Hormone unresponsive：chemotherapy
Isolated liver,brain or lung metastasis (impending)pathologic fracture,spinal cord compression,and pericardial effusion
Multiple brain metastasis,impending pathologic fracture,spinal cord compression severe bone pain
Indications for surgery、palliative radiotherapy、regional treatment
Pleural effusion,pericardial effusion and leptomeningeal metastasis

BASIC REQUIREMENTS OF PATHOLOGY EXAMINATION

Excision biopsy with no prior suspicion for malignancy

•Exact tumor size and type of tumor
•Tumor histological and/or nuclear grade
•Margin status (exact distance in mm)
•Status of lymphovascular permeation
•ER/PR /Her-2 study

Ductal carcinoma in situ with wide excision only

•Nuclear grade
•Status of tumor necrosis
•Tumor size
•Margin status (exact distance in mm)
•ER/PR /Her-2 study

Invasive carcinoma with wide excision and axillary lymph node dissection or modified radical mastectomy

•Exact tumor size and type of tumor
•Tumor histological and/or nuclear grade
•Margin status (exact distance in mm)
•Status of multifocality and multicentricity
•Presence of DCIS present within the invasive tumor
•Presence of DCIS outside the main tumor
•Status of peritumoral LVI (defined as one high power distance from the general contours of the main tumor)
•Number of involved and total axillary lymph nodes with the largest size recorded, total number of axillary nodes examined should not be less than 10.
•If any involvement of skin
•ER/PR /Her-2 study

註解：

NSABP：National Surgical Adjuvant Breast and Bowel Project

TAC：Taxotere +Adriamycin+Cyclophosphamide

LVI：Lymphatic-vascular space invasion

ECS：Extracapsular spread of axillary LNs

Pathologic status of ER,PR and HER-2/new

Pathologic status of ER,PR and HER-2/new

★病理：任何轉移的病灶均要有 ER、PR 及 HER-2 的染色報告
★病理：任何的病灶均要有 ER、PR %

IORT Patient selection criteria (皆符合):

Unicentric only、Clinical size ≤3cm、Negative surgical margin、

pN0 (Sentinel lymph node evaluation or Axillary lymph node dissection)

Principles of radiation therapy:
Indication of breast/chest wall RT：

1.early stage breast cancer s/p BCS；DCIS s/p lumpectomy with moderate risk
- ●Target：breast tissue with/without IMN & SCN
- ●Dose Design：45~50Gy / 25-28 Fxs
- ●boost tumor bed 10-16Gy/5-8Fxs if high risk for recurrence (young age, N+, LVI+, close margin)

2.locally advanced stage s/p neoadjuvant chemotherapy followed by BCS
- ●Target：breast tissue + chest wall & SCN +/- IMN
- ●Dose Design：45~50Gy / 25-28 Fxs then boost tumor bed 10-16Gy/5-8Fxs

3.locally advanced stage (tumor>5cm) or positive surgical lymphnodes(≧4or1-3 #)with patient had 3 risk factor〔nuclear grade 2or3,LVI(+),ECS(+),tumor＞2cm(T2),age＜40y,ER(-)〕
- ●Target：chest wall + SCN + IMN
- ●Dose Design：45~50Gy / 25-28 Fxs then boost tumor bed 10-16Gy/5-8Fxs

Indication of Axillary region RT

1.cN+ without axillary lymph node dissection / sentinel lymph node sampling
- ●Target：Level I, II, III axillary lymph nodes
- ●Dose Design：45~50Gy / 25-28 Fxs

名詞解釋：
- ●**Early stage breast cancer**：Stage I, II
- ●**Locally advanced breast cancer**：Stage III, IV
- ●**DCIS** s/p lumpectomy with moderate risk：New Van Nuys Prognostic Index Scoring System≧7
- ●**DCIS**：Ductal carcinoma in situ
- ●**BCS**：Breast-conservative surgery
- ●**SCN**：supra-clavicular lymph nodes
- ●**IMN**：internal mammary lymph nodes

Neoadjuvant /Adjuvant chemotherapy

AC

Doxorubicin	60 mg/m2 iv	d1
Cyclophosphamide	600 mg/m2 iv	d1
Q3w x 4 cycles		

Muss HB et al. Standard chemotherapy (CMF or AC) versus capecitabine in early-stage breast cancer (BC) patients agec 65 or older: results of CALGB/CTSU 49907. 2008 ASCO annual meeting. Abstract 507 .
Fisher, B et al. Treatment of axillary lymph node-negative, estrogen receptor-negative breast cancer: updated findings from National Surgical Adjuvant Breast and Bowel Project clinical trials. J Natl Cancer Inst 2004; 96:1823 .

EC

Epirubicin	75 - 100 mg/m2 iv	d1
Cyclophosphamide	600 mg/m2 iv	d1
Q3w x 4 cycles		

Piccart MJ et al. Phase III trial comparing two dose levels of epirubicin combined with cyclophosphamide with cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer. J Clin Oncol.2001; 19:3103.

TC

Docetaxel	60 - 100 mg/m2 iv	d1
Cyclophosphamide	600 mg/m2 iv	d1
Q3w x 4 cycles		

Jones SE et al. Phase III trial comparing doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. J Clin Oncol 2006; 24:5381.

CMF po

Cyclophosphamide	100 mg/m2/d po	d1-14
Methotrexate	40 mg/m2 iv	d1, 8
5- FU	600 mg/m2 iv	d1, 8
Q4w x 6 cycles		

Muss HB et al. Standard chemotherapy (CMF or AC) versus capecitabine in early-stage breast cancer (BC) patients agec 65 or older: results of CALGB/CTSU 49907. 2008 ASCO annual meeting. Abstract 507.

CMF iv

Cyclophosphamide	600 mg/m2 iv	d1
Methotrexate	40 mg/m2 iv	d1
5-FU	600 mg/m2 iv	d1
Q3w x 6 cycles		

Weiss RB et al. Adjuvant chemotherapy after conservative surgery plus irradiation versus modified radical mastectomy. Analysis of drug dosing and toxicity. Am J Med 1987; 83:455.

FAC

5-FU	500 mg/m2 iv	d1
Doxorubicin	50 mg/m2 iv	d1
Cyclophosphamide	500 mg/m2 iv	d1
Q3w x 6 cycles		

Martin M et al. Doxorubicin in combination with fluorouracil and cyclophosphamide (i.v. FAC regimen d1, 21) versus methotrexate in combination with fluorouracil and cyclophosphamide (i.v. CMF regimen d1, 21) as adjuvant chemotherapy for operable breast cancer: a study by the GEICAM group. Ann Oncol 2003; 14:833.

FEC

5-FU	500 - 600 mg/m2 iv	d1
Epirubicin	50 - 100 mg/m2 iv	d1
Cyclophosphamide	500 - 600 mg/m2 iv	d1
Q3w x 6 cycles		

Bonneterre J et al. Epirubicin increase long term survival in adjuvant chemotherapy of patients with poor prognosis, node positive, early breast cancer: 10 years follow up results of the French Adjuvant Study Group 05 randomized trial. J Clin Oncol 2005; 23:2686.

AC/EC→Paclitaxel Qw (or Paclitaxel→AC/EC)

Paclitaxel	80 mg/m2 iv	d1
Qw x 12 cycles		

Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.

AC/EC→Docetaxel Q3w (or Docetaxel→AC/EC)

Docetaxel	60-100 mg/m2 iv	d1
Q3w x 4 cycles		

Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.

TAC

Docetaxel	50 - 75 mg/m2 iv	d1
Doxorubicin	50 mg/m2 iv	d1
Cyclophosphamide	500 mg/m2 iv	d1
Q3w x 6 cycles		

Martin M et al. Adjuvant docetaxel for node-positive breast cancer. N Eng J Med 2005; 352:2302 .

TEC

Docetaxel	50-75 mg/m2 iv	d1
Epirubicin	50-75 mg/m2 iv	d1
Cyclophosphamide	500 mg/m2 iv	d1
Q3w x 6 cycles		

P Piedbois et al. Dose-dense adjuvant chemotherapy in node-positive breast cancer: docetaxel followed by epirubicin/cyclophosphamide (T/EC), or the reverse sequence (EC/T), every 2 weeks, versus docetaxel, epirubicin and cyclophosphamide (TEC) every 3 weeks. AERO B03 randomized phase II study. Ann Oncol. 2007; 18: 52.

Adjuvant Targeted therapy

Trastuzumab

Trastuzumab can be given after completion of chemotherapy as well，loading dose 8 mg/kg，followed by 6 mg/kg，iv q3w for a total of 1 year.
Trastuzumab 4 mg/kg loading dose followed by 2 mg/kg iv qw during chemotherapy，then 6 mg/kg iv q3w，for a total of 1 year

Smith I et al. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomized controlled trial. Lancet 2007; 369:29.

Romond EH et al. Trastuzumab plus adjuvant chemotherapy for operable Her2-positive breast cancer. N Eng J Med 2005; 353:1673

Chemotherapy for Metastatic breast cancer

Doxorubicin

Doxorubicin	60-75 mg/m2 iv	d1
Q3w		

or

Doxorubicin	20 mg/m2 iv	d1
Qw		

Chan S et al. Prospective randomized trial of docotaxel versus doxorubicin in patients with metastatic breast cancer. J Clin Oncol 1999;17:2341.
Gasparini G et al. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinial trial. Am J Clin Oncol 1991;14:38.

Epirubicin

Epirubicin	60-90 mg/m2 iv	d1
Q3w		

or

Epirubicin	20 mg/m2 iv	d1
Qw		

Bastholt L et al. Dose-response relationship of epirubicin in the treatment of postmenopausal patients with metastatic breast cancer: a randomized study of epirubicin at four different dose levels performed by the Danish Breast Cancer Cooperative Group. J Clin Oncol 1996;14:1146.
Gasparini G et al. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinial trial. Am J Clin Oncol 1991;14:38.

Liposomal doxorubicin

Liposmal doxorubicin d1	35- 50 mg/m2 iv
Q3-4w	

O'Brien ME et al. Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCL versus conventional doxorubicin for first line treatment of metastatic breast cancer. Ann Oncol 2004;15:440.

Cisplatin

Cisplatin	75 mg/m2 iv	d1
Q3w		

Caboplantin

Caboplantin	6 mg/m2 iv	d1
Q3w		

Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.

Docetaxel

Docetaxel	60-100 mg/m2 iv	d1
Q3w		

or

Docetaxel	25 -40 mg/m2 iv	d1
Qw		

Harvey V et al. Phase III trial of comparing three doses of docetaxel for second-line treatment of advanced breast cancer. J Clin Oncol 2006; 24:4963.

Burstein, HJ et al. Docetaxel administered on a weekly basis for metastatic breast cancer. J Clin Oncol 2000; 18:1212.

Paclitaxel

Paclitaxel	80 mg/m2 iv	d1
Qw		

Bishop, JF et al. Initial paclitaxel improves outcome compared with CMFP combination chemotherapy as front-line therapy in untreated metastatic breast cancer. J Clin Oncol 1999; 17:2355.

Seidman AD et al. Randomized phase III trial of weekly compared with every-3-weeks paclitaxel for metastatic breast cancer, with trastuzumab for all Her-2 overexpressors and random assignment to trastuzumab or not in Her-2 nonoverexpressors: Final results of Cancer and Leukemia Group B Protocol 9840. J Clin Oncol 2008; 26:1642.

Gemcitabine

Gemcitabine	800-1200 mg/m2 iv	d1, 8, 15
Q4w		

Carmichael, J et al. Advanced breast cancer: a phase II trial with gemcitabine. J Clin Oncol 1995; 13:2731.

Vinorelbine

Vinorelbine	20 - 25 mg/m2 iv、50-80 mg/m2 po	d1,8
Q3w		

Gasparini, G et al. Vinorelbine is an active antiproliferative agent in pretreated advanced breast cancer patients: a phase II study. J Clin Oncol 1994; 12:2094.

Capecitabine

Capecitabine	800 - 1250 mg/m2 po bid	d1-14
Q3w		

Fumoleau, P et al. Multicentre, phase II study evaluating capecitabine monotherapy in patients with anthracycline- and taxane-pretreated metastatic breast cancer. Eur J Cancer 2004; 40:536.

AC

Doxorubicin	60 mg/m2 iv	d1
Cyclophosphamide	600 mg/m2 iv	d1
Q3w		

Nabholtz JM et al. Docetaxel and doxorubicin compared with doxorubicin and cyclophosphamide as first-line chemotherapy for metastatic breast cancer: results of a randomized, multicenter, phase III trial. J Clin Oncol 2003;21:968.

EC

Epirubicin	75 mg/m2 iv	d1
Cyclophosphamide	600 mg/m2 iv	d1
Q3w		

Langley RE et al. Phase III trial of epirubicin plus paclitaxel compared with epirubicin plus cyclophosphamide as first-line chemotherapy for metastatic breast cancer: United Kingdom National Cancer Research Institute Trial AB01. J Clin Oncol 2005; 23:8322.

Target therapy for Metastatic breast cancer

Trastuzumab +/- Chemotherapy

Trastuzumab 6mg/kg iv over 90 min first wk followed by 2 mg/kg iv over 30 min q3w

Cobleigh, MA et al. Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease. J Clin Oncol 1999; 17:2639.

Bevacizumab + Chemotherapy

Bevacizumab	10 mg/kg iv	d1
Q2w		

or

Bevacizumab	15 mg/kg iv	d1
Q3w		

Miller KD et al. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. N Eng J Med 2007; 357:2666.
Miles D et al. Randomized, double-blind, placebo-controlled, phase III study of bevacizumab (BV) with docetaxel (D) or docetaxel with placebo (PL) as first-line therapy for patients with locally recurrent or metastatic breast cancer (mBC): AVADO. 2008 ASCO annual meeting. LBA1011.

Lapatinib + Xeloda

Lapatinib	1250mg	
Xeloda	2000mg/m(2)	d1-14

Lancet Oncol 2013 Jan;14(1):64-71.doi:10.1016/S1470-2045(12)70432-1.Epub 2012 Nov.

BEEP

Bevacizumab	15 mg/kg iv	d1
Etoposide	70 mg/m2/d	d2, 3, 4
Cisplatin	70 mg/m2	d2
Q3w		

Lu YS, et al. Bevacizumab preconditioning followed by etoposide and cisplatin (BEEP) is a highly effective treatment for brain metastases of breast cancer progressing from radiotherapy — result of a multi-center phase II study. ECC 2013:1878.

七、安寧緩和照護原則

若預期疾病難以治癒時，病人存活期小於 6 個月便適合安寧療護(Pomeranz & Brustman, 2005；Waldrop & Rinfrette, 2009) 。

若藉由症狀、檢驗數據、及確切的腫瘤診斷，證實臨床上該惡性腫瘤已經廣泛侵犯、或進展快速；功能分數（Palliative Performance Scale）低於 70%；拒絕進一步腫瘤治癒性治療，或者在治療之下仍持續惡化者，即可轉介緩和醫療團隊（彭等，2006）。

十一、參考文獻(Reference)

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3. American Society of Breast Surgeons Guidelines for APBI
4. 2009 Astro Guidelines
5. 2010 ESTRO Guidelines for PBI
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12. Bonneterre J et al. Epirubicin increase long term survival in adjuvant chemotherapy of patients with poor prognosis, node positive, early breast cancer: 10 years follow up results of the French Adjuvant Study Group 05 randomized trial. J Clin Oncol 2005; 23:2686.
13. Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.
14. Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.
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21. Bastholt L et al. Dose-response relationship of epirubicin in the treatment of postmenopausal patients with metastatic breast cancer: a randomized study of epirubicin at four different dose levels performed by the Danish Breast Cancer Cooperative Group. J Clin Oncol 1996;14:1146.
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25. Harvey V et al. Phase III trial of comparing three doses of docetaxel for second-line treatment of advanced breast cancer. J Clin Oncol 2006; 24:4963.
26. Burstein, HJ et al. Docetaxel administered on a weekly basis for metastatic breast cancer. J Clin Oncol 2000; 18:1212.
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28. overexpressors and random assignment to trastuzumab or not in Her-2 nonoverexpressors: Final results of Cancer and Leukemia Group B Protocol 9840. J Clin Oncol 2008; 26:1642.
29. Carmichael, J et al. Advanced breast cancer: a phase II trial with gemcitabine. J Clin Oncol 1995; 13:2731.
30. Gasparini, G et al. Vinorelbine is an active antiproliferative agent in pretreated advanced breast cancer patients: a phase II study. J Clin Oncol 1994; 12:2094.
31. Fumoleau, P et al. Multicentre, phase II study evaluating capecitabine monotherapy in patients with anthracycline- and taxane-pretreated metastatic breast cancer. Eur J Cancer 2004; 40:536.
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35. Miller KD et al. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. N Eng J Med 2007; 357:2666.
36. Miles D et al. Randomized, double-blind, placebo-controlled, phase III study of bevacizumab (BV) with docetaxel (D) or docetaxel with placebo (PL) as first-line therapy for patients with locally recurrent or metastatic breast cancer (mBC): AVADO. 2008 ASCO annual meeting. LBA1011.
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