Outline 大綱

• Introduction to Radiation Oncology
  • 放射腫瘤學概論
• Use of Radiation Therapy in Breast Cancer
  • 使用放射治療乳腺癌
• Breast Cancer Trials
  • 乳腺癌試驗
Introduction to Radiation Oncology
放射腫瘤學概論
U.S. Cancer Statistics

美国癌症统计

• 140万新病例的侵袭性癌症/年
• 900,000 nonmelanomatous皮膚癌
• 70%的病人的癌症部位得以确诊, 30% 癌症转移
• 60%患有侵襲性癌接受 X射線治療

» American Cancer Society
• 10 Leading Sites, 按性别，美国

- 前列腺 • 33%
- Lung & bronchus • 14%
- Colon & rectum • 11%
- Urinary bladder • 6%
- Melanoma of skin • 4%
- Non-Hodgkin’s lymphoma • 4%
- Kidney • 3%
- Oral cavity • 3%
- Leukemia • 3%
- Pancreas • 2%
- All other sites • 17%

- 32% 乳腺癌
- 12% Lung & bronchus
- 11% Colon & rectum
- 6% Uterine corpus
- 4% Ovary
- 4% Non-Hodgkin’s lymphoma
- 3% Melanoma of skin
- 3% Thyroid
- 2% Pancreas
- 2% Urinary bladder
- 20% All other sites

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
<table>
<thead>
<tr>
<th>癌症类型</th>
<th>男</th>
<th>女</th>
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<tr>
<td>所有癌症</td>
<td>43% (1 in 2)</td>
<td>38% (1 in 3)</td>
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<tr>
<td>乳腺癌</td>
<td>13% (1 in 8)</td>
<td>13% (1 in 8)</td>
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<tr>
<td>前列腺癌</td>
<td>17% (1 in 6)</td>
<td>17% (1 in 6)</td>
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<tr>
<td>結腸 / 直腸癌</td>
<td>5.9% (1 in 17)</td>
<td>5.6% (1 in 18)</td>
</tr>
</tbody>
</table>
腫瘤學學科

• 外科手術
  – General, Specialist
• 醫學腫瘤科
• 放射腫瘤學
• 放射診斷科
• 病理學
治療方案

• 局部治療
• 手術
  – 放射治療
• 全身治療
• 化療
  – 激素治療
什麼是放射治療?

- 其中一個主要的治療方法，在癌症治療（治療）
- 臨床學科的科學和人類醫學
  - 解決治療和預防癌症
  - 單獨利用電離輻射或與其他治療方法
電離輻射損傷

• 作用在分子水平上
• 損害癌症的 DNA
• 通過直接與 DNA 電離
  - 間接通過形成自由基（電離水）
  - 損害: 通過單鍊 DNA 斷裂，雙鍊斷裂，基礎傷害，DNA - 蛋白質交聯或組合
• Use high energy X-rays (typically to treat cancers and non-malignant diseases)
• 使用高能量X射線（通常是治療癌症和非惡性疾病）
放疗的歷史

- X射線轟擊表面在真空產生的高速電子
- 1896, X光機正式展出由H.史密斯
- 娛樂行業的接管，馬戲團顧客支付查看自己的骨骼和雙手戴首飾
放疗的歷史

- 1899, 1st 放射治療, 在此之前只有手術治療癌症
- 到19世紀結束，放射治療用於痣，痤瘡，紅斑狼瘡，濕疹，乳房胸部復發
- 由early1900s，更多的惡性淋巴瘤的治療，其中包括食道癌
放疗的歷史

- 1896年 2例乳腺癌治療在芝加哥
- 1896年 4yr old treated with RT for cancer in Vienna and followed for 70 years
- 1903 第一成功治療利用鐳放射治療記錄在聖彼得堡
- 1922 年，放射腫瘤學形成
- 20世紀初 上半場，工程接管，以提供更高穿透 X射線
放射治療進展

• 20世紀 40年代之前，主要是治療的患者
  千伏 X光機或放射源，有限的滲透性，重要
  的皮膚反應

• X光機，可以產生光束為 1MV 被稱為兆
  伏級機
生存曲線的作用劑量

• 生存曲線
Therefore...

- In order to kill cancers deep in the body, a larger amount of dose would need to be distributed to the outer, more superficial structures
- I.E. Prostate cancer
放射治療適應症

• 通用和姑息治療 Definitive and palliative treatment

• 優勢
  - organ conservation (breast, prostate, bladder)
  - less invasive
  - outpatient
  - decrease surgical morbidities
  - non-surgical candidates
• 缺點
  – 漫長的治療過程
  – 輻射關聯 morbitidies
  – 交通運輸
  – contraindications
  – given only once a one site
放射腫瘤學目標

• 提供精確劑量
• 消除腫瘤的同時最大限度地減少損害正常結構
• 幫助維持較高的生活質量，通過保存器官功能和解剖的完整性
治療序列

• 術前 減少腫瘤負荷
  – sterilize surgical fields/ nodes
  – 轉換不可操作的可操作性腫瘤
  – 保留功能（直腸）
与手術並行
  - 腫瘤有争议的边界区
  – 增加劑量，同時盡量減少發病率
• 術後
  – 侵害性病理結果
  – 降低復發率
  – 腫瘤有争议的边界区
• 單独使用通用放射治療
• 同步化療
  – 器官 sparing
  – aggressive tumors
放射治療類型

• Teletherapy 遠距離治療
• Brachytherapy 近距離治療
  – Prostate 前列腺
  – breast
  – Sarcoma 肉瘤
  – Cardiac 心臟

• 有針對性的治療
  – 放射免疫療法
  – 放射性同位素
Treatments

• 周一到周五 5-20 分钟
• 5-7 周
• Imaging of port films taken regularly
• Weekly MD visit for skin reaction
• Electrons/ high energy x-rays
Use of Radiation Therapy in Breast Cancer

使用放射治療乳腺癌
Anatomy 解剖

• 乳腺位於
  - 對胸大肌
    - 範圍從2至第6肋骨
    - 從胸骨到腋窩
• 由脂肪，管道，肺葉分為小葉，纖維組織緻密
• 乳房組織表面上是籠罩在胸鰭淺筋膜和深刻的胸深筋膜，
• 在更年期，纖維組織較軟
Anatomy

• 淋巴管
  – drain to 腋窩淋巴結之間的第二和第三肋間
    通過胸大肌的鎖骨上窩
  – 通過乳房內部肋間和胸大肌，接近胸骨
流行病學

- 在西方主要國家的問題
- 每年20萬例的案件
- 45,000 每年 死亡率
- 一生中 1 / 8 概率
- #1 nonskin癌症 in 美國
- #2 營症有關的死亡在美國
- 32％的女性癌症
- 19％的癌症死亡婦女
- Leading cancer related death is US among women 2-59 yrs of age
風險

- 年齡
- 家族史 (1st degree relatives)
- Self history (breast, Hodgkin’s Disease)
- BRCA1 or 2 genotype
- 未產婦
- 月經初潮早 / 晚絕經
- 生第一兒童在 30 后
- 飲食，激素，環境
- 75% 的患者無危險因素
- ADH/LCIS, 9x risk
有家族史的风险 > 4

- Age
- 出生地點（北美或北歐）
- 絕經前血胰島素樣生長因子（IGF）-1水平升高
- 絕經後血液中雌激素水平升高
- 母親和一個姐妹有乳腺癌歷史
相關的因素，相對風險 2-4

- High socioeconomic status
- 年齡在第一足月妊娠 >30 years
- 一個乳房癌歷史
- 任何直系親屬的乳腺癌史
- 良性增生性病變，乳腺增生的變化，以及高劑量的電離輻射到胸部的歷史
有關因素相對風險 1.1-1.9

- Nulliparity
- 月經初潮早 (age <11 y)
- 絕經期晚 (age >55 y)
- 絕經後肥胖
- 高脂肪的飲食 / 飽和脂肪豐富的飲食
- 居住在城市地區，美國北部
- 白色人種 - > than 45 years
- 黑色人種 - < than 45 years
- 子宮內膜或卵巢癌歷史
Identified factors with a protective role against breast cancer 確定的因素有保護作用，防止乳腺癌

- 初潮年齡 > 15 years
- 母乳喂養時間超過 1年
- 不飽和脂肪酸豐富的飲食
- 體力活動
- 絕經前肥胖？
Benefits to Screening

- 每年乳房X線照片檢查
- Older studies (Health Insurance Plan New York (1963-1968)/Swedish Study (began 1977) show 30% decrease in mortality in five years, greatest benefit in women over 50
- National Breast Cancer Screening Study of Canada (1980-1985), no evidence mammograms of benefit for women 40-49yrs (1st 7 years) controversial, design criticized
Breast Cancer Detection Project
乳腺癌檢測

- 1972-1981
- Mammogram and physical exam
- 40% cancers detected mammograms alone
- 10% by PE alone (not seen on mammograms)
- 50% detected by both
- 显然是有很大的改善成像技術在過去二十年
Detection 乳腺癌檢測

- Not all seen or felt
- Many diagnosed while small in breast
- Believed screening mammograms translated to 25% improvement in breast cancer mortality rate

Recommendations:
- 每月的自我檢查 (access for changes, 80% felt on self exam are benign)
- 年度體檢
- 年度乳房 X 光照片後，40 歲
- Baseline (35-40) or depending on FH
Clinical Findings

• Many are detected now through screening
• Some still present with symptoms

• 悪性
  - Hard
  - Irregular
  - Painless
  - Bloody discharge
  - Fixed
  - Skin dimpling
  - Nipple Retraction

• Benign
  - Firm rubbery
  - Regular
  - Painful
  - No bloody discharge
  - Not fixed
  - No dimpling
  - No retraction
Histology

- 乳腺癌的類型

- 80%的入侵，20%的原位

- 源於線槽（多數）或葉

- 浸潤性導管，乳腺導管內（原位癌），
  侵襲性小葉，原位小葉很少炎症 invasive ductal, in situ ductal (DCIS), invasive lobular, in situ lobular (LCIS)
  - rarely inflammatory
Treatment Options 治療方案

- 大多數婦女今天有幾種治療選擇，but depends on Stage
- 治療是局部和全身
  - local is addressing the breast itself (surgery, radiation)
  - systemic is addressing entire body (chemotherapy, hormones)
Local Treatment 局部治療

- 兩個主要的選擇對大多數婦女
- Equivalent survival 等效生存率
- 乳房切除或腫塊切除術與輻射 (Breast Conservation Therapy)
- 大小，類型和位置影響選擇
Consultations

- Surgeon 外科醫生
- Medical Oncologist
- Radiation Oncologist 放射腫瘤學家
- Radiologist
- Pathologist
乳房切除 Vs. BCT

- Factors to consider:
- 個人選擇
- Cosmesis
- Convenience
- Co-Morbidities
- Complications from each
- 有時輻射乳房切除後無論如何是需要
Lymph Node Sampling

- Standard for invasive disease
- 乳腺癌腋窩淋巴結是主要排瀉
- 傳統上，腋窩淋巴結採樣
- 前哨淋巴結活檢 (most women)
  - unless large lymph nodes under arm
  - large tumor
  - poor features
Prognostic Features

- Lymph node status (size, number, extracapsular involvement)
- Imaging studies if needed (CT scans, Bone scans, CXR)
- Tumor size
- Tumor grade
- Hormonal status
- Extent of Spread
Breast Conservation Therapy
保乳治療

• Lumpectomy with clean margins
• treats typically 整個乳房
• 大約 4週後手術或化療後
• M-F 5-7 weeks
• better cosmetic result
• 類似的生存率=乳房切除術
Early Breast Trials 早期乳腺癌試驗

• Mainly involved “more conservation” surgery (lumpectomy, quadrantectomy, simple mastectomy, with lymph node dissection) Vs. radical mastectomy and modified radical mastectomy

• Major International Studies
  – Milan Trial, NSABP-04/06, NCI, Institut Gustave-Roussy, EORTC, Danish Trial
Milan Trial *

- Prospective randomized trial, 701 women
- 2 arms
  - quadrantectomy with axillary lymph node dissection plus XRT (50 Gy breast plus 10 Gy boost to tumor bed)
  - Vs. radical mastectomy
  - all women with +LNs underwent 12 cycles CMF chemotherapy

*Veronesi, U. NEJM 1981;305:6-11
## Milan - Results

<table>
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<tr>
<th>@ 8yrs</th>
<th>OS</th>
<th>DFS</th>
<th>LF</th>
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<tbody>
<tr>
<td>BCT</td>
<td>83%</td>
<td>77%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Radical Mastectomy</td>
<td>85%</td>
<td>80%</td>
<td>2.3%</td>
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</table>
NSABP-06

- 1581 pts 1976-84, Stages I-II
- < 4cm tumor, 62% LN-, 26% 1-3 nodes, 12% 4+ nodes, ER available data in 75% women (64%+), + surgical margins 10% with lumpectomy
- All with ALND
- RT 50Gy no boost
- LN+ melphalan + 5FU
- Total mastectomy vs lumpectomy vs lumpectomy +RT
NSABP-06 Results

- At 12 years, no difference in survival in 3 arms, but meta-analysis of large trials show survival benefit with XRT Vs. Lumpectomy alone
- However, 40% local recurrence in lumpectomy alone arm
- LR with XRT 5-10% (LN+ at 5%, received chemo also)
20 year update

• NEJM 2002, Oct 17;347(16):1233-41
• 73%, 复发 15 年之内，18% 在5至10年，8%，10年後
• No difference in OS survival in 3 groups at 20 years
• Unpublished, node – subgroup with survival advantage
Without RT for older women

- Intergroup (CALGB 9343, RTOG 97-02, ECOG) 2004 (94-99)
  - NEJM 2204; Sept 2; 35(10): 971-7
  - 70 years or older, T1N0, ER+
  - 636 pts randomized tamoxifen +/- RT
  - 5 yr LRF 4% vs 1% favoring RT
  - No diff 5yr OS (87%/86%)
• Princess Margaret Study 1992-2000
• 50 yrs + (ave 68yrs)
• NEJM 2004 Sept 2;351(10):963-70
• 5 yr LR 7.7% vs 0.6%, DFS 84% vs 91%
• No diff DM or OS
Tumor Boost Trials

- EORTC 22881/10882 (1989-96)
- NEJM 2001 Nov9;345(19):1378-87
- Stage I-II
- 50Gy/25 Fx +/- 16Gy boost
- Boost was lumpectomy plus 1.5cm
- 5yr LR 4.3% vs 7.3% (40% reduction)
- Most benefit younger pts (10.2% vs. 19.5%)
- No diff OS
Breast RT on Survival

- Early Breast Cancer Trialists’ Collaborative Group
- Lancet 2000 May 20;335(9217):1757-70
- Meta-Analysis of 40 trials
- 10 and 20 year results looking at cause specific mortality (1/2 were LN+)
- RT associated with 2/3 reduction in LR (8.8% vs 27.2% at 10 years)
- Breast Cancer Mortality Reduced but increase other mortality (cardiac)
- Criticism: older RT techniques
• Van de Steene 2000
• “Adjuvant radiotherapy for breast cancer significantly improves overall survival: the missing link.”
• Radiother Oncol 2000 June;55(3):263-72
• Analysis of Early Breast Cancer Trialists’ Collaborative Group study showed survival benefit (12% reduction) for recent trials using standard fractionation.
Contraindications to Breast Preservation
禁忌保乳治療

• Absolute contraindications to lumpectomy/RT
  – Pregnancy 妊娠
  – 已放疗过乳房
  – 兩個或兩個以上的癌症總灶在不同的象限同乳腺癌
  – X線結果暗示暗示瀰漫地區惡性腫瘤
  – Failure to obtain negative margins despite several surgical attempts
Relative contraindications to lumpectomy/RT

- Tumors larger than 5 cm
- Very small breasts
- Collagen Vascular Disease
- Extensive DCIS
辐射对局部晚期乳腺癌

- T3/T4
- postop, usually follows chemo
- chest wall XRT plus LN XRT
- Studies shown LC and OS benefit
  - Ragaz (BC 318pts, Stages I-II, +LN, 17% benefit DFS premenopausal),
  - Fowble (identified risk factors for LR)
Indications postoperative XRT

- Diffuse multifocal disease
- T3/T4
- close or positive surgical margins
- positive LN, premenopausal
- >4 LNs all pts, extracapsular extension of LN, >2cm +LN, pectoral fascial involvement (Fowble’s data from ECOG studies showed >7 LNs less benefit from XRT secondary to DM)
Danish Breast Cancer Cooperative Group*

- 1708 pts
- s/p mastectomy for pathological stage II-III
- prospectively randomized
  - 8 cycles CMF plus chest wall and LN XRT
  - Vs. cycles CMF
- median F/U 114 months

*Overgaard, M. NEJM 1997;337:949-955
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<tr>
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<th>LR +/- DM</th>
<th>OS</th>
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<tr>
<td>CMF alone</td>
<td>32%</td>
<td>45%</td>
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<tr>
<td>p&lt;0.001</td>
<td></td>
<td></td>
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<tr>
<td>CMF + XRT</td>
<td>9%</td>
<td>54%</td>
</tr>
<tr>
<td>p&lt;0.001</td>
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Danish Study- Results
Canadian Adjuvant RT Trial

- 318 pts, node +, premenopausal women
- Mastectomy >> CMF (cyclo 600mg/m², metho 40mg/m², 5FU 600mg/m² IV q 21 days)
- RT 37.50 Gy chest wall and lymphatics
- 15 yrs, reduce LR 33%, reduce breast cancer mortality 29%
- DFS 60% RT, 44% no RT
- OS 68% RT, 58% no RT
Systemic Treatment 全身治療

• 化療
• Hormones 激素
• 取決於幾個因素
  – 淋巴結狀態
  – 絕經狀態
  – 激素受體狀態
  – 病人情況
  – 其他的病理特徵
Sequence of Treatment 治療序列

- Surgery > Chemotherapy > XRT > Hormones
- Surgery > XRT > Hormones
- Surgery > XRT
- Surgery (Mastectomy, good prognostic features)
- Surgery > Systemic Treatment
- Neoadjuvant Chemo > Surgery > XRT
Sequencing Chemo and RT

- Joint Center Trial
- NEJM ’96 May 23
- 244 pts Stages I-II
- High risk, +LN or –ER, +lymph vasc
- Chemo>>RT or RT>>Chemo
- Chemo 4 cycles (12 weeks)
  metho, leucovorin, cyclo, pred, doxo
## 5 yr 精算結果

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<tr>
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<th>Recurrence any site</th>
<th>DM</th>
<th>OS</th>
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<tr>
<td>RT first</td>
<td>38%</td>
<td>36%</td>
<td>73%</td>
</tr>
<tr>
<td>Chemo first</td>
<td>31%</td>
<td>25%</td>
<td>81%</td>
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## 5 yr. crude 1\(^{st}\) recurrence

<table>
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<th>LR</th>
<th>DM</th>
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<tr>
<td>RT first</td>
<td>5</td>
<td>32</td>
</tr>
<tr>
<td>Chemo first</td>
<td>14</td>
<td>20</td>
</tr>
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</table>
Conclusions 結論

• 低風險的病人 可以放射治療的第一
• 高危患者應得先化療
• If RT starts within 50 days of surgery, LR 2%, if longer LR 6%
• HOWEVER, updated data JCO 2005 ;23(9):1934-40 shows no difference in time to any event, metastases or death
NSABP-17*

• BCT is also an alternative for patients with DCIS
• In situ studies have also shown no difference in survival between BCT and mastectomy
• NSABP 17, 391 pts
• 2 arms, lumpectomy alone Vs. lumpectomy+XRT

* Fisher, B. NEJM 1993;328:1581-1586
**NSABP 17 Results**

<table>
<thead>
<tr>
<th></th>
<th>Noninvasive IBT</th>
<th>Invasive IBT</th>
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<tbody>
<tr>
<td>Lumpectomy alone</td>
<td>13.4%</td>
<td>13.4%</td>
</tr>
<tr>
<td>With XRT (50Gy)</td>
<td>8.2%</td>
<td>3.9%</td>
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</tbody>
</table>
Current DCIS Studies

- **NSABP 21**
  - occult disease <1cm
  - BCT + Tam, BCT + placebo, lumpectomy alone
  - involves Tamoxifen in 2 arms (as large NSABP 24 DCIS study, 1804 pts, showed positive benefit with Tamoxifen after BCT, decrease 13.4% to 8.2% IBT, 3.4% to 2% contralateral at 5yrs).
Van Nuys Prognostic Index

- GENERAL guidelines to help determine patients who are candidates for breast preservation and whether they need adjuvant RT

- **Four** significant predictors of local recurrence: overall tumor size [largest single-direction size measure], closest clear surgical margin width [thinnest width], pathologic nuclear grade classification, and patient age. Scores of 1 (best) to 3 (worst) are assigned for each of the 4 predictor parameters and then summed/totaled to give an overall VNPI score ranging from 4 to 12.
General Guidelines

- **Age**
  - 61 or older…1pt
  - 40-60…2pts
  - <40…3pts

- **Surgical Margin**
  - 1cm or more…1pt
  - 1mm-9mm…2pts
  - <1mm…3pts

- **Grade**
  - Nuclear grade 1,2,3

- **Size**
  - 1.5mm or less… 1 pt
  - 1.6-4mm… 2pts
  - 4.1mm or greater… 3pts
Breast Brachytherapy
乳腺癌近距放射治療

• Criteria 標準
  – 階段 0, I, II <3cm
  – DCIS or invasive adeno 原位癌或腺病毒入侵
  – Clear margins 邊緣清晰
  – No multicentric disease 沒有多中心
  – 3 or less nodes per NSABP39
  – No extracapsular nodal extension even microscopic
  – No paget’s
Breast Brachytherapy

• Rationale 理由:
  – Only 10-40% pts who are candidates for BCT receive it across country
  – Transportation/time issues
  – 大多数在乳房肿瘤切除术腔复发 Veronesi et al *. 20 yr 在同侧乳腺出腔一样对侧乳房发生，类似的调查结果 in Yale group**
  – 避免副作用外照射

Data

• Many mature phase I-II trials, 5 yr data with LC comparable to WBI

• Interstitial Data-
  – Vicini ’93 pilot trial LDR brachytherapy, 120 pts enrolled by ’01 5 yr f/u, median 82 months, 0.9% recurrence
  – Second trial with HDR 70 pts, combined data * 5yr actuarial recurrence 1.2%

• Mammosite- user friendly catheter
  – Over 2000 cases now
  – Preliminary single institution evaluation –good cosmesis and LC

## APBI > 5 Yr Follow up

<table>
<thead>
<tr>
<th>Institution</th>
<th># Cases</th>
<th>Median F/U (mo)</th>
<th>5-Yr Actuarial Recurrence Rate Total (%)</th>
<th>5-Yr Elsewhere Failure Rate (%)</th>
<th>Cosmesis Good/Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBH</td>
<td>199</td>
<td>96</td>
<td>1.6</td>
<td>0.8</td>
<td>92</td>
</tr>
<tr>
<td>120/HDR 79 LDR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tufts/Brown U</td>
<td>33</td>
<td>82</td>
<td>9</td>
<td>9</td>
<td>88</td>
</tr>
<tr>
<td>RTOG 95-17 HDR</td>
<td>99</td>
<td></td>
<td>4</td>
<td>2</td>
<td>--</td>
</tr>
<tr>
<td>HDR</td>
<td>66</td>
<td>78</td>
<td>3</td>
<td>2</td>
<td>--</td>
</tr>
<tr>
<td>LDR</td>
<td>34</td>
<td>85</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIO, Hungary Phase I/II Trial</td>
<td>45</td>
<td>80</td>
<td>6.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>84</td>
</tr>
<tr>
<td>NIO, Hungary Phase III Trial</td>
<td>127</td>
<td>66</td>
<td>4.7</td>
<td>3.1</td>
<td>81</td>
</tr>
<tr>
<td>Ochsner Clinic</td>
<td>164</td>
<td>65</td>
<td>3</td>
<td>0</td>
<td>75</td>
</tr>
<tr>
<td>TOTAL</td>
<td>667</td>
<td>65-96</td>
<td>maj. &lt;5</td>
<td>maj. &lt;5</td>
<td>maj. &gt;80</td>
</tr>
</tbody>
</table>
NSABP 39 Trial

- Title: A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I, or II Breast Cancer
- Anticipated 4300 women enrolled by 2011.
- Currently >3000 women enrolled
<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard Treatment</strong></td>
<td><strong>Test Treatment</strong></td>
</tr>
<tr>
<td>Whole Breast Irradiation (WBI)</td>
<td>Partial Breast Irradiation (PBI)</td>
</tr>
<tr>
<td>Chemotherapy, if needed</td>
<td>Multi-catheter Brachytherapy</td>
</tr>
<tr>
<td><em>Followed by</em></td>
<td><em>or</em></td>
</tr>
<tr>
<td>Whole Breast Irradiation</td>
<td>MammoSite® Balloon Catheter</td>
</tr>
<tr>
<td><em>(1 treatment a day, 5 days a week for</em></td>
<td><em>or</em></td>
</tr>
<tr>
<td>5-7 weeks)*</td>
<td>3-D Conformal External Beam Irradiation</td>
</tr>
</tbody>
</table>

Hormonal therapy (only if your tumor has a positive hormone receptor test) will be chosen by your doctor and will continue for at least 5 years. The timing for when the hormonal therapy will begin depends on whether or not you will receive chemotherapy.
Daily Treatments

- Mon-Fri
- approximately 7 weeks
- 1.8-2 Gy/fraction to 50.4 total dose plus boost
- 5-10 min a day
- painless
Hypofractionated

- Canadian/UK trials
- Fewer treatments
- More Convenience
- Side effects/Cure?
- Cosmesis?
Randomized Trial of Breast Irradiation Schedules After Lumpectomy for Women With Lymph Node-Negative Breast Cancer

- Results initially with median follow-up of 69 months (JNCI 2002;94:1143-50)
  - 1234 pts, T1-2 N0 disease, lumpectomy with negative margins, 2 arm randomization
  - 622 received 42.5 Gy in 16 fractions and 612 received 50 Gy in 25 fractions
  - Primary endpoint local recurrence
  - Secondary endpoints were distant recurrence, cosmesis, and late radiation toxicity
Randomized Trial of Breast Irradiation Schedules After Lumpectomy for Women With Lymph Node-Negative Breast Cancer

<table>
<thead>
<tr>
<th>Variable</th>
<th>Short arm</th>
<th></th>
<th>Long arm</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>5-y local recurrence rate, %</td>
<td>No. of patients</td>
<td>5-y local recurrence rate, %</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;50 y</td>
<td>157</td>
<td>3.6</td>
<td>148</td>
<td>7.2</td>
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<tr>
<td>50–59 y</td>
<td>186</td>
<td>2.9</td>
<td>155</td>
<td>2.6</td>
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<tr>
<td>60–69 y</td>
<td>181</td>
<td>3.1</td>
<td>200</td>
<td>1.0</td>
</tr>
<tr>
<td>≥70 y</td>
<td>98</td>
<td>1.0</td>
<td>109</td>
<td>2.9</td>
</tr>
<tr>
<td>Tumor size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1 cm</td>
<td>183</td>
<td>1.7</td>
<td>192</td>
<td>1.6</td>
</tr>
<tr>
<td>&gt;1–2 cm</td>
<td>317</td>
<td>2.1</td>
<td>302</td>
<td>3.5</td>
</tr>
<tr>
<td>&gt;2 cm</td>
<td>122</td>
<td>6.4</td>
<td>118</td>
<td>5.4</td>
</tr>
<tr>
<td>Systemic therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>298</td>
<td>3.0</td>
<td>295</td>
<td>3.9</td>
</tr>
<tr>
<td>Yes</td>
<td>324</td>
<td>2.6</td>
<td>317</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Local in-breast recurrence data from original study with 5 year follow-up
Long-term Results of a Randomized Trial of Accelerated Hypofractionated Whole Breast Irradiation Following Breast Conserving Surgery in Women with Node-Negative Breast Cancer

- Median follow-up now 144 months
- Local Recurrence at 10 years
  - 6.2% (hypofrac)
  - 6.7% (standard frac)
- Cosmesis at 10 years (EORTC Rating System)
  - 70% excellent (hypofrac)
  - 71% excellent (standard frac)
- Late mod-severe skin/sub-Q toxicity at 10 years
  - 6% skin & 8% sub-Q (hypofrac)
  - 3% skin & 4% sub-Q (standard frac)
Side Effects 副作用

• Localized 局部
  – Skin 皮膚
  – Fatigue 疲勞
  – Pneumonitis 肺炎
  – secondary ca
  – arm edema 手臂水腫
  – Ribs 肋骨
  – Heart 心臟
  – Cosmesis 美容外观
Treatment Management 治療管理

- Weekly visits 每週訪問
- Antioxidants 抗氧化劑
- skin care 皮膚護理
  - Shaving 剃須
  - Deodorants 除臭劑
  - moisturizers/soaps
  - Chlorine
Survival 存活率

- 依賴於癌症 階段 /治療（全身）
  - Stage 0 (DCIS) 97-100%
  - Stage I- approx 80%-85%
  - Stages II-IV
    - depends on LN status, extent of spread, systemic treatment
• 常見的問題有許多相關的風險
• Advancements in treatment less 2 decades
  – More conservation surgery (lumpectomy, sentinel node)
  – Radiation therapy greater role (BCT, Brachytherapy)
• 病人的選擇，需要充分了解
• Curable 可治愈的