Panel Discussion 1: Apr. 20. Lotus Hall
Elderly Breast Cancer

Local Therapy

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- Introduction
- Geriatric Surgical Oncology
- Practice Guidelines of Local Therapy
- Breast Surgery
- Management of the Axilla
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- Conclusions

Born in 1931 (86 year-old)
Carmen Dell'Orefice
(the world's oldest working model)
Definition of the ‘older’ or ‘elderly’ person

- **WHO website** (http://www.who.int/healthinfo/survey/ageingdefnolder/en/)
  - Most developed world countries: chronological age of **65 years** as a definition of 'elderly' or ‘older’ person.
  - The United Nations: cutoff is **60+ years** to refer to the older population.

- **NCCN Task Force Report** (JNCCN 2008;6[suppl 4]:S1-S25)
  - Some members: ‘**≥ 70 years**’ be used to define “older” patients.
  - **Little or no data** exist to make evidence-based decisions because this population is dramatically under-represented in breast cancer clinical trials.
  - Therefore, **expert-driven consensus** is recommended for this population.
Life Expectancy at age 65 years old

- The average number of years: a person at certain age can be expected to live, assuming that age-specific mortality levels remain constant.

- The actual age-specific death rate of any particular birth cohort cannot be known in advance.

- If death rates are falling, actual life spans will be higher than life expectancy calculated using current death rates.

- The methodology used to calculate life expectancy can vary slightly between countries.

Older Adult Oncology

**Upper, Middle, and Lower Quartiles of Life Expectancy for Women and Men at Selected Ages**

- **Life Expectancy for Women**
  - Top 25th Percentile
  - 50th Percentile
  - Lowest 25th Percentile

**Years**
- 70: 22.0, -24.1%
- 75: 16.6, -24.1%
- 80: 12.6, -27.8%
- 85: 9.1, -31.9%
- 90: 6.8, -35.0%
- 95: 4.6, -35.0%

**Data from the Life Tables of the United States 2008.**
See the life expectancy tables in the National Vital Statistics Reports at [http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_03.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_03.pdf)
Future Life Expectancy: projections with a Bayesian model ensemble

Women at birth in 2030.

Clinical Questions of Geriatric Oncology

• **Basic questions** are…
  ✓ Is the patient going to **die with cancer or of cancer**?
  ✓ Is the patient going to **experience the consequence of cancer** during his or her lifetime?
  ✓ Is the patient able to **tolerate cancer treatment**?
  ✓ What are the **long-term consequences of cancer and cancer treatment** in older aged persons?

• **Chronologic age** is a weak surrogate for patient function and comorbidities.
  • In addition, **the social consequences** include the health of the home caregiver and the economic implications of caring for an aging patient.
# Comprehensive Geriatric Assessment and Clinical Implications

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Clinical Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FUNCTIONAL STATUS</strong></td>
<td></td>
</tr>
<tr>
<td>Activities of daily living and instrumental activities</td>
<td>Relation to life expectancy, functional dependence, and tolerance of stress</td>
</tr>
<tr>
<td><strong>COMORBIDITY</strong></td>
<td></td>
</tr>
<tr>
<td>No. of comorbid conditions and comorbidity indices</td>
<td>Relation to life expectancy and tolerance of stress</td>
</tr>
<tr>
<td><strong>MENTAL STATUS</strong></td>
<td></td>
</tr>
<tr>
<td>Folstein Mini-Mental Status Examination</td>
<td>Relation to life expectancy and functional dependence</td>
</tr>
<tr>
<td><strong>EMOTIONAL CONDITION</strong></td>
<td></td>
</tr>
<tr>
<td>Geriatric Depression Scale</td>
<td>Relation to life expectancy may indicate motivation to receive treatment</td>
</tr>
<tr>
<td><strong>NUTRITIONAL STATUS</strong></td>
<td></td>
</tr>
<tr>
<td>Mini Nutritional Assessment</td>
<td>Reversible condition; possible relationship to survival</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>Risk of drug interactions</td>
</tr>
<tr>
<td><strong>GERIATRIC SYNDROMES</strong></td>
<td></td>
</tr>
<tr>
<td>Delirium, dementia, depression, falls, incontinence, spontaneous bone fractures, neglect and abuse, failure to thrive, vertigo</td>
<td>Relation to survival and functional dependence</td>
</tr>
</tbody>
</table>
## Physiologic Decline with Aging

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Major Physiologic Changes</th>
</tr>
</thead>
</table>
| Cardiovascular | - **Decreased** number of myocytes, ventricular and arterial compliance, and β-adrenergic responsiveness  
- Fibrosis of conducting pathways with increased arrhythmias  
- Increased dependence on preload (including atrial kick), diastolic dysfunction, and silent ischemia                                                                                                                                                                      |
| Respiratory    | - **Decreased** chest wall compliance, maximum inspiratory and expiratory force, lung elasticity (small airway collapse), PaO2 but no change in PaCO2, FVC and FEV1, ventilator responses to hypoxemia and hypercapnia, and normal airway protective mechanisms (increased risk for aspiration)  
- Ventilation-perfusion mismatch                                                                                                                                                                                                 |
| Renal          | - **Decrease** in number of functional nephrons and tubular cells, renal blood flow, GFR, CrCl despite normal serum Cr level, tubular function (loss of concentrating ability), clearance of certain drugs  
- Increased susceptibility to dehydration, and lower urinary tract dysfunction and infection                                                                                                                                                                                                       |
| Hepatobiliary  | - **Decreased** liver volume, number of hepatocyte mitochondria, hepatic blood flow  
- Increased hepatocyte size and ploidy, sensitivity to and decreased clearance of certain drugs, and incidence of gallstones and gallstone-related diseases  
- Synthetic capacity unchanged                                                                                                                                                                                                                                                                 |
| Immune         | - **Involution** of thymus gland  
- **Decreased** production and differentiation of naïve T cells, and T cell mitogenic activity  
- Increase in inflammatory cytokines and autoantibodies                                                                                                                                                                                                                                                                 |
The American College of Surgeons (ACS) and The American Geriatric Society (AGS)

Best Practice Guidelines for the Geriatric Surgical Patient

Preoperative Assessment

In addition to conducting a complete and thorough history and physical examination of the patient, the following assessments are strongly recommended:

- Assess the patient's cognitive ability and capacity to understand the anticipated surgery (see Section I.A, Section I.B, and Appendix I).
- Screen the patient for depression (see Section I.C).
- Identify the patient's risk factors for developing postoperative delirium (see Section I.D).
- Screen for alcohol and other substance abuse/dependence (see Section I.E).
- Perform a preoperative cardiac evaluation according to the American College of Cardiology/American Heart Association (ACC/AHA) algorithm for patients undergoing noncardiac surgery (see Section II and Appendix II).
- Identify the patient's risk factors for postoperative pulmonary complications and implement appropriate strategies for prevention (see Section III).
- Document functional status and history of falls (see Section IV).
- Determine baseline frailty score (see Section V and Appendix III).
- Assess patient's nutritional status and consider preoperative interventions if the patient is at severe nutritional risk (see Section VI and Appendix IV).
- Take an accurate and detailed medication history and consider appropriate perioperative adjustments. Monitor for polypharmacy (see Section VII, Appendix V, Appendix VI, and Appendix VII).
- Determine the patient's treatment goals and expectations in the context of the possible treatment outcomes (see Section VIII).
- Determine patient's family and social support system (see Section VIII).
- Order appropriate preoperative diagnostic tests focused on elderly patients (see Section IX).
**NCCN Guidelines Version 2.2016**

**Older Adult Oncology**

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**APPROACH TO DECISION MAKING IN THE OLDER ADULT**

- **Life expectancy**
  - Is the patient at moderate or high risk of dying or suffering from cancer considering his or her overall life expectancy? \(^{a,b}\)
  - No → Symptom management/supportive care (See NCCN Guidelines for Palliative Care)
  - Yes →

- **Patient's decision-making capacity**
  - Does this patient have decision-making capacity? \(^{c,d}\)
    - Yes →
    - No →
      - Obtain information from:
        - Patient's proxy
        - Advance directive
        - Living will
        - Health care power of attorney
        - Clinician's documentation
        - Consider consult from ethics committee or social worker or consider palliative care (See NCCN Guidelines for Palliative Care)

- **Patient's goals & values**
  - Assess the patient's goals and values regarding the management of his or her cancer
  - Are the patient's goals and values consistent with wanting anti-cancer therapy? \(^e\)
    - No → Symptom management/supportive care (See NCCN Guidelines for Palliative Care)
    - Yes → Assessment of Risk Factors (See OAO-2)
Assessment of Risk Factors

Comorbidities
- cardiovascular, renal, neuropathy, anemia, osteoporosis, liver, diabetes, lung, hearing/vision loss, prior cancer Dx & Tx, chronic infection, decubitus/pressure ulcers

Geriatric Syndromes
- ADL, IADL, mobility problems, falls, dementia, delirium, depression, nutritional deficiency, polypharmacy

Socioeconomic Issues
- poor living conditions, no caregiver or limited social support, low income, transportation barriers/access problems, under-insurance/high out-of-pocket costs for medications

Special considerations for patients able to tolerate treatment

Surgery
- In general, age is not the primary consideration for surgical risk.
- Emergency surgery carries increased risk of complications.
- Assess physiologic status and the ACS/AGS guidelines for older patients.
- Increased need for functional assistance pre-surgery predicts postop. complications, extended hospital stay, and 6-month mortality.
- Impaired cognitive status is a risk factor for postop. complications, prolonged length of stay, and 6-month overall postop. mortality.
- Older age is a risk factor for postoperative delirium.
- Delirium is a risk factor for functional and cognitive decline.
- Preventive measures exist for delirium (Yale Delirium Prevention Trial and Hospital Elder Life Program (HELP); NICE Guideline for Prevention of Delirium)

Radiation Therapy
- Use caution with concurrent chemoradiation therapy; dose modification of chemotherapy may be necessary.
- Nutritional support and pain control for radiation therapy-induced mucositis.
DISEASE-SPECIFIC ISSUES RELATED TO AGE

Breast Cancer

- Multiple studies have shown that older women often do not receive “standard of care” treatment, and do not do as well as younger women with the same stage of breast cancer.
- Women older than 75 years receive less aggressive treatment and have higher mortality from early-stage breast cancer than younger women.¹⁻³ Biologic as well as chronologic age should be considered in selecting treatments for older women with breast cancer.

See NCCN Guidelines for Breast Cancer
A preliminary retrospective study of Korea Big 5 Hospitals

N = 5,395 underwent surgery from 2005 to 2010; Median FU periods = 73.0 months

Unpublished data.
Tumor Biology between older and young women with breast cancer

- **Older** women tend to have **fewer adverse prognostic features**.
  - Increased ER/PR-positive tumors
  - Lower HER2-positive tumors
  - Lower aggressive other markers; tumor grade, proliferative marker, p53 mutation, S-phase fraction, lymphovascular invasion..

- By a process of **natural selection**, it is reasonable to expect a concentration of more indolent tumors among older persons.

Balducci L. Cancer in the Elderly: Biology, Prevention, and Treatment
Management of elderly patients with breast cancer: Updated recommendations of the SIOG and EUSOMA

<table>
<thead>
<tr>
<th>Therapy</th>
<th>2012 Recommendations of the International Society of Geriatric Oncology (SIOG) / European Society of Breast Cancer Specialists (EUSOMA)</th>
</tr>
</thead>
</table>
| Surgery | - **Patients 70 years or older should be offered the same surgery as younger patients.**  
- Standard of care is **BCS plus WBRT**, or mastectomy with or without postoperative radiotherapy.  
- **Mastectomy** is indicated for large or multifocal tumours not amenable to conservative excision, patients who are not fit for WBRT, and patients who prefer mastectomy to BCS plus WBRT.  
- **ALND** is indicated for clinically positive or highly suspected nodes.  
- In clinically node negative disease, axillary staging by **SLNB** with completion ALND for tumour-positive SLNB remains the standard of care.  
- **Omission of SLNB and completion ALND** might be reasonable in some older patients. |
| Radiotherapy | - **WBRT after BCS, with a boost to the tumour bed, should be considered in all elderly patients since it decreases risk of local relapse.**  
- There is no subgroup of fit older patients in whom post-BCS WBRT can be systematically omitted.  
- **Post-mastectomy chest-wall radiation** should be considered for elderly patients with at least four nodes (N2-3) or a pT3/4 tumour (>5cm).  
- **Hypofractionated radiation** schedules offer similar local-regional control and adverse effects as standard WBRT.  
- The evidence for **PBI in older patients** is not sufficiently robust to recommend it as standard therapy. |

Surgery of the primary lesion in the elderly patients

- Older women should be offered the option of breast conservation, because body image and the loss of breast are important issues regardless of age.
- Operative mortality rate for breast surgery: very low (<1%)
- BCS is a much less morbid procedure and preferable to mastectomy.

- Main factor influencing surgical mortality is not age but the presence of significant comorbidity.
- There may be at least a short-term decrease in cognitive function after general anesthesia.
- Attention should be paid to functional status and comorbid illness in making decisions about surgical management.
## Omitting Primary Surgery

* No significant, † Significant, ‡ Not reported

<table>
<thead>
<tr>
<th>Ref</th>
<th>Patients, n</th>
<th>Follow-up, months</th>
<th>Treatment</th>
<th>Overall Survival</th>
<th>Local Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentiman et al. Eur J Cancer 2003</td>
<td>164</td>
<td>120</td>
<td>Tamoxifen Surgery</td>
<td>39.0%</td>
<td>57.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>27.0%*</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9.0%†</td>
</tr>
<tr>
<td>van Dalsen et al. J Surg Oncol 1995</td>
<td>171</td>
<td>41</td>
<td>Tamoxifen Surgery</td>
<td>68.0%</td>
<td>27.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>72.0%*</td>
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<td></td>
<td></td>
<td></td>
<td>6.0%†</td>
</tr>
<tr>
<td>Robertson et al. BMJ 1988</td>
<td>135</td>
<td>24</td>
<td>Tamoxifen Surgery</td>
<td>85.0%</td>
<td>44.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>74.6%*</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>24.6%‡</td>
</tr>
<tr>
<td>Gazet et al. Eur J Surg Oncol 1994</td>
<td>200</td>
<td>72</td>
<td>Tamoxifen Surgery</td>
<td>67.0%</td>
<td>56.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>72.0%*</td>
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<td></td>
<td></td>
<td>44.0%*</td>
</tr>
<tr>
<td>Mustacchi et al. Ann Oncol 2003</td>
<td>474</td>
<td>80</td>
<td>Tamoxifen Surgery and Tamoxifen</td>
<td>38.7%</td>
<td>47.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>45.6%*</td>
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<td></td>
<td></td>
<td>11.0%†</td>
</tr>
<tr>
<td>Fennessy et al. Br J Surg 2004</td>
<td>455</td>
<td>151</td>
<td>Tamoxifen Surgery and Tamoxifen</td>
<td>28.8%</td>
<td>50.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>37.7%†</td>
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<td></td>
<td></td>
<td></td>
<td>16.0%†</td>
</tr>
</tbody>
</table>

Cochrane review (Surgery ± TAM vs. TAM alone)

- **Surgery ± TAM** showed no significant difference in OS but superior local disease control than TAM alone.

- Short estimated life expectancy of < 2–3 years, since it is the median duration of response to TAM.

- Still no data of aromatase inhibitors but may be another option.

Breast Reconstruction

- The oldest aged woman underwent immediate breast reconstruction at my hospital: Implant; 78 yrs, LD flap; 68 yrs, and TRAM flap; 64 yrs.

- In USA (n = 127,501; TM+IBR),
  - 10.3%; age ≥ 65 yrs (1.5%; ≥ 75 yrs)
- 27.4% of age ≥ 65 yrs and TM+IBR
- Contralateral prophylactic mastectomy
- 30-day unplanned re-admission
  - 3.7% (≥65 yrs) vs 2.9% (<65 yrs), p<0.001

Systematic review of breast reconstruction

• 42 articles (31-USA; 3-UK; 2-Italy, Canada; 1-Australia, France, Netherlands, Spain)

• Breast reconstruction rate of 6.1% among mastectomy patients aged ≥ 60 years from 1987 to 2002.

• The majority of studies favored implant-based breast reconstruction for those aged ≥ 60.

• Mostly, complication rates were not higher in older women, and QoL outcomes were similar to younger women.

• Age alone should not be an exclusion criterion.

Management of the Axilla

• **SLNB** is preferred in **clinically node-negative** disease.

• For elderly women with **clinically positive ALNs** who can tolerate surgery and **do not meet the Z0011 criteria**, **axillary dissection** represents the best treatment because no long-term difference in arm movement or pain between axillary clearance and not.

• **ALND may be omitted** in older patients had **BCS** and **positive node based on the eligibility criteria for the Z0011 trial**.
  (negative margins, T1 or T2 tumor, SLN ≤ 2 involved, not matted LN, no extranodal extension, no preoperative therapy)
**ALND vs Axillary RTx for SLN-positive Disease**

- Alternative to completion ALND for SLN-positive disease is **axillary irradiation** (EORTC 10981-22023 AMAROS trial).


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**Lymphoedema**

<table>
<thead>
<tr>
<th>Clinical sign of lymphoedema in the ipsilateral arm</th>
<th>Axillary lymph node dissection</th>
<th>Axillary radiotherapy</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>3.655 (5.3%)</td>
<td>0.586 (9%)</td>
<td>0.25</td>
</tr>
<tr>
<td>1 year</td>
<td>114/410 (28%)</td>
<td>62/410 (15%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3 years</td>
<td>5/373 (23%)</td>
<td>47/341 (14%)</td>
<td>0.003</td>
</tr>
<tr>
<td>5 years</td>
<td>5/322 (23%)</td>
<td>31/286 (11%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Arm circumference increase >10% of the ipsilateral upper or lower arm, or both**

<table>
<thead>
<tr>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.497</td>
</tr>
<tr>
<td>0.332</td>
</tr>
<tr>
<td>0.080</td>
</tr>
<tr>
<td>0.0009</td>
</tr>
</tbody>
</table>

Data are n/N (%), unless otherwise specified.

---

**5-yr axillary recurrence (95% CI)**

- **ALND**: 0.43% (0.00-0.92)
- **Axillary RTx**: 1.19% (0.31-2.08)
Omission of Axillary Staging: Systematic review and meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Accrual period</th>
<th>Population</th>
<th>Follow-up (range)</th>
<th>Axillary surgery / No axillary surgery</th>
<th>Primary outcome</th>
<th>Secondary outcome</th>
<th>Adjuvant treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martelli et al. (Single center)</td>
<td>1996–2000</td>
<td>Age 65–80 (median 70), cT1N0</td>
<td>50 (125–175)</td>
<td>109 / 110</td>
<td>OS and BCSS</td>
<td>Ipsilateral and contralateral breast cancer, distant metastasis. Overt axillary disease for no Axillary Dissection</td>
<td>WBRT, TAM 5 yrs</td>
</tr>
<tr>
<td>Rudenstam et al. (Multicenter)</td>
<td>1993–2002</td>
<td>Age &gt; 60 (median 74), node-negative</td>
<td>79</td>
<td>234 / 237</td>
<td>Quality of life</td>
<td>OS, DFS, and breast cancer Mortality</td>
<td>RTx for BCS, TAM 5 yrs</td>
</tr>
</tbody>
</table>

In-Breast recur (surgery); RR = 0.24, p=0.04

Distant recur (surgery); RR = 1.17, p=0.48

Overall survival (surgery); RR = 0.99, p=0.92

Omission of Axillary Staging

• Axillary evaluation may not always be necessary in the elderly women with clinically benign preoperative nodal exam.
• $T \leq 2\text{cm}$, ER-positive or PR-positive, and BCS
  -> axillary evaluation, even with SLNB, has little utility.
  -> Omission of SLNB might be possible in some elderly patients.

• $T > 2\text{cm}$, ER-negative and PR-negative
  -> SLNB to determine who might best benefit from adjuvant chemotherapy or axillary treatment.
Radiation Therapy

- Older women **tolerate breast irradiation** with good to excellent cosmesis.
- Chronologic age alone should not be a limiting factor in its inclusion.

- EBCTCG meta-analysis confirm radiotherapy after BCS reduces the risk of local failure as well as death rate.
- But local recurrence was inversely associated with patients’ age therefore, the benefit might be less significant as increasing age.
- In elderly with **advanced disease (T3-4 or N2-3)**, PMRT improves the survival but still remains debatable in patients with N1 status or individual risk factors of local recurrence.
Booster after BCS

- EORTC 22881-10882 Trial (16 Gy booster vs no; median 10.8 yrs)
  - Higher dose improved local control but severe fibrosis increased.
  - No difference in survival.

# Omitting Radiation Therapy

A systematic review & meta-analysis

<table>
<thead>
<tr>
<th>Ref (year)</th>
<th>N (total)</th>
<th>N (70+)</th>
<th>Study period</th>
<th>Age</th>
<th>Tumor</th>
<th>Hormone receptor</th>
<th>Surgery (BCS)</th>
<th>Axillary staging</th>
<th>Adj. EndoTx</th>
<th>Intervention</th>
<th>Control</th>
<th>Primary outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRIME II (2015)</td>
<td>1,326</td>
<td>1,326</td>
<td>03-09</td>
<td>≥65</td>
<td>≤3cm, N0</td>
<td>ER/PR+ (-) margin (≥1mm)</td>
<td>SLNB or ALND</td>
<td>TAM 5yr; other ET allowed</td>
<td>WBRT (40–50 Gy); boost 10–15 Gy permitted</td>
<td>No RT</td>
<td>IBTR</td>
<td></td>
</tr>
<tr>
<td>CALGB 9343 (2004)</td>
<td>636</td>
<td>636</td>
<td>94-99</td>
<td>≥70</td>
<td>≤2cm, N0</td>
<td>ER+ (-) inked margin</td>
<td>Clinical ALND allowed, but discouraged</td>
<td>TAM 5yr</td>
<td>WBRT (45 Gy); boost up to 14 Gy</td>
<td>No RT</td>
<td>Local or regional recurrence</td>
<td></td>
</tr>
<tr>
<td>Fyles (2004)</td>
<td>769</td>
<td>325</td>
<td>92-00</td>
<td>≥50</td>
<td>≤5cm, N0</td>
<td>Any (81% ER+) (-) inked margin</td>
<td>ALND or Clinical TAM 5yr</td>
<td>WBRT (40 Gy); boost 12.5 Gy</td>
<td>No RT</td>
<td>DFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fisher (2002)</td>
<td>673</td>
<td>100</td>
<td>89-94, 96-98</td>
<td>Any</td>
<td>&lt;1cm, N0</td>
<td>Any (-) margin</td>
<td>ALND</td>
<td>TAM (BID) 5yr</td>
<td>WBRT (50 Gy); no boost</td>
<td>No RT</td>
<td>IBTR</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect (95% CI)</th>
<th>Illustrative comparative risks, per 1000 patients (95% CI)</th>
<th>Risk difference, per 1000 patients (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Assumed risk TAM alone</td>
<td>Corresponding risk TAM and RTx</td>
</tr>
<tr>
<td>IBTR at 5 yrs (n=2387)</td>
<td>0.18 (0.10–0.34)</td>
<td>60</td>
<td>10 (6–20)</td>
</tr>
<tr>
<td>IBTR at 10 yrs (n=891)</td>
<td>0.27 (0.13–0.54)</td>
<td>80</td>
<td>20 (10–40)</td>
</tr>
<tr>
<td>Axillary Recurrence at 5 yrs</td>
<td>0.28 (0.10–0.81)</td>
<td>12</td>
<td>3 (1–10)</td>
</tr>
<tr>
<td>(n=2287)</td>
<td></td>
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<tr>
<td>Distant Recurrence at 5 yrs</td>
<td>1.49 (0.87–2.54); N-S</td>
<td>22</td>
<td>30 (20–50)</td>
</tr>
<tr>
<td>(n=2287)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Survival at 5 yrs</td>
<td>0.98 (0.79–1.22); N-S</td>
<td>165</td>
<td>160 (130–200)</td>
</tr>
<tr>
<td>(n=2287)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- For elderly women (≥ 70 yrs), **radiotherapy reduces the risk of breast and axillary recurrence**, but does not impact DRFS, BCCS, or OS in EBC treated with BCS and TAM.
- The value of this risk reduction must be weighed by women and their physicians when considering the omission of adjuvant radiotherapy.

BCT among elderly women (≥ 70 yrs) with T1-2 N0 ER-Negative breast cancer

• SEER-Medicare-linked data, N = 3,432

• **Radiotherapy** after BCS in elderly with T1-2N0 ER(-) is associated with a reduced incidence of future mastectomy and breast cancer death.

• Probably smaller benefit in women aged ≥ 80 years or T1 tumors.

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**Adjusted Cumulative Incidence of Mastectomy Curves Comparing the Effect of Radiotherapy**

- **HR 2.25**
  - **unadjusted 5-yr incidence P-value**
    - RTx: 4.9% <0.0001
    - No RTx: 10.8%

**Adjusted Cumulative Incidence of Breast Cancer Death Curves Comparing the Effect of Radiotherapy**

- **HR 2.14**
  - **unadjusted 5-yr incidence P-value**
    - RTx: 8.3% <0.0001
    - No RTx: 24.1%

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Schedule of Radiation Therapy

✓ The schedule and duration of RTx may be obstacles in the elderly.

• Hypofraction radiation schedule (13-16 vs standard 25 fractions): Comparable locoregional relapse and less common toxicity.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Treatment: hypofractionation versus WBRT</th>
<th>Local recurrence rate</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bentzen et al; START A (2008)</td>
<td>BCS or mastectomy 39 Gy in 13 fractions over 5 weeks versus 41.6 Gy in 13 fractions over 5 weeks versus 50 Gy in 25 fractions over 5 weeks</td>
<td>5.2% (5 year) 3.5% (5 year) 3.6% (5 year)</td>
<td>--</td>
</tr>
<tr>
<td>Bentzen et al; START B (2008)</td>
<td>BCS or mastectomy 40 Gy in 15 fractions over 3 weeks versus 50 Gy in 25 fractions over 5 weeks</td>
<td>2.2% (5 year) 3.3% (5 year)</td>
<td>Better breast cosmesis with hypofractionation</td>
</tr>
<tr>
<td>Whelan et al; Canadian trial (2010)</td>
<td>BCS, Ti-2N0M0, clear resection margins 42.5 Gy in 16 fractions over 3 weeks versus 50 Gy in 25 fractions over 5 weeks</td>
<td>6.2% (10 year) 6.7% (10 year)</td>
<td>No significant difference in breast cosmesis and late cardiotoxicity between treatment groups</td>
</tr>
</tbody>
</table>

WBRT—whole-breast radiotherapy. BCS—breast-conserving surgery.

Table 3: Studies of hypofractionation versus standard fractionation WBRT

PBI for the elderly

- **Accelerated partial breast irradiation (PBI)**
  - Intra/postoperative brachytherapy (interstitial implants, MammoSite balloon catheter)
  - targeted intraoperative radiotherapy (TARGIT), and
  - electron intraoperative radiotherapy (ELIOT)

- A meta-analysis of RCT showed PBI was associated with higher risk of local & axillary failure but comparable OS & distant metastasis were demonstrated.  

- This might be an option for low-risk elderly patients.
Conclusion (I)

• **Management of elderly** breast cancer is **complex** because this population is also **heterogeneous**.

• **Limited data** are available, mainly because the aging population is poorly represented, especially in randomized clinical trials.

• It is appropriate for patient to participate in decision-making process, since elderly preferences often favor quality of life and independence.

• **Local treatment of breast and axilla for elderly** women should be managed similarly to young women.

• **Chronologic age alone** does not provide adequate information.
Conclusion (II)

• Considering life expectancy, CGA, the risk/benefit of treatment, tumor biology and available data, optimal local therapy should be determined for elderly patients with breast cancer.

• Clinicians should inform their patients that under-treatment strongly increases the risk of loco-regional recurrence but not survival.

• Multidisciplinary approach between oncology and geriatrics teams can result in the facilitation of treatment and the coordination of care for elderly cancer patients.
Thank You for Your Attention.