The role of new radiation techniques for metastases treatment

Birgitte Vrou Offersen,
Professor, clinical oncologist
Dept. Experimental Clinical Oncology
Danish Center for Particle Therapy
Dept. Oncology, Aarhus University Hospital, Denmark
I have no conflicts of interest
The natural history of breast cancer

Hypothesis of Halsted (1894)

BC is an orderly disease spreading through the lymphatics to the lymph nodes and subsequently to distant sites, but not hematogenously
The natural history of breast cancer

Systemic theory

"that breast cancer is a systemic disease involving a complex spectrum of host-tumor interactions, and that variations in effective local regional treatment are unlikely to affect survival substantially"

Bernard Fisher
Karnovsky lecture 1980
Spectrum theory

Breast cancer is a heterogeneous disease - a spectrum ranging from a disease that remains local throughout its course to a disease which is systemic when first detectable. Thus there could be situations where metastases would develop as a consequence of residual inadequately treated loco-regional disease.

Samuel Hellman
Karnovsky lecture 1994
Oligometastases

From considerations of these theories of cancer dissemination, in the light of the emerging information on the multistep nature of cancer progression, we propose the existence of a clinical significant state of **oligometastases**. For certain tumors, the anatomy and physiology may limit or concentrate these metastases to a single or a limited number of organs. The likelihood of the oligometastatic

An attractive consequence of the presence of a clinically significant oligometastatic state is that some patients so affected should be amenable to a **curative therapeutic** strategy. The occasional success of surgical excision or

tions. Not only is there a spectrum of malignancy, but there is an accompanying spectrum of potentially curative treatments. Tumors early in their progression should be amenable to **localized therapy**. Patients with oligometastases, either de novo or following systemic treatment, should be cured by ablation of these lesions. More advanced disease will require more aggressive and effective systemic treatment.
Hypothesis: Radical RT may improve 2-yr PFS from 30% to 50%

Inclusion: Oligometastasis ≤5 metastatic lesions (no brain) and primary tumour controlled

Material & Method: Total 54 patients with 94 lesions (85% had max 2 lesions)
Clinical examination, CT, MR and FDG PET/CT
Stereotactic body radiation therapy (SBRT) 30-45 Gy/3 fr (44 pts) or IMRT 60 Gy/25 fr (10 pts)

Results: Median follow up 30 months. 1 yr PFS 75%, 2 yr PFS 53%
2 yr local control 97%, 2 yr OS 95%
No patients with ≥3 toxicity. Only 2 pts with grade 2 toxicity (pain & fatigue)
Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial


Lancet 2019; 393: 2051-58

Aim: Assess the effect of Stereotactic Ablative RT (SABR) on survival, oncological outcome, toxicity and QoL
Oligometastasis is ≤5 metastases

Randomization 1:2
Standard care
Standard care + SABR

Primary endpoint: OS based on a randomised phase 2 screening design with 2-sided α of 0.20 (thus p<0.20 designates a positive trial)
Cohort: 99 patients
Median follow up 25 months

Results: Median OS 28 months (95% CI 19-33) in controls versus 41 months (95% CI 26-not reached) in the SABR group, HR 0.57 (95% CI 0.30-1.10; p=0.090).

Adverse events ≥ grade 2: 9% in controls versus 29% in SABR group, p=0.026, an absolute increase of 20% (95% CI 5-34)
Treatment related death 0 in controls versus 4.5% in SABR group
Overall survival

Median follow up
SABR: 26 months
Control: 25 months

Progression free survival
NRG-BR002: A phase IIIR/III trial of standard of care therapy with or without stereotactic body radiotherapy (SBRT) and/or surgical ablation for newly oligometastatic breast cancer (NCT02364557).

**Authors:**

**Institutions:**
The University of Chicago Medicine, Chicago, IL; Statistical Center, Radiation Therapy Oncology Group, Philadelphia, PA; The University of Chicago, Chicago, IL; University of Colorado Comprehensive Cancer Center, Aurora, CO; University of Chicago, Chicago, IL; University of Michigan, Ann Arbor, MI; University of Rochester Medical Center, Rochester, NY; Duke University Medical Center, Durham, NC; Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; NRG Oncology, and The Ohio State University Comprehensive Cancer Center, Columbus, OH

**Summary:**
Newly diagnosed oligo-metastatic breast cancer ≤4 lesions (no brain)
Max 12 months first line systemic therapy without progression, primary tumour controlled

**Randomization:**
standard of care versus standard of care + SABR or surgical resection

**Phase II:**
median PFS improvement 10.5 to 19 months, 128 patients

**Phase III:**
5 yr OS improvement 28% to 42.5%, additional 232 patients (total 360 patients)

**Accrual:**
Jan 31, 2019: 105 patients accrued.
Local radiotherapy and granulocyte-macrophage colony-stimulating factor to generate abscopal responses in patients with metastatic solid tumours: a proof-of-principle trial

Encouze B Golden, Arpit Chhabra, Abraham Chachova, Sylvia Adams, Martin Donach, Maria Fenton-Kerimian, Kent Friedman, Fabio Ponzo, James S Babb, Judith Goldberg, Sandra Demaria, Silvia C Formenti

Abscopal effect:
Radiotherapy-induced immune-mediated tumour regression at sites distant to the irradiated site

Background for this study:
Dendritic cells are pivotal to immunity
Granulocyte-macrophage colony-stimulating factor stimulates differentiation of dendritic cells
Abscopal responses are mediated by effector T-cells

Simon’s optimal two-stage design:
Phase 1: at least 1 / 10 first patients with an abscopal effect
Abscopal effect definition: at least 30% decrease in longest diameter of non-irradiated lesion

Primary outcome: Proportion of patients with abscopal effect. Expected 20%

Phase 1: abscopal effect seen in 4 patients
Phase 2: accrue additional 19 patients
Two later amendments: total 41 patients accrued

RT: 35Gy/10 fr
CT reduced during RT

Overall abscoopal response seen in 11 / 41 patients, 26.8%

<table>
<thead>
<tr>
<th>Patients diagnosed</th>
<th>Patients completing scheduled therapy</th>
<th>Patients not assessable for best abscoopal response</th>
<th>Patients assessable for best abscoopal response who completed their scheduled therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PD</td>
<td>SD</td>
<td>PR</td>
</tr>
<tr>
<td>Non-small-cell lung cancer</td>
<td>18 (44%)</td>
<td>13 (32%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>14 (34%)</td>
<td>11 (27%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Thymic cancer</td>
<td>2 (5%)</td>
<td>2 (5%)</td>
<td>..</td>
</tr>
<tr>
<td>Urothelial cancer</td>
<td>2 (5%)</td>
<td>0</td>
<td>..</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>2 (5%)</td>
<td>0</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Eccrine cancer</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>..</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>..</td>
</tr>
<tr>
<td>Small-cell lung cancer</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>..</td>
</tr>
<tr>
<td>Total</td>
<td>41 (100%)</td>
<td>30 (73%)</td>
<td>4 (10%)</td>
</tr>
</tbody>
</table>

PD = progressive disease. SD = stable disease. PR = partial response. CR = complete disease.

Table 2: Best abscoopal responses based on patient diagnoses and completion of scheduled therapy

Median OS (responder) 21 months
Median OS (non-responder) 8 months
HR 2.06 (95% CI, 1.04-4.11)

This is the first evidence that an abscopal effect can predict better OS
>50 clinical studies are ongoing testing addition of RT to immunotherapy

Persistent Use of Extended Fractionation Palliative Radiotherapy for Medicare Beneficiaries With Metastatic Breast Cancer, 2011 to 2014

James B. Yu, MD, MHS,*†‡ Craig E. Pollack, MD,§|| Jeph Herrin, PhD,‡¶ Weiwei Zhu, MPH,‡# Pamela R. Soulos, MPH,‡# Xiao Xu, PhD,‡** and Cary P. Gross, MD†‡##

N=7547 patients
2013: ASTRO Choosing Wisely guideline

Mean price per course, 2016 adjusted USD
6597 $ 3566 $ 2074 $ 633 $

FIGURE 1. Percentage of patients treated with radiation courses involving 1, 2 to 10, 11 to 19, and 20 to 30 fractions, respectively, for bone metastases from breast cancer in 2011 to 2014.
### Analysis 5.1. Comparison 5 Intention-to-treat, Outcome 1 Overall response.

**Review:** Palliation of metastatic bone pain: single fraction versus multifraction radiotherapy

**Comparison:** 5 Intention-to-treat

**Outcome:** 1 Overall response

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Single fraction</th>
<th>Multifraction</th>
<th>Odds Ratio M-H Fixed 95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall pain response</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPTVP 1999</td>
<td>274/383</td>
<td>257/378</td>
<td>20.2 %</td>
<td>1.18 [0.87, 1.61]</td>
</tr>
<tr>
<td>Cole 1989</td>
<td>14/16</td>
<td>11/13</td>
<td>0.4 %</td>
<td>1.27 [0.15, 10.53]</td>
</tr>
<tr>
<td>Foro 1998a</td>
<td>19/25</td>
<td>21/25</td>
<td>1.4 %</td>
<td>0.60 [0.15, 2.47]</td>
</tr>
<tr>
<td>Foro 1998b</td>
<td>19/25</td>
<td>22/25</td>
<td>1.5 %</td>
<td>0.43 [0.09, 1.97]</td>
</tr>
<tr>
<td>Gaze 1997</td>
<td>108/151</td>
<td>99/144</td>
<td>7.9 %</td>
<td>1.14 [0.69, 1.88]</td>
</tr>
<tr>
<td>Kagel 1990</td>
<td>12/14</td>
<td>12/13</td>
<td>0.5 %</td>
<td>0.50 [0.04, 6.28]</td>
</tr>
<tr>
<td>Koswig 1999</td>
<td>44/52</td>
<td>45/55</td>
<td>2.5 %</td>
<td>0.83 [0.32, 2.15]</td>
</tr>
<tr>
<td>Nielsen 1998</td>
<td>52/122</td>
<td>56/199</td>
<td>8.9 %</td>
<td>0.84 [0.50, 1.39]</td>
</tr>
<tr>
<td>Oszaraz 2001a</td>
<td>27/36</td>
<td>28/38</td>
<td>1.9 %</td>
<td>1.07 [0.38, 3.04]</td>
</tr>
<tr>
<td>Oszaraz 2001b</td>
<td>27/36</td>
<td>29/35</td>
<td>2.0 %</td>
<td>0.62 [0.19, 1.98]</td>
</tr>
<tr>
<td>Price 1986</td>
<td>29/140</td>
<td>34/148</td>
<td>7.2 %</td>
<td>0.88 [0.50, 1.53]</td>
</tr>
<tr>
<td>Steenland 1999</td>
<td>392/579</td>
<td>361/578</td>
<td>32.1 %</td>
<td>1.26 [0.99, 1.61]</td>
</tr>
<tr>
<td>Ward 2001</td>
<td>45/200</td>
<td>63/198</td>
<td>135 %</td>
<td>0.02 [0.40, 0.97]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>1779</td>
<td>1769</td>
<td>100.0 %</td>
<td>1.03 [0.89, 1.19]</td>
</tr>
</tbody>
</table>

Total events: 1059 (Single fraction), 1038 (Multifraction)

Heterogeneity: Chi² = 12.57, df = 12 (P = 0.40); I² = 5%

Test for overall effect: Z = 0.42 (P = 0.67)

Test for subgroup differences: Not applicable

Cochrane meta-analysis
11 RCT comparing single fraction with multifraction RT (3435 patients)
Metastatic bone pain

Sze et al, Cochrane Database Syst Rev 2004; 2: CD004721
### Analysis 5.2. Comparison 5 Intention-to-treat, Outcome 2 Complete response.

Review: Palliation of metastatic bone pain: single fraction versus multifraction radiotherapy

**Comparison:** 5 Intention-to-treat

**Outcome:** 2 Complete response

**Endpoint:** Overall complete pain response

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Single fraction</th>
<th>Multifraction</th>
<th>Odds Ratio M-H.Fixed 95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPTWP 1999</td>
<td>199/383</td>
<td>192/378</td>
<td>3.34 %</td>
<td>1</td>
</tr>
<tr>
<td>Gaze 1997</td>
<td>50/151</td>
<td>47/144</td>
<td>2.02 %</td>
<td>1.63</td>
</tr>
<tr>
<td>Kagei 1990</td>
<td>8/14</td>
<td></td>
<td>0.91 %</td>
<td>0.40</td>
</tr>
<tr>
<td>Koswig 15</td>
<td>77/165</td>
<td>74/165</td>
<td>0.82 %</td>
<td>0.36</td>
</tr>
<tr>
<td>Nielsen 19</td>
<td>131/650</td>
<td>134/650</td>
<td>1.06 %</td>
<td>0.47</td>
</tr>
<tr>
<td>Price 1986</td>
<td>18/148</td>
<td>19/148</td>
<td>1.62 %</td>
<td>0.94</td>
</tr>
<tr>
<td>Steenland 1999</td>
<td>199/579</td>
<td>175/578</td>
<td>1.11 [0.94, 1.30]</td>
<td>1.54</td>
</tr>
</tbody>
</table>

**Total (95% CI):**

- Single fraction: 1441
- Multifraction: 1435

Total events: 497 (Single fraction), 463 (Multifraction)

Heterogeneity: $\chi^2 = 2.98$, df = 6 ($P = 0.81$); $I^2 = 0.0\%

Test for overall effect: $Z = 1.23$ ($P = 0.22$)

Test for subgroup differences: Not applicable

---

**Fraction**

<table>
<thead>
<tr>
<th>Pathological fractures:</th>
<th>Single</th>
<th>Multi</th>
<th>OR 1.82 (95% CI 1.06-3.11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-treatment rate:</td>
<td>21.5%</td>
<td>7.4%</td>
<td>OR 3.44 (95% CI 2.67-4.43)</td>
</tr>
</tbody>
</table>

---

We need a revision of the reimbursement system so payment is independent of number of fractions.
FAST-Forward phase III randomised controlled trial of 1-week hypofractionated breast radiotherapy: 3-year normal tissue effects

Professor Murray Brunt
University Hospitals of North Midlands and Keele University, UK

Joanne Haviland, Mark Sydenham, Abdulla Alhasso, David Bloomfield, Charlie Chan, Mark Churn, Suzy Cleator, Charlotte Coles, Marie Emson, Andrew Goodman, Clare Griffin, Adrian Harnett, Penelope Hopwood, Anna Kirby, Cliona Kirwan, Daniel Megias, Carolyn Morris, Elinor Sawyer, Navita Somaiah, Isabel Syndikus, Maggie Wilcox, Duncan Wheatley, Judith Bliss, John Yarnold

Presented as late breaking abstract ESTRO 2018
Aim

To test a 1-week course of curative whole breast radiotherapy against a standard 3-week schedule in terms of local cancer control and late adverse effects (AE) in patients with early breast cancer.
Trial design

Eligible patients
Invasive carcinoma of the breast
pT1-3 pN0-1 M0
N=4000
Recruitment and consent

Randomise

40Gy in 15 # (2.67Gy) 3 wks
27Gy in 5 # (5.4Gy) 5 days
26Gy in 5 # (5.2Gy) 5 days

Radiotherapy +/- boost (16Gy/8# or 10Gy/5#)

Annual clinical assessment for 10 years
Photos at 2, 5 and 10 years
PROMS at 3, 6, 12 months, 2, 5 and 10 years

Primary endpoint:
- ipsilateral local tumour control

Median follow-up: 4 years

Secondary endpoints:
- early & late AE in normal tissues
- quality of life
- contralateral primary tumours
- regional & distant metastases
- survival
Acute toxicity study

Clinical assessments of skin toxicity graded by CTCAE criteria in 150 evaluable non-boost patients (7 centres)
Clinical assessments of late AE at 3 years, N=3305)

Breast shrinkage

<table>
<thead>
<tr>
<th>Radiation Dose</th>
<th>Not at all</th>
<th>A little</th>
<th>Quite a bit</th>
<th>Very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 Gy</td>
<td>6%</td>
<td>8%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>27 Gy</td>
<td>4%</td>
<td>5%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>26 Gy</td>
<td>4%</td>
<td>5%</td>
<td>3%</td>
<td></td>
</tr>
</tbody>
</table>

Breast induration

<table>
<thead>
<tr>
<th>Radiation Dose</th>
<th>Not at all</th>
<th>A little</th>
<th>Quite a bit</th>
<th>Very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 Gy</td>
<td>4%</td>
<td>5%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>27 Gy</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>26 Gy</td>
<td>4%</td>
<td>5%</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>

Breast distortion

<table>
<thead>
<tr>
<th>Radiation Dose</th>
<th>Not at all</th>
<th>A little</th>
<th>Quite a bit</th>
<th>Very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 Gy</td>
<td>4%</td>
<td>5%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>27 Gy</td>
<td>4%</td>
<td>5%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>26 Gy</td>
<td>4%</td>
<td>5%</td>
<td>3%</td>
<td></td>
</tr>
</tbody>
</table>

Telangiectasia

<table>
<thead>
<tr>
<th>Radiation Dose</th>
<th>Not at all</th>
<th>A little</th>
<th>Quite a bit</th>
<th>Very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 Gy</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>27 Gy</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>26 Gy</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>

Courtesy Murray Brunt
Any moderate/marked clinician-assessed late AE in the breast, 3 yr

% with no moderate/marked breast AE

Estimated 3-year cumulative incidence, 95% CI (%)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Estimated absolute difference in 3-year cumulative incidence vs. 40 Gy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>27 Gy</td>
<td>+7.2 (3.8, 11.0)</td>
</tr>
<tr>
<td>26 Gy</td>
<td>+1.3 (-1.7, 4.5)</td>
</tr>
</tbody>
</table>

Includes distortion, shrinkage, induration, telangiectasia, oedema

26 Gy / 5 versus 40 Gy / 15 fr is now tested in Fast Forward Nodal

Courtesy Murray Brunt
Considerations for you!
Equal dose 2 Gy (EQD2Gy)

<table>
<thead>
<tr>
<th></th>
<th>$\alpha/\beta = 2$ Gy</th>
<th>$\alpha/\beta = 4$ Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 Gy / 25 fr</td>
<td>50 Gy</td>
<td>50 Gy</td>
</tr>
<tr>
<td>40 Gy / 15 fr</td>
<td>46.7 Gy</td>
<td>44.5 Gy</td>
</tr>
<tr>
<td>26 Gy / 5 fr</td>
<td>46.8 Gy</td>
<td>39.9 Gy</td>
</tr>
<tr>
<td>30 Gy / 10 fr</td>
<td>37.5 Gy</td>
<td>35 Gy</td>
</tr>
</tbody>
</table>
Considerations for you!

Equal dose 2 Gy (EQD2Gy)

<table>
<thead>
<tr>
<th></th>
<th>( \alpha/\beta = 2 \text{ Gy} )</th>
<th>( \alpha/\beta = 4 \text{ Gy} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 Gy / 25 fr</td>
<td>50 Gy</td>
<td>50 Gy</td>
</tr>
<tr>
<td>40 Gy / 15 fr</td>
<td>46.7 Gy</td>
<td>44.5 Gy</td>
</tr>
<tr>
<td>26 Gy / 5 fr</td>
<td>46.8 Gy</td>
<td>39.9 Gy</td>
</tr>
<tr>
<td>30 Gy / 10 fr</td>
<td>37.5 Gy</td>
<td>35 Gy</td>
</tr>
</tbody>
</table>

Breast adenocarcinoma

In favour of 26 Gy / 5 fr:
1 week therapy, little burden to the patient, short delay if systemic therapy is paused
High anti-cancer dose
Modest acute morbidity
Optimizing whole brain radiotherapy dose and fractionation: Results from a prospective phase III trial (NCCTG N107C (Alliance)/CEC.3)

Daniel M. Trifiletti, MD, Karla V. Ballman, PhD, Paul D. Brown, MD, S. Keith Anderson, MS, Xiomara W. Carrero, BS, Jane H. Cerhan, PhD, Anthony C. Whitton, MD, Jeffrey Greenspoon, MD, Ian F. Parney, MD, Nadia N. Laack, MD, Jonathan B. Ashman, MD, Jean-Paul Bahary, MD, Costas G. Hadjipanayis, MD, James J. Urbanic, MD, Fred G. Barker, II, MD, Elana Farace, PhD, Deepak Khuntia, MD, Caterina Giannini, MD, Jan C. Buckner, MD, Evanthia Galanis, MD, David Roberge, MD

Stereotactic radiosurgery

Surgical resection followed by adjuvant whole brain RT (WBRT)

194 patients with ≤4 brain metastases randomized.
Before start, institutions decided on WBRT either 37.5 Gy / 15 or 30 Gy / 10 fr
Optimizing whole brain radiotherapy dose and fractionation: Results from a prospective phase III trial (NCCTG N107C (Alliance)/CEC.3)

Daniel M. Trifiletti, MD, Karla V. Ballman, PhD, Paul D. Brown, MD, S. Keith Anderson, MS, Xiomara W. Carrero, BS, Jane H. Cerhan, PhD, Anthony C. Whitton, MD, Jeffrey Greenspoon, MD, Ian F. Parney, MD, Nadia N. Laack, MD, Jonathan B. Ashman, MD, Jean-Paul Bahary, MD, Costas G. Hadjipanayis, MD, James J. Urbanic, MD, Fred G. Barker, II, MD, Elana Farace, PhD, Deepak Khuntia, MD, Caterina Giannini, MD, Jan C. Buckner, MD, Evanthia Galanis, MD, David Roberge, MD

194 patients with ≤4 brain metastases randomized. Before start, institutions decided on WBRT either 37.5 Gy / 15 or 30 Gy / 10 fr

Primary analysis showed no differences btw randomization arms (tumour control endpoints). This analysis investigates treatment related toxicities and tumour control among 92 patients randomized to surgical resection and WBRT
92 patients randomized to surgical resection + WBRT and had either 30 Gy/10 fr (53%) or 37.5 Gy/15 fr (47%)

Median follow up, cognitive failure: 10.2 mths (30 Gy) and 12.6 mths (37.5 Gy), p=0.18
76 % had 1 brain metastasis

Cognitive failure by 30 Gy/10 fr vs 37.5 Gy/15 fr P=0.658
CNS failure free survival by 30 Gy/10 fr vs 37.5 Gy/15 fr P=0.094
Surgical-bed recurrence free survival by 30 Gy/10 fr vs 37.5 Gy/15 fr
Overall survival by 30 Gy/10 fr vs 37.5 Gy/15 fr P=0.18
Conclusion:

- Protracted WBRT courses do not reduce cognitive deficit, neither improve tumour control in the hypoxic surgical cavity, or otherwise improve the therapeutic ratio.
- Adverse effects were significantly higher with protracted WBRT.
- Shorter course regimens remain the standard of care.

Table 2: Physician reported severe adverse events (grade ≥3 or any grade 1-2 experienced by more than 10% of patients) following whole brain radiotherapy (WBRT), stratified by WBRT dose and fractionation (adverse events with <3% frequency reported in supplemental table).
Conclusion

The oligometastatic stage of breast cancer will attract more focus and research to identify breast cancer patients who can be cured for breast cancer. Stereotactic radiotherapy is likely to play a pivotal role in the new treatments to be developed, and likely combined with immunotherapy to obtain abscopal effect.

Unfortunately, some institutions still use protracted radiation therapy courses for painful bone metastases despite overwhelming evidence in favour of single fraction therapy.

One week adjuvant radiation therapy courses are being tested, so it is time to also consider one week courses in palliative therapy.

Protracted whole brain radiation therapy (10 fr vs 15 fr) is not beneficial for the patient with resected brain metastases, neither for tumour control nor for cognitive decline.
Thank you

Acknowledgements:
Murray Brunt, Charlotte Coles, Philip Poortmans, Liesbeth Boersma, Youlia Kirova & many other colleagues inside the ESTRO