Parallel Session 9.1: Late effects

- Sanne Schagen: Effects of chemotherapy on cognition and brain structure in pts with non-CNS disease
- Olga Husson: Health-related quality of life and disease specific symptoms among thyroid cancer survivors
- Gabriela Armuand: Fertility-related distress and health-related quality of life among cancer survivors
- Cecilie Sperling: The impact of comorbidity on the survival of ovarian cancer patients
Effects of chemotherapy on cognition and brain structure in pts with non-CNS disease

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Literature on cognitive effects of cancer and cancer therapy

Cognitive dysfunction in pts with CNS disease due to:

- Disease burden
- Surgery, radiotherapy, chemotherapy
- Seizure and seizure therapy

Pts without CNS disease may also experience cognitive functioning

- **Chemotherapy not intended to target the CNS**
PRO ≠ Cognitive Function

- Not mutually exclusive
- Self-report more strongly related to mood and fatigue than cognitive problems as assessed with NP tests
Rapidly developing body of research:

Neuropsychological studies
Imaging studies
Pre-clinical studies
Cross-sectional neuropsychological studies: chemotherapy and cognition

23 studies

Sample size $n = 17 - 295$, total of 1466 pts with CT examined
Most studies assessed pts within 2 years after CT
Mean age around 50 (only 2 studies pts >65)

- 78% of studies (18/23) concluded there is evidence of treatment-related cognitive impairment
- Incidence of cognitive impairment ranges from 17-75%
- Most common domains affected: learning and memory, processing speed and executive functioning

Wefel & Schagen, Curr Neurol Neurosci Rep, 2012
BC patients CMF chemotherapy n=196; Reference group n=1509
On average 21 years after completion of treatment

Koppelmans V, Breteler MM, Booger W, Seynaeve C, Gundy C, Schagen SB
JCO, 2012
The magnitude of the effects is comparable to approximately six years of age-related decline in cognitive function.
Prospective neuropsychological studies: chemotherapy and cognition I

26 studies
23 with a pre-chemotherapy assessment

Sample size n=16 –136, total of 1462 pts with CT examined
Most studies assessed pts within a year after completion of CT
Pts on average in their forties (only 4 studies pts >60)

- 17 studies reported on pre-chemotherapy cognitive functioning
- 8 studies found lower than expected cognitive performance in cancer pts compared to controls
Prospective neuropsychological studies: chemotherapy and cognition III

69% of studies (16/23) concluded that there was evidence of chemotherapy related cognitive decline

- Incidence of cognitive decline ranges from 19%-78%
- Most common domains affected: learning and memory, processing speed and executive functioning - consistent with a frontal-subcortical profile
Risk factors for cognitive problems

Treatment-related:
• High dose exposure
• Multi-agent therapy with additive/synergistic effects (ET?)

Patient-related:
• None consistently identified
  (age, education, depression, anxiety, fatigue, treatment induced menopause)

But given the small sample sizes, exploration of risk factors is likely underpowered
Mechanisms

• Myelin damage
• Vascular injury
• Inflammation
• Decreased neurogenesis
• Neurochemical changes

Not mutually exclusive, many factors involved
• regimen, dosimetry, sequence & timing
• Individual differences
Grey matter volume

1 month after anthracycline-based chemotherapy ($n=17$)

Yoshikawa et al., Breast Cancer Res Treat, 2005
Inagaki et al., Cancer, 2007
McDonald et al., Breast Cancer Res Treat, 2010
Koppelmans et al., Breast Cancer Res Treat, 2012
White matter integrity (diffusion tensor imaging [DTI])

3 months after FEC or FEC + paclitaxel (n=34)

Abraham et al., Clinical Breast Cancer, 2008
Deprez et al., Human Brain Mapping, epub 2011
Deprez et al., JCO, 2012
De Ruiter et al., Human Brain Mapping, 2011
Koppelmans et al., HBM, in press
“Doctor, Will the Treatment You Are Recommending Cause Chemobrain?”

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See accompanying article on page 274
Preclinical studies

- Preclinical studies show that many common cytotoxic agents have an adverse effect on neurobiology and behavior
- Studies teach us that many different mechanisms are involved in cognitive and brain changes following chemotherapy
- Studies have implications for the design of intervention studies
Cognition and cancer research

Our field is ready to embark on large systematic studies to illuminate:

- Long-term trajectory of cognitive change
- Specific toxicity profiles
- Groups at risk for treatment-related impact on brain structure, function and consequent behavior
- Intervention strategies – tailored to the symptoms and based on the hypothesized mechanism
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