Estimated risk of radiation-induced lung cancer in paediatric patients following electron, photon and proton therapy

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Introduction

Radiation induced secondary cancer following cranio-spinal irradiation of paediatric patients

- Cranio-Spinal Irradiation (CSI) remains an important technique in the management of medulloblastoma, a common childhood cancer disease

- Young cancer patients are more susceptible to radiation carcinogenesis and calls for models for secondary cancer induction particularly tailored to paediatric patients

- In addition to the age dependence, secondary cancer risk is influenced by dose-level and heterogeneity, as well as gender and type of tissue irradiated

*Our objective was to estimate organ specific radiation induced cancer risk after electron, photon and proton radiotherapy, and we will here focus on the results for a female and male paediatric patient*
Treatment planning procedures

- CSI plans* were created on CT images (in prone position) for six patients (VMAT for two cases only)

- Treatment plan techniques:
  - Conformal photons
  - Electrons and photons combined
  - Volumetric arc therapy (VMAT)
  - Double scattering (DS) protons
  - Intensity-modulated proton therapy (IMPT)

- Standard risk medulloblastoma: 23.4 Gy(RBE) to brain and spine

- Vertebrae included in target volume for proton plans

- Common field configuration,
  - exception: VMAT technique with continuous arcs from 275-85°

*Eclipse, Varian Medical Systems, Palo Alto, CA, USA

Field setup: Two posterior spinal fields and two oblique cranial fields

Age specific target volume for proton techniques: Vertebrae included for paediatric patients in order to prevent asymmetric growth. [Giebeler et al 2013]
We analysed the risk of radiation-induced cancer for organs either in or near the spinal fields where the different dose-response scenarios were expected to have much impact: lungs, stomach, colon, liver, thyroid, bladder, breast, prostate.

To cover a range of possible dose-risk relationships, we included:

- Linear No Threshold (LNT)
- Plateau response above 4.5 Gy [Hall, 2003]
- Competition model [Dasu, 2005] accounting for cell killing vs induction of carcinogenic mutations
- Organ specific linear-exponential response obtained from fit to Hodgkin’s patient statistics [Schneider, 2005]

Organ Equivalent Dose (OED) concept: a dose-volume distribution can be converted into a single measure (in units of Gy) representing imposed risk on a relative scale.
Secondary Cancer Risk Analysis

Patient- and organ-specific risk coefficients estimated from the BEIR VII report*

<table>
<thead>
<tr>
<th>Lifetime Attributable Risk coefficient R per 1000 persons [Gy⁻¹]</th>
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<tbody>
<tr>
<td>Exposure age</td>
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<tr>
<td>Gender</td>
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<td>Female</td>
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<td>Male</td>
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<td>Breast</td>
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<td>Prostate</td>
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Life Attributable Risk of cancer incidence: \( LAR = OED \times R(\text{exposure age}, \text{sex}, \text{tissue}) \)

For absolute risk estimates the preferred models for age- and sex-dependent site-specific solid cancer from the BEIR* VII report has been used in combination with the four dose-response models

- Elevated risks for children compared to adults
- Gender variations

*Board on Biological Effects of Ionizing Radiation, 2006
Estimated risk of radiation-induced cancer following paediatric cranio-spinal irradiation with electron, photon and proton therapy

- Life attributable risk of cancer incidence for six paediatric CSI patients
- Accumulated risk in organs either in or near the spinal fields were about six times higher for the conventional photons and electrons compared to the proton techniques
- The lungs and the thyroid contributed the most to the total risk from all techniques in the patient population

*Life attributable risk of cancer incidence for six paediatric CSI patients stratified by technique.*

*weighted 2:1 for male:female*

*Stokkevåg et al, Acta Oncol 2014 (in press)*
Estimated risk of radiation-induced cancer following paediatric cranio-spinal irradiation with electron, photon and proton therapy

- OEDs for the proton techniques were in general significantly lower than for the photon and electron techniques, typically 4-8 times lower.

- Uncertainty in the LAR measure is significant: Nominal values compared in favour of the proton techniques for all patients and all organs included.

- Differences between female and male patients observable.

Representative results: Colon OED and LAR grouped by technique. Patient sequence from left to right: female: 5 y, 7y, 8y, male: 8y, 8y, 11y. [95% conf. interval]

Stokkevåg et al, Acta Oncol 2014 (in press)
Female 8 years, results for the lung: VMAT, conventional photons, electrons, DS protons, and IMPT

- The proton plans generally achieved lower lung doses compared to the photon and electron techniques. The volumes receiving doses below 10 Gy were significantly reduced with the proton techniques.

- Lower risks for the proton techniques for all dose-response models considered: 3-8 times higher risk from VMAT compared to proton techniques.

- Higher risks for female patients: 2.3 times higher (scales as risk factor).

*Neutron doses estimated from Taddei et al, Phys Med Biol 2009*
Results

Life attributable risk of cancer incidence using a linear exponential model

- Higher risks for the female patient relative to the male patient, much due to the higher susceptibility for female thyroid and lung cancer

- For the female patient, the LARs were 13 times higher with both photon techniques compared to the proton techniques

- Reduced doses to the thyroid by using electrons contributes to reduced LAR for the female patient by employing electrons

*Risk relative to IMPT: 13:13:8:1:1
*Risks relative to IMPT: 9:8:8:1:1

*Neutron doses estimated from Taddei et al, Phys Med Biol 2009
Conclusive remarks

- The proton techniques compared favourably with respect to LAR of radiation-induced cancer by all models with higher risks for the female than for the male patient.

- Male 8 years: Inherent differences in total LAR between electrons, conformal photons and VMAT were minor.

- Female 8 years: The LAR from the electron technique was somewhat lower compared to photons and VMAT.
Thank you!

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