Radiobiological optimization including consideration of secondary cancer risk: A treatment modality comparison study for pediatric medulloblastoma

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Svensk Förening för Radiobiologi – Radiofysikdagarna hösten 2011
Tack!

• Per Munck af Rosenschöld

• Marianne Aznar

• Per Nilsson

• Thomas Björk-Eriksson

• Ivan Vogelius
Late effects after cancer treatment

• Late effects are a big issue for modern day cancer patients

• Attributable to better treatment
  • Surgery
  • Chemotherapy
  • Radiotherapy

• Secondary cancers
  • Increased awareness - especially for young patients
  • Several risk modeling strategies proposed
  • Radiotherapy being the main contributor
Secondary cancers

• Nearly 14% of cancer survivors develop a second cancer within 25 years after treatment

• Second cancer ≠ recurrence or metastasis

• Higher risk for younger patients
Late effects after cancer treatment

• Late effects are a big issue for modern day cancer patients

• Attributable to better treatment
  • Surgery
  • Chemotherapy
  • Radiotherapy

• Secondary cancers
  • Increased awareness - especially for young patients
  • Several risk modeling strategies proposed
  • Radiotherapy being the main contributor

• Non-cancer adverse effects
  • e.g. lung and heart complications
Childhood Cancer Survivor Study (CCSS)

![Graph showing survival probability over attained age for different groups: Males (U.S. general population), Females (U.S. general population), Males (CCSS cohort), Females (CCSS cohort), Males (CCSS cohort) - Extrapolated, Females (CCSS cohort) - Extrapolated.](image)
Radiotherapy

- 3D conformal (3D CRT)
- Intensity-modulated (IMRT)
- Rotational therapy (RapidArc, Tomotherapy, VMAT)
- Particle therapy (Protons, Ions)
Treatment planning today

• Advanced treatment modalities used to create highly conformal dose distributions
  • Enables sparing of organs at risk to some extent

• Currently sparing is focused on minimizing early appearing toxicity
  • Bowel toxicity
  • Brainstem injury
  • Rectal bleeding
  • Also some later appearing toxicity like e.g. xerostomia
Purpose of study

• Estimate risks of secondary cancer risks and risks of non-malignant toxicities for pediatric medulloblastoma patients

• Compare these estimates between different treatment techniques

• Attempt to optimize the radiotherapy plans with respect to long-term risks
Risk modelling – OED (Organ-equivalent dose)

• Concept developed by Schneider et al. in 2005

• A model which describes the secondary cancer risk from an inhomogeneous dose distribution

• Using the data from a DVH one can calculate an OED given in Gy that represents:
  • The same secondary cancer risk as a homogeneous irradiation to that dose would yield

• Requires empirical data
Risk modelling – OED (Organ-equivalent dose)

- Plateau model
- Linear model
- Bell shape model

Excess absolute risk per 10,000 person years

Homogeneous irradiation dose (Gray)
Secondary lung cancer risk

- OED - Plateau model
- OED - Bell shape model
- Competition model
- LNT-model

Homogeneous irradiation dose [Gy]

Secondary cancer risk
Pediatric medulloblastoma

• Primitive neuroectodermal tumor in the posterior fossa

• ~20% of childhood brain tumors

• 5-year survival ~80% for standard risk patients

• Treatment consists of:
  • Surgery
  • Post operative radio- and chemotherapy

• The impact of chemotherapy is not considered in this study!
Paediatric craniospinal irradiation
Results – Normal tissue toxicity

Pneumonitis

Complication risk

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<th>0%</th>
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</table>
Results – Normal tissue toxicity

Heart failure

Complication risk

- 3DCRT
- IMPT
- RapidArc
- RapidArc_Re-opt
Results – Normal tissue toxicity

Ototoxicity

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<th>Treatment</th>
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<tr>
<td>IMPT</td>
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<tr>
<td>RapidArc</td>
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<td>RapidArc Re-opt</td>
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</table>
Results – Risk of solid secondary cancer

Plateau model - All patients

Excess absolute risk vs. Attained age (y)
Results – Risk of solid secondary cancer

Plateau model - All patients

Excess absolute risk

Attained age (y)
Optimizing with respect to secondary cancer risk

• Promising results, the risk can be manipulated

• PTV coverage remained the same

• But…

• The coverage of the spinal part of the PTV was somewhat deteriorated
Conclusions and future prospects

• Optimizing treatment plans for medulloblastoma patients appears promising

• Not enough to look at only tumor control or only late effects, consider the big picture

• Integrating it into the treatment planning would allow for direct risk based optimization – Visionary, but we are working on it
Thank you for your attention!

Supervisors and colleagues:
Per Munck af Rosenschöld
Marianne Aznar
Ivan Vogelius
Maja Maraldo
Anne Kiil-Berthelsen
Lena Specht

Thomas Björk-Eriksson
Per Nilsson
Ingrid Kristensen

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Även ett stort tack till Børncancerfonden!