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Craniospinal radiotherapy in children: Electron- or photon-based technique of spinal irradiation

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ABSTRACT

Background: The prone position and electron-based technique for craniospinal irradiation (CSI) have been standard in our department for many years. But this immobilization is difficult for the anaesthesiologist to gain airway access. The increasing number of children treated under anaesthesia led us to reconsider our technique.
Aim: The purpose of this study is to report our new photon-based technique for CSI which could be applied in both the supine and the prone position and to compare this technique with our electron-based technique.
Materials and methods: Between November 2007 and May 2008, 11 children with brain tumours were treated in the prone position with CSI. For 9 patients two treatment plans were created: the first one using photons and the second one using electron beams for spinal irradiation. We prepared seven 3D-conformal photon plans and four forward planned segmented field plans. We compared 20 treatment plans in terms of target dose homogeneity and sparing of organs at risk.
Results: In segmented field plans better dose homogeneity in the thecal sac volume was achieved than in electron-based plans. Regarding doses in organs at risk, in photon-based plans we obtained a lower dose in the thyroid but a higher one in the heart and liver.
Conclusions: Our technique can be applied in both the supine and prone position and it seems to be more feasible and precise than the electron technique. However, more homogeneous target coverage and higher precision of dose delivery for photons are obtained at the cost of slightly higher doses to the heart and liver.

1. Background

The entire craniospinal axis is the standard radiation volume for the treatment of primary brain tumours with a risk of leptomeningeal spread.[1] Many of these tumours are found in young children who may require anaesthesia during their therapy. The prone position during CSI was standard for many years. But this therapeutic immobilization is difficult for the anaesthesiologist to gain airway access. Some authors report that the supine position is simple and together with airway access provides other advantages. It is more comfortable and more reproducible.[2–5] But this position constrains application to only the photon-based technique for spine irradiation. In young children, especially, severe toxicity is of our interest. Adverse effects connected with neuraxis irradiation include

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neuroendocrine and neurocognitive dysfunctions, but in addition, the exit dose of the photon beam for spinal irradiation is potentially associated with late cardiac, pulmonary and bone damage.[2,3,6–9] Electrons are more conformal and potentially spinal irradiation with electrons is more protective for structures outside the target volume on the beam path.[3,10]

The CSI technique in our department has evolved over the last decades. High-energy electrons for spine irradiation have been used since 1986 and this 2D technique and treatment results in 158 children with medulloblastoma were published previously.[11] In the next report we presented the outcome and patterns of failure for 95 patients with medulloblastoma treated with 3D-conformal radiotherapy.[12] New equipment installed in our department (accelerators with CBCT and TPS with forward IMRT planning) together with an increasing number of young children treated under anaesthesia led us to reconsider our technique of craniospinal irradiation. Therefore we propose a new, photon-based technique with characteristic features: two isocentres, intrafraction moving beam junction, and oblique beams in the thyroid region between lateral cranial and posterior spinal beams.

2. Aim

The aim of this study is to report our new photon-based technique for CSI which could be applied in both the supine and the prone position and to compare this technique with the old electron-based technique. The treatment plans were compared in terms of dose homogeneity in the target volume and sparing of organs at risk.

3. Materials and methods

During 6 months, between November 2007 and May 2008, 11 children, aged 4–13 years (median 6 years), were treated with craniospinal irradiation. The diagnoses included medulloblastoma/PNET in 7, anaplastic ependymoma in 2 and atypical teratoid rhabdoid tumour in 2 patients. Patients received 25.05 or 35.07 Gy CSI in 15 or 21 fractions. The primary tumour site was subsequently boosted to the dose of 54–55.11 Gy. All children were immobilized in the prone position with an individual thermoplastic mask for the head. For 9 patients two treatment plans for spinal irradiation were created: the first one using photons and the second one using 18–22 MeV electron beams. In two cases the spine was localized too deep for the electron beam and these patients had only photon treatment plans.

The treatment planning was based on the 3 mm spaced CT slices from the top of the head to the level of the aortic arch and 9 mm elsewhere. The brain and the whole length of the thecal sac were contoured and defined as the $\mathrm{CTV}_{\mathrm{brain}}$ and $\mathrm{CTV}_{\mathrm{spine}}$. $\mathrm{PTV}_{\mathrm{brain}}$ encompassed a 4 mm margin around the $\mathrm{CTV}_{\mathrm{brain}}$ in all directions. In $\mathrm{PTV}_{\mathrm{spine}}$ the lateral margin was set to 10 mm because of the possibility of a child moving. Organs at risk that we additionally outlined were the thyroid, heart, lungs, liver, kidneys and vertebral body.

Our electron technique was reported previously.[11,12] Our new photon-based technique is a two-isocentre treatment technique which could be applied for both the supine and prone position. We performed two methods of planning: conformal 3D (for 7 patients) and forward planned segmented fields (for 4 patients). In our photon-based technique the brain with the upper cervical part of the spine (usually to the C3 level) was treated with 6 MV photon lateral beams with zero collimator angle. Custom blocks together with the MLC were used in both cranial fields to improve shielding of eye lens and the target conformity in the vicinity of the cribriform plate. The spine besides the thyroid region was treated with a 6 MV posterior photon beam. The width of the spinal fields was comparable with the width of the electron fields, which was about 5.5 cm. Between cranial and spinal beams two additional oblique fields were added in the thyroid region in order to reduce the dose to the thyroid gland. Such beam arrangement also helped to avoid irradiation of the mandible and oral cavity. These 15 MV photon beams, isocentric with cranial beams, covered the part of the spine in the vicinity of the thyroid gland. Gantry angles for cervical fields were 70° and 290°. The edges of these fields matched cranial fields from one side and the posterior spinal field from the other.

To ensure an even dose distribution at the match lines intrafraction feathering technique was used with two- and three-level intrafraction junctions for conformal 3D and forward planned segmented fields plans, respectively. Our standard CSI treatment plan with segmented fields comprised in total five beams. This number doubled for conformal 3D planning with two-level junctions. In our standard CSI treatment plan with segmented fields small weight segments were added to the cranial and spinal beams to improve dose homogeneity within the spine volume and to reduce the maximum dose to organs at risk. Four, three and five segments existed typically in each cranial, cervical and spinal field, respectively.

We compared target dose homogeneity and sparing of organs at risk for 20 treatment plans (11 photon and 9 electron). For all plans we calculated the standard deviation of the dose distribution in $\mathrm{CTV}_{\mathrm{spine}}$ and $\mathrm{PTV}_{\mathrm{spine}}$ for the total dose and the average doses to organs at risk as the percentage of the average dose in the $\mathrm{CTV}_{\mathrm{spine}}$. Additionally we compared the average values of standard deviation for photon conformal 3D and forward planned segmented field plans.

4. Results

Standard deviations of dose distribution in the spine are presented in Tables 1 and 2.

In the photon f-IMRT plans for the spine the dose homogeneity in CTV and PTV was better than in electron-based plans. However, the comparison of the values of the standard deviations of dose distribution in the spine does not reflect the existing radiobiological differences between plans. The photon beam junctions were moved within each fraction while the electron beam junctions were changed once during the whole CNS treatment, after the first half of the therapy. Better dose homogeneity in the spine for photons is radiobiologically enhanced by the introduction of a three-level intrafraction beam junction.

The average doses in the organs at risk are presented in Table 3.

Table 1 – The dose homogeneity in the target volume for photon and electron plans.

Target		Photons (11 plans)	Electrons (9 plans)
PTV_{spine}	σ_{min} [%]	2.8	2.8
	σ_{max} [%]	4.2	3.6
	σ_{av} [%]	3.3	3.3
CTV_{spine}	σ_{min} [%]	2.0	2.6
	σ_{max} [%]	3.3	3.4
	σ_{av} [%]	2.5	2.9

$\sigma_{min}, \sigma_{max}, \sigma_{av}$—the minimum, maximum and average value of standard deviation

Table 3 – The average doses in critical structures presented as the percentage of the average dose in the spine.

Organ at risk	Photons	Electrons
Thyroid gland	21 ± 6	35 ± 6
Lung left	16 ± 8	19 ± 5
Lung right	18 ± 7	24 ± 4
Heart	50 ± 7	28 ± 7
Kidney left	9 ± 3	16 ± 6
Kidney right	14 ± 8	25 ± 7
Liver	20 ± 4	10 ± 4
Vertebral body	92 ± 1	90 ± 3

In the photon-based plans we obtained a lower dose in the thyroid gland, lungs and kidney, but a higher one in the heart and liver. We managed to obtain a lower dose to the thyroid for photons due to the presence of the oblique beams in this region. The average dose in vertebral bodies was comparable in photon and electron plans but in our electron plans we used relatively high electron energies.

5. Discussion

Craniospinal irradiation is a very complex technique and the use of newer conformal methods is needed to limit doses to surrounding healthy tissues. A wide range of the technique with various radiation modalities has been used to irradiate the entire craniospinal axis.[1–5,13]

The presented results showed that our photon-based technique for spinal irradiation, which may be applied in both the supine and prone position, is superior to the electron-based technique in respect to target dose homogeneity. The supine position is more comfortable and is better tolerated by children, as well as being considered safer if anaesthesia is required.[2–4]

Some young patients with brain tumours will survive many years and late effects of radiation therapy such as somatic and carcinogenic effects may be observed during the follow-up period. Long-term side effects associated with spinal treatment include hypothyroidism, increased incidence of cardiac disease, restrictive lung disease (RLD), direct effects on bone growth and second malignancies. Many of these effects are dose related.[2,3,6–9,14–18]

Primary hypothyroidism is a well-known late effect from CSI. It is caused commonly by the direct effect of ionizing radiation on the thyroid gland. Up to one-third of patients develop primary hypothyroidism after CSI.[6,15–17] Reduction of the CSI dose from 36 to 23.4 Gy does not produce any detectable difference in thyroid toxicity.[15] Reduction in this damage was observed only in hyperfractionated regimens and when the thyroid gland was spared from the exit dose of the spinal field.[16,17] In our report, in the photon-based technique, the thyroid was spared by adopting two oblique fields in this region. The dose was reduced from 12 to 7 Gy when 35 Gy was applied for the spine.

Radiation-induced heart disease is well described after mediastinum irradiation in children.[19] Jakacki et al. described cardiac toxicity also in children who received craniospinal irradiation for medulloblastoma.[7] Spinal irradiation can deliver a significant exit dose to the heart. A relatively large percentage of the heart is in the beam path, especially when craniospinal irradiation is delivered using conventional 2D technique. In our analysis in photon plans the dose to the heart was nearly doubled compared to electron plans. Average doses for the heart were 17.5 Gy vs. 10 Gy, respectively, when 35 Gy was applied for the spine. Parker and coworkers reported that in the IMRT plans less than 1% of the heart volume was irradiated to doses above 15 Gy vs. 46% for 3D CRT plans.[3]

The use of photons or electrons for the spinal fields did not produce any detectable difference in pulmonary toxicity. In our report in the photon plans the dose was slightly lower than in electron plans. Studies of pulmonary function after CSI have rarely been undertaken, perhaps because of the small volume of lung included in a spinal field. In patients after CSI, the decreased growth of the spine is often connected with the reduced chest volume and this could be the cause of restrictive lung disease. But in the majority of survivors RLD was asymptomatic.[9,18]

Adult height is often reduced in medulloblastoma survivors. This can be attributed to GH deficiency, early puberty and impaired spinal growth due to direct RT toxicity on the growing vertebral bodies. Decrease in sitting height is connected with the spine dose and younger age.[8] In our report there was no difference in the value of the dose applied to the vertebral bodies between the photon- and electron-based method.

Table 2 – The dose homogeneity in the target volume for conformal 3D and forward planned segmented fields plans.

Target		Photons conformal 3D (7 plans)	Photons forward planned segmented fields (4 plans)
PTV_{spine}	σ_{av} [%]	3.5	2.9
CTV_{spine}	σ_{av} [%]	2.7	2.2

σ_{av}—the average value of standard deviation

In this analysis we also compared doses received by the liver and kidney. In the literature there are no reports about late toxicity from these organs after CSI.

Parker and coworkers in a treatment planning study for spinal irradiation for IMRT technique achieved a better target coverage than for 3D-CRT and spared healthy tissues better in the high dose region, but increased the volume of tissues receiving middle and low doses outside the target.[3] These doses can be especially dangerous in paediatric oncology due to their carcinogenic effect.[14] Secondary cancer is one of the most severe side effects of therapy in children. Hall warned against the unnecessary use of IMRT, estimating an increase in frequency of second cancers from 1% to 1.75%.[14,20] However, in a large population study the dose response for the excess relative risk for secondary cancer of the CNS was linear.[21] In our forward planned segmented field technique the volume receiving intermediate and low doses is comparable with other posterior photon-based techniques. It can be only slightly higher due to the oblique fields in the thyroid region.

Proton therapy seems to be ideally suited to spinal irradiation, and would provide the best sparing of organs at risk as well as the smallest dose to non-target tissues, but is not yet widely available. Reduction in the risk of radio-induced malignancy is a strong theoretical argument in favour of this therapy.[6]

6. Conclusions

Our photon technique can be applied in both the supine and prone position. It seems to be more feasible and precise than the electron technique. The forward planned segmented field technique with three-level intrafraction junction is superior to conformal 3D planning with two junction levels in terms of dose homogeneity in the target volume, potential of shaping isodose distribution, and the beam delivery. Very good dose homogeneity can be obtained for the forward planned segmented fields plans. Doses to lungs, kidneys and the thyroid gland for our photon-based technique are comparable or even slightly lower than for electrons. However, more homogeneous target coverage and higher precision of dose delivery for photons are obtained at the cost of higher doses to the heart and liver.

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