

The use of flattening filter free irradiation mode in normo-fractionated treatments

Purpose

The option to irradiate patients without a flattening filter in the beam path is aiming at increased dose rates and reduced beam-on times. Since the flattening filter is a source of scatter radiation, its removal has the positive side effect of lowering out-of-field doses, which might reduce the risk of radiation induced second cancers in peripheral tissue.

A variety of planning studies has proven that the flattening filter free (FFF) mode of a linac allows reducing delivery times in stereotactic treatments with high fraction doses. The challenge in FFF treatment planning is, however, treatment of large targets due to dose decrease with distance from the central beam axis. In addition delivery times are influenced to a larger extent by mechanical constraints of the gantry and the multi leaf collimator in normo-fractionated treatments with fraction doses around 2 Gy.

Four studies have been performed at our department comparing the two irradiation modes with (FF) and without flattening filter for normo-fractionated intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) of prostate cancer¹, breast cancer^{2,3}, hypopharyngeal cancer⁴, and childhood ependymoma. The aim of this study was to review the data of these studies and to identify general advantages and disadvantages of the FFF irradiation mode independent of the target site.

Material and methods

Planning

For each of the 4 studies VMAT and IMRT plans had been created for at least 10 patients in FF and FFF mode with identical dose volume objectives. Target sites and prescription doses are listed in table 1. Common measures of plan quality were V95%, Conformity Index (CI), and Homogeneity Index (HI) for the target volumes. OAR measures were dependent on the target type and therefore not suitable as general measures.

Target	Prescription dose	# fractions
Hypopharynx PTV / SIB	54 Gy / 66 Gy	30
Breast PTV / SIB	50.4 Gy / 63 Gy	28
Prostate PTV / SIB	62.5 Gy / 72.6 Gy	33
Ependymoma PTV	50.4 Gy	28

Table 1: Target sites and prescription doses.
PTV: Planning Target Volume,
SIB: Simultaneous Integrated Boost volume

Dosimetry

All treatment plans were verified by a 2D-ionization-chamber-array, and delivery times were measured from first beam on to last beam off. Out-of-field doses were determined with an ionization chamber at 31 cm from isocenter. The radiation induced second cancer risk is proportional to dose up to around 2 Gy. The measurement setup is shown in figure 1.

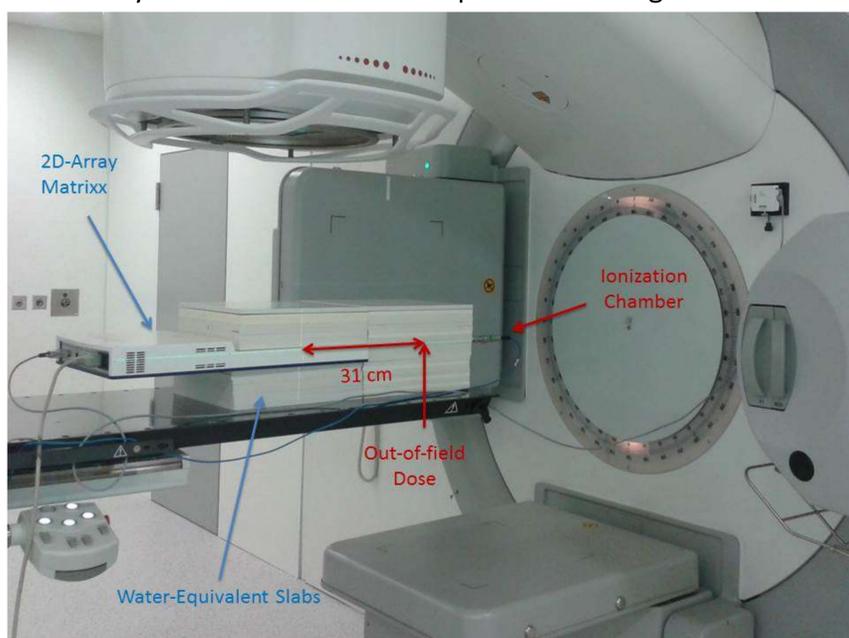


Figure 1: Measurement setup

Statistical evaluation

The data of the common measures of the four studies were pooled for statistical evaluation. To allow comparison of the measures despite differences in prescription dose, the data were normalized to the value of the measure in FF mode. Differences between the irradiation modes were calculated in percent of the value in FF mode.

The two sided Wilcoxon signed rank test was used to detect relevant differences with a significance level of $\alpha = 0.05$. Due to multiple pairwise comparisons, the Bonferroni-Holm method for multiple testing was applied to control the maximum experimentwise error rate by adjusting the level of significance: All hypotheses are sorted in order of smallest p-value to largest. The m-th hypothesis out of n is rejected if $p_m \leq \alpha / (n+1-m) = \alpha_{n,m}$. The process is stopped when one hypothesis is accepted.

Results

All plans passed the dosimetrical verification. The results of the statistical evaluation are shown in figure 2 and table 2.

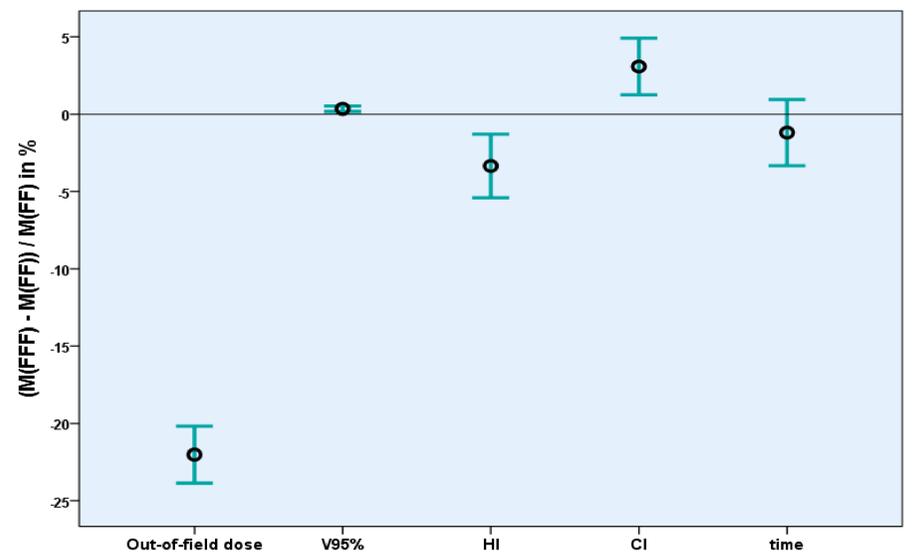


Figure 2: Graphical illustration of the relative differences (mean value and standard deviation over all cases) between FFF and FF for the five common measures M in % of the reference value M(FF).

Measure M	$(M(FFF)-M(FF)) / M(FF)$	p	$\alpha_{n,m}$
Out-of-field dose	- 20.1 %	0.000	0.0100
Target V95%	0.3 %	0.000	0.0125
Target HI	- 1.8 %	0.002	0.0167
Target CI	1.8 %	0.043	0.0250
Delivery time	- 1.2 %	0.156	0.0500

Table 2: Relative differences between FFF and FF irradiation mode for the 5 common measures M in % of the reference value M(FF) (mean over all cases). Bold values indicate statistically significant improvements of FFF versus FF.

Statistically significant differences were found for out-of-field dose, target V95% and HI, all of them in favour of FFF. Differences of target V95% and HI were, however, below 2% and are therefore considered of limited clinical relevance.

The out-of-field dose as a measure of radiation induced second cancer risk in peripheral organs was substantially reduced in FFF mode. The reduction amounted to 20% averaged over all cases.

Conclusion

The only statistically significant and clinically relevant advantage of the FFF mode was a reduction in dose to peripheral organs, corresponding to a mean reduction of 20% in radiation induced second cancer risk in these organs.

Acknowledgement

This work was supported by the Bavarian State Ministry of the Environment and Consumer Protection (Bayerisches Ministerium für Umwelt und Verbraucherschutz)

Literatur

- Treutwein M. et al. Volumetric-modulated arc therapy and intensity-modulated radiation therapy treatment planning for prostate cancer with flattened beam and flattening filter free linear accelerators. J Appl Clin Med Phys, 2017. 18(5): p. 307-314.
- Maier J. et al. Simultaneous integrated boost (SIB) radiation therapy of right sided breast cancer with and without flattening filter - A treatment planning study. Radiat Oncol, 2016. 11(1): p. 111.
- Dobler B. et al. Second Cancer Risk after simultaneous integrated boost radiation therapy of right sided breast cancer with and without flattening filter. Strahlenther Onkol, 2016. 192(10): p. 687-95.
- Dobler B. et al. Simultaneous integrated boost therapy of carcinoma of the hypopharynx/larynx with and without flattening filter - a treatment planning and dosimetry study. Radiat Oncol, 2017. 12(1): p. 114.