Il trattamento VMAT con alto dose rate (FFF)

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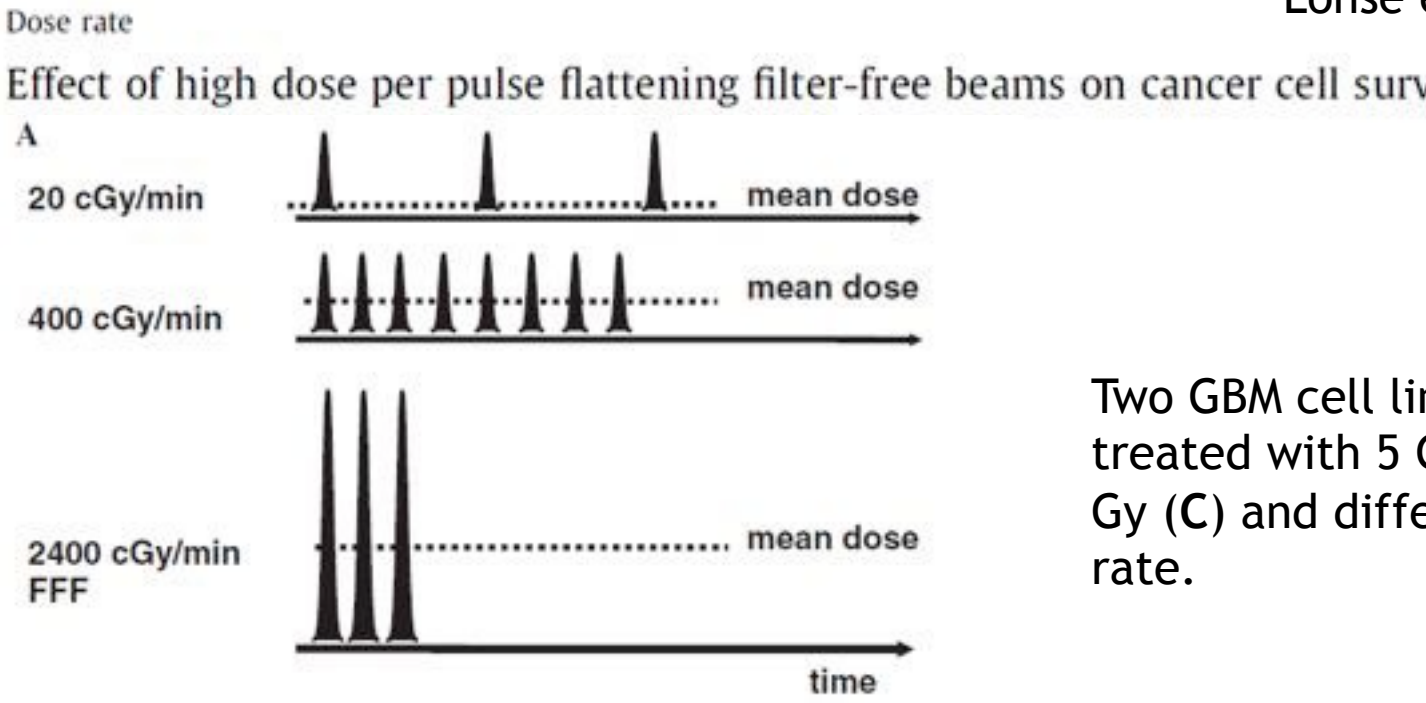
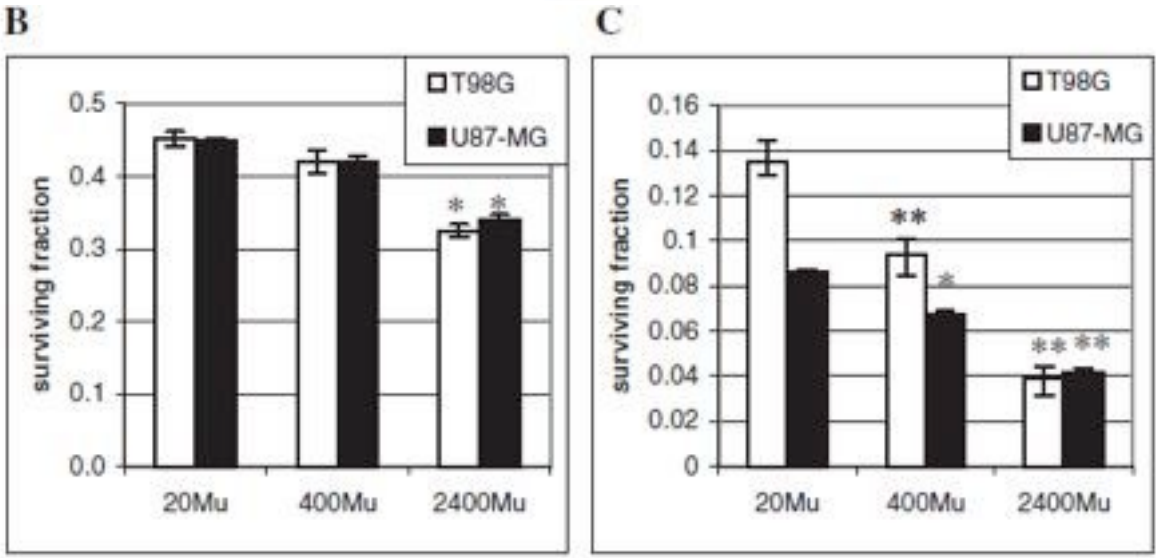
Radiobiology high-dose-rate

Lohse et al, 2011 R&O



Two GBM cell lines were treated with 5 Gy (**B**) or 10 Gy (**C**) and different dose-rate.



Clonogenic survival is statistically reduced if total dose is delivered with a higher dose per pulse.

HIGHER DOSES/PULSE

↑ DNA DEMAGE INDUCTION

↑ DSB

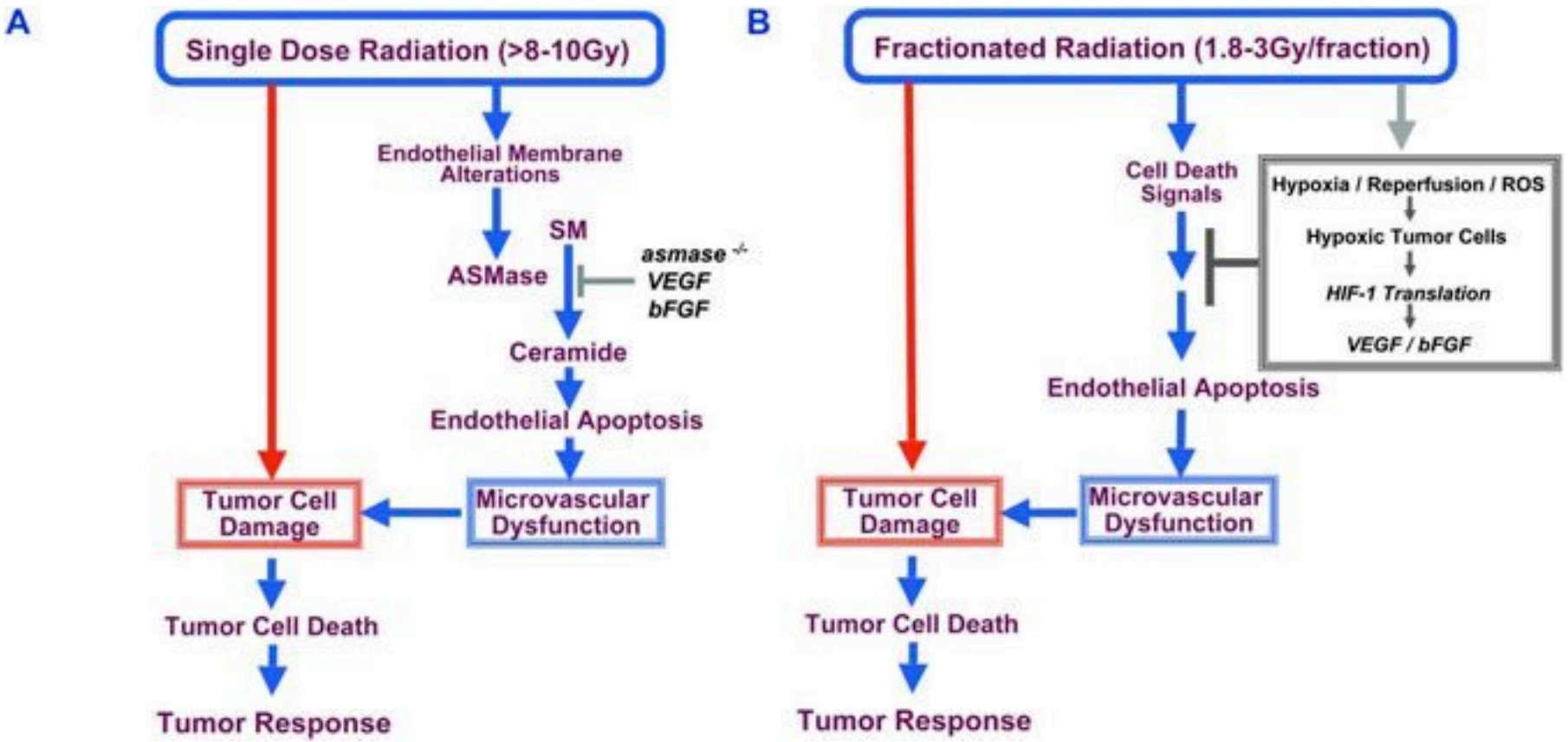
↑ CHANGES IN PROTEIN

↑ CHANGES IN FATTY ACIDS

Hamilton J, et al. IJROBP 2009
Jeggo P, et al. IJROBP 2009
Yoshida H, et al. IUBMB 2009

Results: The results presented here demonstrate that irradiation of glioblastoma cell lines using the FFF beam is more efficient in reducing clonogenic cell survival than the standard flattened beam, an effect which becomes more significant the higher the single dose. Interestingly, in our experimental setting, the radiobiological effect of the FFF beam is dependent on dose per pulse rather than on delivery time. The used radiobiological models are able to describe the observed dose rate dependency between 6 and 24 Gy/min.

Effect of Single High Dose



(Fuks, 2005)

Radiobiology high-dose-rate

"An in vitro study of the radiobiological effects of flattening filter free radiotherapy treatments"

King RB, et al Phys. Med. Biol. 2013

To determine the radiobiological impact of the increased dose-rates from FFF exposures a Varian Truebeam medical linear accelerator was used to irradiate two human cancer cell lines *in vitro*, **DU-145 prostate and H460 non-small cell lung**, with both flattened and FFF 6 MV beams.

↓

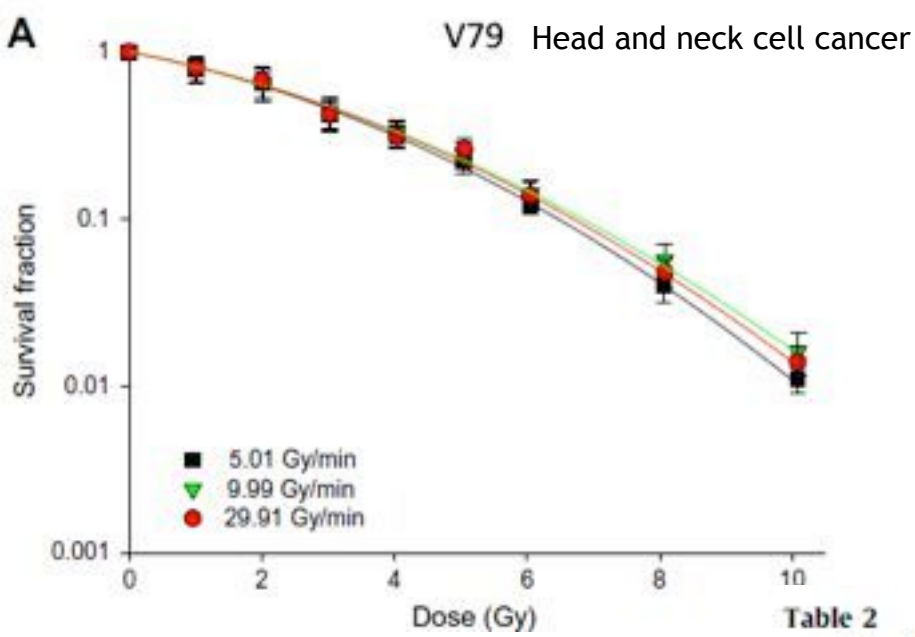
For both cell lines there appeared to be no significant change in cell survival. Collective damage behaviour does not occur at the instantaneous dose-rates investigated and the use of either modality should result in the same clinical outcome, however this will require further validation *in vivo*.

Radiobiology high-dose-rate

Sorensen et al, 2011 R&O

Dose rate

Dependence of cell survival on instantaneous dose rate of a linear accelerator



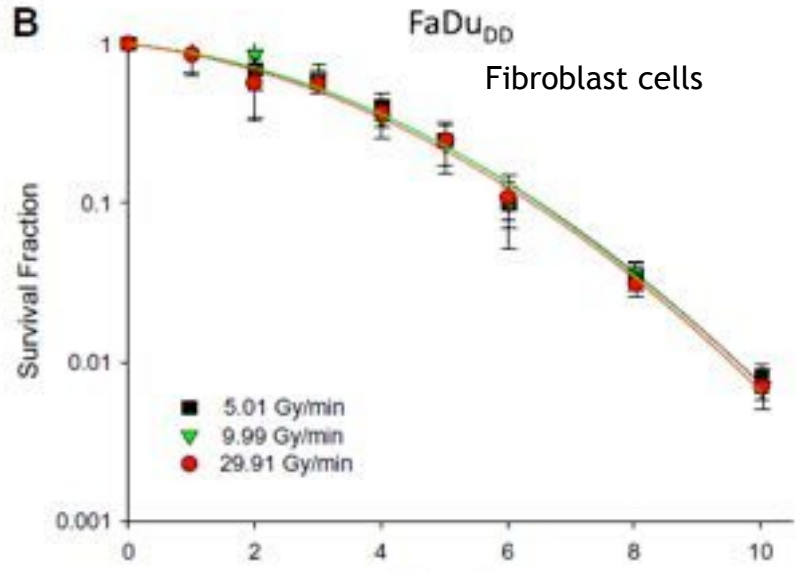


Table 2

α and β values of the fitted curves in Fig. 2. The indicated errors are standard errors.

Cell line	Dose rate (Gy/s)	α (Gy^{-1})	β (Gy^{-2})
V79	56.5	−0.179 ± 0.010	−0.027 ± 0.001
V79	112.8	−0.179 ± 0.009	−0.023 ± 0.001
V79	338	−0.175 ± 0.017	−0.025 ± 0.002
FaDu$_{DD}$	56.5	−0.098 ± 0.033	−0.039 ± 0.004
FaDu$_{DD}$	112.8	−0.088 ± 0.035	−0.041 ± 0.004
FaDu$_{DD}$	338	0.114 ± 0.026	−0.039 ± 0.003

The 3 dose rates have identical effects in cell survival

Solid malignant tumors are characterized by an inadequate vascular system, which can result in the development of hypoxic microregional areas within the tumors.

At high dose rates, a reduction in the biological effect can be found, possible due to consumption of oxygen by a higher radical production.

This study investigated the influence of a high dose rate on clonogenic cell survival for two cell lines at 21% of oxygen, and do not take tumor hypoxia into account.

No effect of the instantaneous dose rate on cell survival was observed.

This suggests that the high instantaneous dose rates of FFF linear accelerators will not influence either treatment outcome nor toxicity.

Radiobiology high-dose-rate – Some open issues

- Controversial results of *in vitro* studies
- Different clinical outcomes in tumour tissues between conventional and high dose rate ?
- Different results in different tumours with different biology ?
- What about healthy tissues (early-late responding) ?
- Which study design do wee need to investigate these issues ?