Cellular and gene expression changes in VH10 and AHH-1 cells after chronic and acute exposure to low doses of low, high and mixed LET ionizing radiation.

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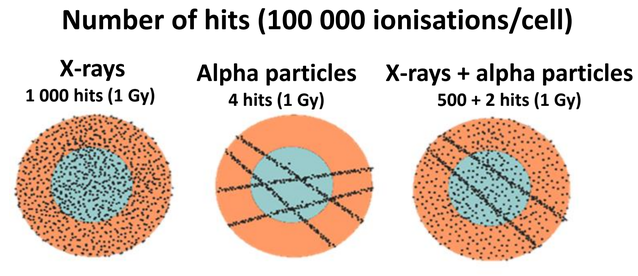
Background

Ionizing radiation exposures often comprise low doses and dose rates of different qualities, but the shape of the dose response curve for cellular effects is unknown. We aimed at better understanding the effects of chronic low doses and dose rates of distinct radiation qualities in two cell types differing in origin and radiosensitivity.



Methods

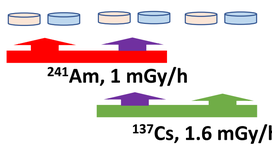
Cells: **VH10** (primary human fibroblasts)

AHH-1 (human B-lymphoblastoid cell line)

Chronic exposure

Doses: 0.05, 0.1, 0.15, 0.2 Gy

Analysis: 0 h post-exposure



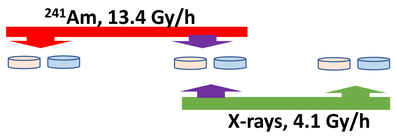
Acute exposure

Doses: 0.05, 0.1, 0.15, 0.2 Gy

Analysis: 24 h post-exposure

Doses: 0.1, 0.2, 1.0 Gy

Analysis: 4, 6, 8, 24 h post-exposure

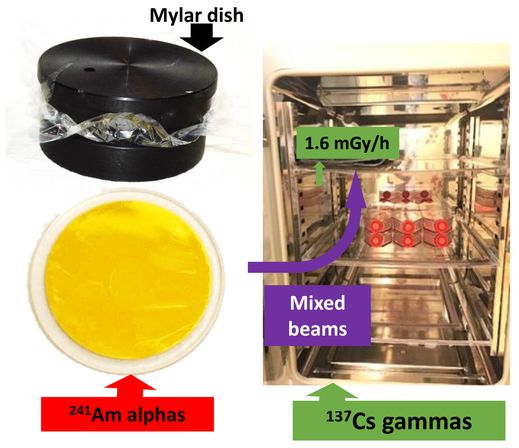


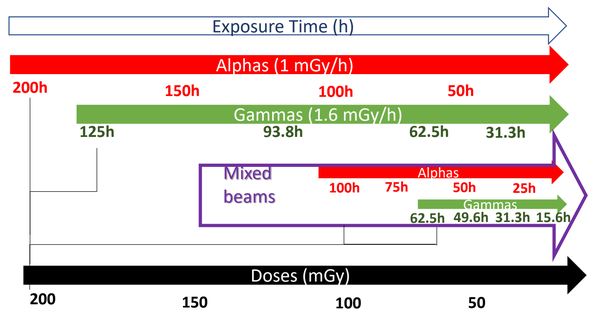
Gene expression (qRT-PCR): *BBC3*, *CDKN1A*, *FDXR*, *GADD45A*, *MDM2*, *XPC*.

Population doublings (trypan blue exclusion assay cell counts).

Micronucleus frequency, apoptosis, senescence, cell cycle arrest and oxidative stress (ongoing).

Chronic exposure



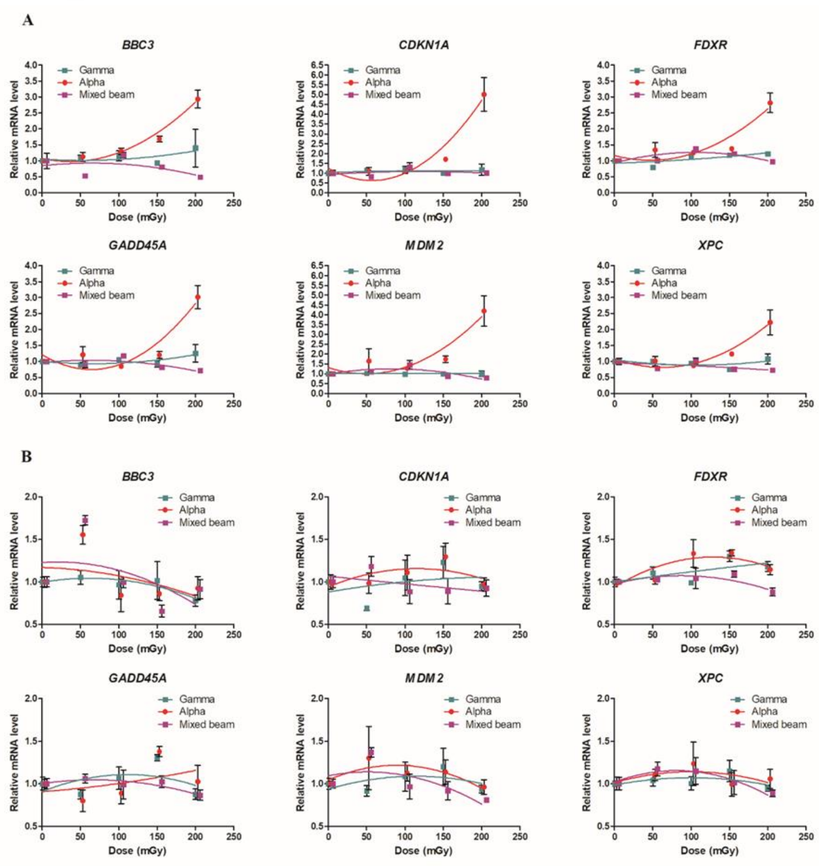


Acute exposure

Results

Chronic exposure

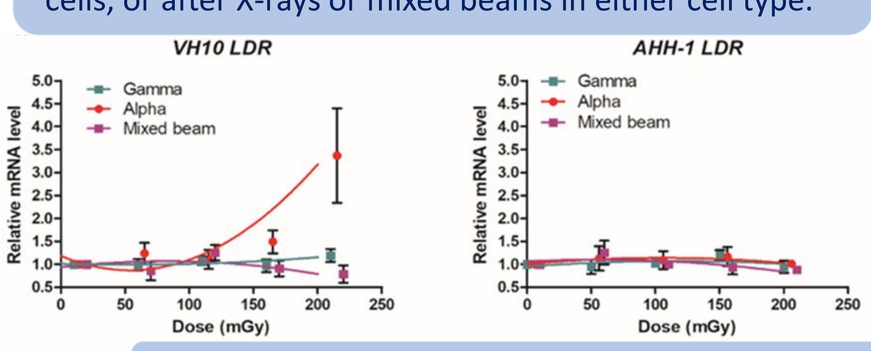
0 h post-exposure



VH10 cells

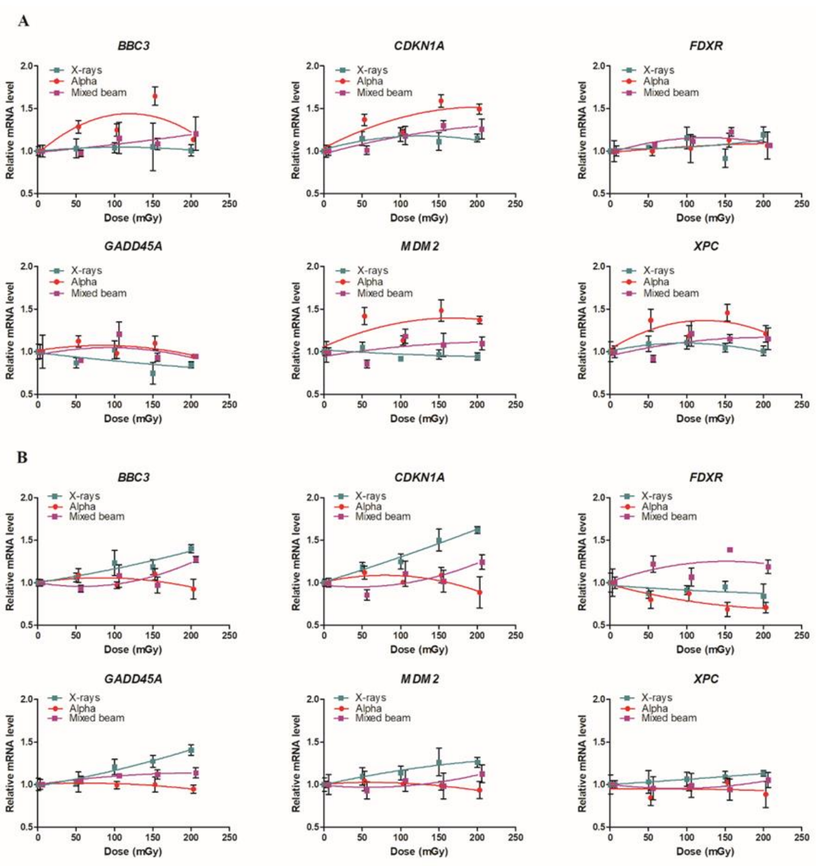
AHH-1 cells

Dose dependent upregulation of most genes at doses >150 mGy after chronic alpha exposure in VH10 cells, but no transcriptional changes relative to control in AHH-1 cells, or after X-rays or mixed beams in either cell type.

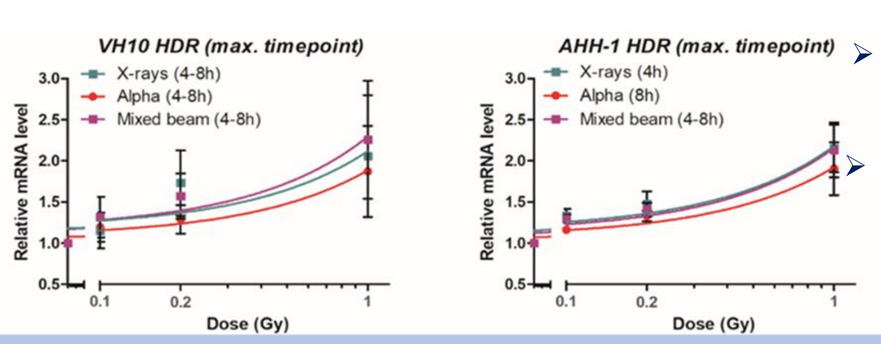


Acute exposure

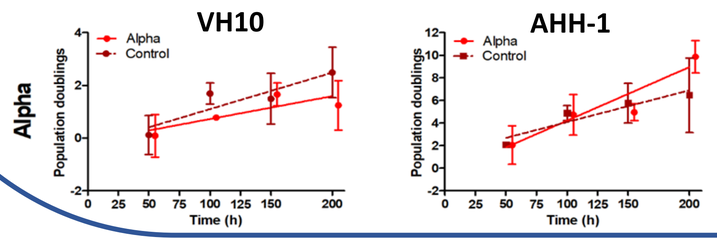
24 h post-exposure



Trend towards upregulation in some genes at 24 h post-acute alpha particle exposure in VH10, and after X-rays in AHH-1 cells.



Lower magnitude of transcriptional response after high dose rate (HDR) alpha exposure as compared to low dose rate (LDR) in VH10, not AHH-1 cells.



Reduced population doublings after chronic alpha particle exposure as compared to control in VH10, opposite trend in AHH-1 cells at 200 mGy.

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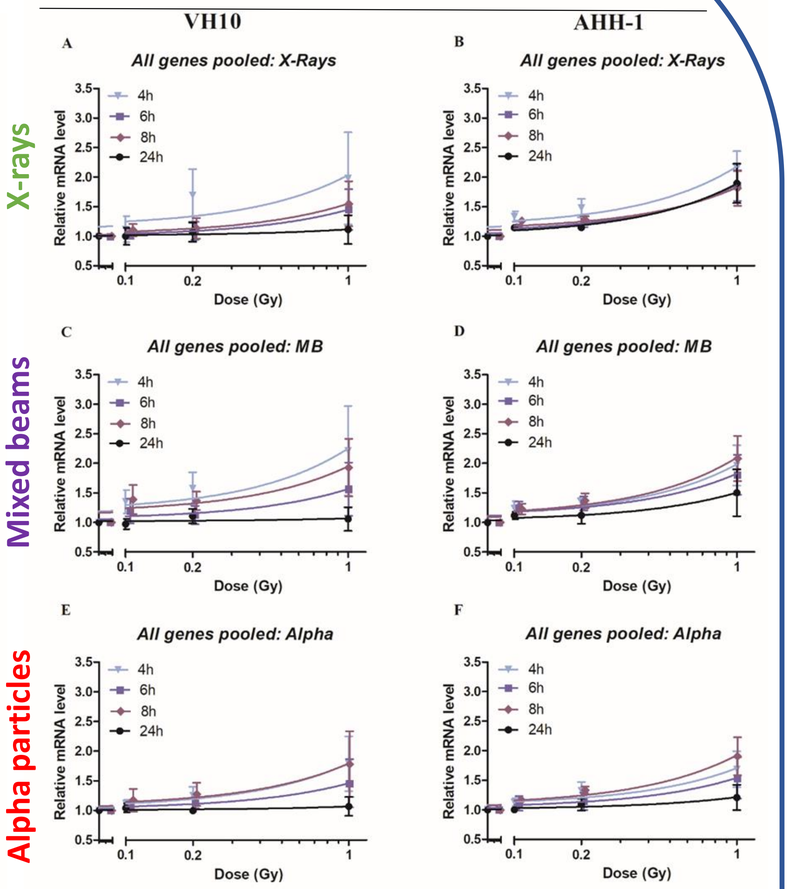
4-24 h post-exposure



- Time-dependent transcriptional responses after acute exposure , higher magnitude at <24 h timepoints.
- More stable effect after X-rays and mixed beams in AHH-1 as compared to VH10.
- Delayed responses after alpha exposure as compared to X-rays (mixed beams intermediate and gene-dependent).
- Similar transcriptional changes in acutely irradiated AHH-1 and VH10 cells at the timepoint of maximum gene induction: highest pooled gene expression for X-rays and mixed beams and lowest for alpha particles.

Conclusion

The transcriptional effect of IR depends on the dose rate, radiation quality, cell type and time point of analysis. The complexity of cellular responses to low doses of radiations of different qualities must be considered in attempts to infer health risks from cell-based studies.

Acknowledgments:

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