DNA DOUBLE STRAND REPAIR DURING HEAD-DOWN-TILT BEDREST: AGBRESA MEETS RADIATION

S. Diegeler[1*], J. Kronenberg[1], C. Schmitz[1], C.E. Hellweg[1], E. Mulder[2], M. Bohmeier[2], I. Schrage-Knoll[2], G. Kraus[2], E. Huth[2], C. Berwanger[2], F. Paulke[3], L. Lecheler[3] J. Jordan[4]

[1]Radiation Biology Department, German Aerospace Center (DLR), Institute of Aerospace Medicine, Cologne Germany, [*]sebastian.diegeler@dlr.de, [2]Muscle and Bone Metabolism Department, DLR, Institute of Aerospace Medicine, Cologne, Germany, [3]Study Team, DLR, Institute of Aerospace Medicine, Cologne, Germany, [4]DLR, Institute of Aerospace Medicine, Cologne, Germany

BACKGROUND

Radiation and reduced gravity impose a major burden on health and performance during human spaceflight. While radiation increases cancer risk and limits tissue regeneration, reduced gravity predisposes to musculoskeletal and cardiovascular deconditioning. Deconditioning could conceivably limit the recovery from radiation damage. Our aim was to develop a terrestrial *ex vivo* model that could be utilized to study the interaction between simulated reduced gravity using head-down-tilt bed rest and radiation on cellular DNA repair.

METHODS

We obtained blood samples from participants of the Artificial Gravity Bed Rest Study 2019 (AGBRESA) 14 days before down bed-rest (BDC -14), 30 and 57 days into bed-rest (HDT 30 and HDT 57), and after 10 days recovery (R +10). The 60 days strict head-down-tilt bedrest compares two short-arm centrifugation protocols as a countermeasure with a control group. We assessed the repair of *ex vivo* induced DNA double strand breaks in human peripheral blood mononuclear cells (PBMC). PBMC isolated through Histopaque-1077 in density gradient centrifugation were exposed to 1 and 4 Gy X-rays to induce DNA double strand breaks. Cells were fixed 0.5, 1, 2, 4 and 24 h after X-irradiation. DNA double strand breaks were detected via immunofluorescence staining of γH2AX and quantified using flow cytometry.

RESULTS

At BDC-14 the relative γH2AX fluorescence signal of PBMC increased starting at 0.5 h (1 Gy: 2.21 ± 0.30, 4 Gy: 3.76 ± 0.58, $n = 16$) and reached a peak 2 h post-irradiation (1 Gy: 2.77 ± 0.21, 4 Gy: 4.80 ± 0.71, $n = 16$). The γH2AX signal decreased at 4 h to levels similar to the 0.5 h time point (1 Gy: 2.13 ± 0.23, 4 Gy: 4.03 ± 0.34, $n = 16$). Over 24 h, the signal for 1 Gy X-irradiated PBMC returned to baseline (0.98 ± 0.09, $n = 16$), while exposure to 4 Gy X-rays resulted in residual damages (1.52 ± 0.17, $n = 16$).

CONCLUSION

The results from BDC -14 provide a baseline for DNA double strand break repair capacity of human PBMC. We will now assess how DNA repair capacity following radiation exposure is affected by simulated reduced gravity through head-down tilt bed-rest and short-arm centrifugation countermeasures.

ACKNOWLEDGEMENTS

The AGBRESA study was funded cooperatively by NASA and ESA and was conducted at the :envihab facility of the DLR Institute of Aerospace Medicine.