

# A model of radiation-induced myelopoiesis in space

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## Abstract

Astronauts' radiation exposure limits are based on experimental and epidemiological data obtained on Earth. It is assumed that radiation sensitivity remains the same in the extraterrestrial space. However, human radiosensitivity is dependent upon the response of the hematopoietic tissue to the radiation insult. It is well known that the immune system is affected by microgravity. We have developed a mathematical model of radiation-induced myelopoiesis which includes the effect of microgravity on bone marrow kinetics. It is assumed that cellular radiosensitivity is not modified by the space environment, but repopulation rates of stem and stromal cells are reduced as a function of time in weightlessness. A realistic model of the space radiation environment, including the HZE component, is used to simulate the radiation damage. A dedicated computer code was written and applied to solar particle events and to the mission to Mars. The results suggest that altered myelopoiesis and lymphopoiesis in microgravity might increase human radiosensitivity in space.

KEYWORDS: Myelopoiesis, space radiation, microgravity, computer code.

## 1. Introduction

Radiation risk to crews of long-term manned space missions are estimated using biophysical models of radiation action. In these models, the space radiation environment is carefully simulated, but the individual radiosensitivity is assumed to be the same on earth and in space. The hematopoietic tissue is the main radiation target for both acute radiation effects (e.g. in case of a solar particle event) and late stochastic risk (caused by low-dose chronic exposure to space radiation). It is known that the immune system function is altered in microgravity [1], yet so far this effect has not been considered in the estimates of astronauts' radiosensitivity.

We have modified a mathematical model of radiation-induced myelopoiesis, which has been widely used to describe the radiosensitivity of humans and animals on Earth [2]. The new model, tested on cancer patients' data treated with radiotherapy, describes the effect of whole and partial-body exposure, both on myelopoiesis and lymphopoiesis. Moreover it allows to consider the microgravity effects of bone marrow kinetics. An equivalent whole body prompt dose (EPD) for any reference radiation, i.e. the dose that would cause the same hematopoietic injury of a prompt exposure, is calculated for each exposure scenario.

## 2. The model

Hematopoietic cells are compartmentalised into normal (n), injured (i), and killed (k). Process by which these populations change are modelled by a set of three differential equations. The five  $\lambda_{xy}$  parameters in these equations describe the transition rates among compartments (from x to y compartment) and are cell- and radiation-type dependant. Parameters can

be evaluated for each exposure scenario.

We assume that cellular radiosensitivity is not modified by space environment, but repopulation rates ( $\lambda_{nn}$ ) of stem and stromal cells are reduced as a function of time in weightlessness. We assume that  $\lambda_{nn}$  varies with time as

$$\lambda_{nn}(t) = \lambda_{nn}(0) e^{-t/\tau}$$

where  $\lambda_{nn}(0)$  is the value in normal conditions and  $\lambda$  is calculated from the experimental value of  $\lambda_{nn}$  after a certain time in weightlessness. We used an 84% decrease after two weeks in space from published data [3].

The complex space radiation field has been divided into two main components: a low-LET component (parameters are calculated from <sup>60</sup>Co  $\gamma$ -rays) and a high-LET component (parameters are calculated from fission neutrons) [4]. The values of the five parameters, for a given cellular type, are obtained as a weighted mean of the values of the parameters for the single components (Table I) using the dose rates of each component (Table II) as weights.

**Table I** – Dose rates for each component of GCR and SPE radiation. These data refer to the period of minimum solar activity during which SPE should be rarer. The 5 g/cm<sup>2</sup> Aluminium shielding is the most likely to be used.

	GCR (cGy/min)		SPE (cGy/min)	
	Low-LET	High-LET	Low-LET	High-LET
5 g/cm <sup>2</sup> Al	1.54·10 <sup>-5</sup>	8.50·10 <sup>-6</sup>	3.92·10 <sup>-2</sup>	4.30·10 <sup>-3</sup>
Mars Surface	8.33·10 <sup>-6</sup>	2.43·10 <sup>-6</sup>	5.90·10 <sup>-3</sup>	5.21·10 <sup>-4</sup>

**Table II** – Values of the parameters of the model for the two components (low- and high-LET) and two space radiation events (galactic cosmic rays for the trip to mars, and solar particle event)

Parameter	Low-LET	High-LET	GCR	SPE
$\lambda_{NI}$ (cGy <sup>-1</sup> )	0.010200	0	$6,57 \cdot 10^{-3}$	$9,37 \cdot 10^{-3}$
$\lambda_{IN}$ (min <sup>-1</sup> )	0.060000	0	$3,86 \cdot 10^{-2}$	$5,51 \cdot 10^{-2}$
$\lambda_{NK}$ (cGy <sup>-1</sup> )	0.003600	0.020000	$9,43 \cdot 10^{-3}$	$4,92 \cdot 10^{-3}$
$\lambda_{IK}$ (cGy <sup>-1</sup> )	0.110000	0	$7,08 \cdot 10^{-2}$	$1,01 \cdot 10^{-1}$
$\lambda_{NN}$ (min <sup>-1</sup> )	0.000220	0.000220	$2,2 \cdot 10^{-4}$	$2,2 \cdot 10^{-4}$

### 3. Results and discussion

A FORTRAN computer code was written and applied to simulate a mission to Mars in the most likely mission scenario [5] considered by NASA (Earth-Mars: 9 months, 14 months on the planet, Mars-Earth: 10 months). Three different cases of the same mission scenario were simulated:

- case 1: both cellular surviving fraction and EPD are calculated using <sup>60</sup>Co  $\gamma$ -rays parameters, and not considering the microgravity effect.
- case 2: as case 1 but using the GCR parameters to calculate cellular surviving fraction.
- case 3: as case 2 but considering the microgravity effect.

Stem cells survival is displayed in Figure 1. In the mission to Mars, cell survival would be very high, being the radiation exposure characterized by a very low dose-rate. However, when the microgravity effect is considered (case 3), survival shows a sharp decrease towards the end of the mission. Even in this

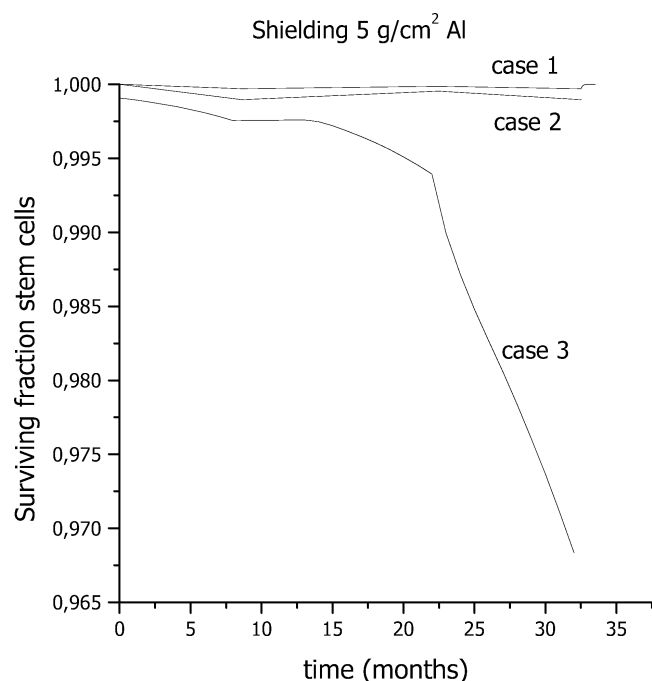


Fig. 1 – Surviving fraction for hematopoietic stem cells during a Mars mission in the three cases described in the text.

**Table III** – EPD for an SPE during a Mars mission. In the first column, the SPE radiation quality is not simulated (gamma rays are used instead), and the effect of microgravity is not included. In the second column, the SPE is simulated as described in Table II, and the microgravity effect is included.

	EPD (cGy)	
	$\gamma$ <sup>60</sup> Co - $\mu$ g	SPE + $\mu$ g
Beginning	78.3	218.2
Mars surface		223.7
End		233.1

**Table IV** – Death and cancer probability calculate from the EPD reported in Table III.

	Death probability		Cancer probability	
	$\gamma$ <sup>60</sup> Co - $\mu$ g	SPE + $\mu$ g	$\gamma$ <sup>60</sup> Co - $\mu$ g	SPE + $\mu$ g
Beginning		0.18		0.08
Mars surface		0.19		0.09
End	0.02	0.22	0.07	0.12

case, however, the cell survival remains so high that no significant cancer risk would be expected.

With the same method we calculated the values of the parameter for a Solar Particle Event (SPE) occurring during the Mars mission (Tables I and II). We simulated an SPE, similar to the August 1972 event [6], at different times from the beginning of the trip. Calculated EPD values are shown in Table 3. Death risk rises from 2% to 22% when microgravity is taken into account, while cancer probability rises from 7% to 12% (Table IV).

The results of these simulations show that altered immune system function can increase individual radiation sensitivity.

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