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A method to predict space radiation biological effectiveness for non-cancer effects following intense Solar Particle Events

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ABSTRACT

In addition to the continuous exposure to cosmic rays, astronauts in space are occasionally exposed to Solar Particle Events (SPE), which involve less energetic particles but can deliver much higher doses. The latter can exceed several Gy in a few hours for the most intense SPEs, for which non-stochastic effects are thus a major concern. To identify adequate shielding conditions that would allow respecting the dose limits established by the various space agencies, the absorbed dose in the considered organ/tissue must be multiplied by the corresponding Relative Biological Effectiveness (RBE), which is a complex quantity depending on several factors including particle type and energy, considered biological effect, level of effect (and thus absorbed dose), etc.

While in several studies only the particle-type dependence of RBE is taken into account, in this work we developed and applied a new approach where, thanks to an interface between the FLUKA Monte Carlo transport code and the BIANCA biophysical model, the RBE dependence on particle energy and absorbed dose was also considered. Furthermore, we included in the considered SPE spectra primary particles heavier than protons, which in many studies are neglected. This approach was then applied to the October 2003 SPE (the most intense SPE of solar cycle 23, also known as "Halloween event") and the January 2005 event, which was characterized by a lower fluence but a harder spectrum, i.e., with higher-energy particles. The calculation outcomes were then discussed and compared with the current dose limits established for skin and blood forming organs in case of 30-days missions.

This work showed that the BIANCA model, if interfaced to a radiation transport code, can be used to calculate the RBE values associated to Solar Particle Events. More generally, this work emphasizes the importance of taking into account the RBE dependence on particle energy and dose when calculating equivalent doses.

1. Introduction

Recently, human space exploration has gained a renewed interest, also thanks to the fact that NASA is planning to go back to the Moon with a human mission and that the Moon may represent an intermediate step towards Mars (www.nasa.gov). Human space missions are subject to many risks, including those due to space radiation, which has been classified as a "red risk" (Patel, 2020, Jul). In free space, Galactic Cosmic Rays (GCR), whose fluence consists of about 87 % protons, 12 % He ions and 1 % heavier ions, are responsible for a continuous exposure to a dose-rate in the order of 1 mSv/day (Durante and Cucinotta, 2011). This value is modulated by solar activity, which varies according to a 11-year cycle. When the activity of the Sun is maximum, the GCR flux is minimum, thanks to the protection provided by the Sun magnetic field; on the contrary at solar minimum the GCR flux is maximum. At solar minimum, the doses involved for sustained lunar operations of 1-year duration have been estimated to be in the range 0.10–0.12 Gy, corresponding to 0.18–0.22 Gy-Eq or 0.3–0.4 Sv (Simonsen et al., 2020). Due to the longer duration, the values would be higher for a Mars mission, for which it has been estimated that the dose would be in the range 0.30–0.45 Gy, that is 0.55–0.80 Gy-Eq or 0.87–1.20 Sv. GCR thus represent a serious hazard for the crewmembers of long-term missions. Several studies are available in the literature where astronauts' exposure has been investigated for different scenarios. In particular, our previous

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work showed that, for a 650-day mission at solar minimum, the calculated effective doses were lower than the career limit recommended by ICRP (1 Sv), but higher than the 600-mSv limit recently adopted by NASA (Ramos et al., 2023). This is the main reason why many authors suggest that a mission at solar maximum would be preferable.

However, a mission at solar maximum would be characterized by an increased probability of Solar Particle Events (SPE), which are occasional injections of high fluxes (up to more than 10^{10} particles cm^{-2} delivered in few hours) of charged particles coming from the Sun. Solar particle events occur when the activity on the Sun, such as a solar flare and/or a coronal mass ejection, accelerates and releases particles into the interplanetary medium. The actual process of solar particle acceleration is still under debate, although it probably consists of some type of shock acceleration process. Due to the high involved doses, intense SPEs represent a concern with respect to the so-called deterministic effects (or "tissue reactions").

With respect to such effects, all space agencies have established dose limits for skin, eye and blood-forming organs (BFO). Furthermore, NASA also considered heart and central nervous system (CNS), whereas JAXA included testes. The NASA limits for missions of different duration are reported in Table 1 (NASA 2022-01-05), whereas the ESA and RSA limits are reported in Table 2 (Cucinotta, 2010). While for skin and BFO the numbers are the same, for eyes the NASA values are higher than the ESA/RSA values by a factor 2. However, a comparison is not straightforward because the NASA limits are expressed in Gy–Eq, that is by multiplying the absorbed dose by the RBE (Relative Biological Effectiveness), whereas the ESA and RSA limits are expressed in Sieverts.

On this subject, it is worth mentioning that large uncertainties are associated to the RBE of space radiation (Durante and Cucinotta, 2008). The RBE values recommended by NCRP for short-term non-cancer effects are reported in Table 3. These values should be used for skin and BFO but not for late effects such as eye cataract, heart effects and CNS effects, for which the uncertainties are particularly large (Durante and Cucinotta, 2008).

Several modelling works are available in the literature on the effects of Solar Particle Event e.g., (Cucinotta, 1999, Kim et al. 1999; Wilson et al., 1999; Parsons and Townsend, 2000; F. Ballarini et al., 2006). Such works share the common philosophy of simulating the interactions of the different SPE spectrum components by means of an analytical or Monte Carlo radiation transport code; in general, the transport is first performed through an Al shield of variable thickness, and then in the human body. The latter is modelled by phantoms characterized by different levels of complexity, from simple water spheres to geometrical or voxel human phantoms that allow a very realistic representation of the various tissues and organs. In many of these works, the absorbed dose is then multiplied by fixed RBE values to get tissue-specific Gy-Equivalent doses that can be compared with the corresponding limits.

In this work we developed a different approach, based on cell survival RBE values calculated by means of the BIANCA biophysical model, developed within our research group e.g. (Ballarini and Carante, 2016; Carante et al., 2018). Specifically, BIANCA was applied to provide a database of particle- and energy-dependent linear and quadratic coefficients describing dose-response curves for in vitro cell survival. According to some studies, the use of the RBE for in vitro cell survival may not be adequate for the estimate of RBE for tissue reaction; in particular, Sato et al. (Sato et al., 2022) concluded that dermal cell survival RBE could lead to an underestimation of the RBE for skin reactions.

However, from a practical point of view, taking into account the actual tissue reactions is not trivial, also considering that even for a given tissue/organ there exist different reaction types (e.g. skin reddening, desquamation, necrosis etc.). As a consequence, since several works evaluate the RBE for tissue reactions based on in vitro cell survival, also in this work we made this pragmatic choice, based on the idea that cell death is thought to be closely related to non-cancer effects: if the number of lost cells is large, observable harm occurs, reflecting the loss of tissue function (Hall and Giaccia, 2012).

The database created by BIANCA was then read by the FLUKA Monte Carlo radiation transport code e.g. (Ferrari et al., 2005; Bohlen et al., 2014, Ballarini et al., 2022), which allowed voxel-by-voxel calculation of dose-averaged linear and quadratic coefficients, and thus of the corresponding RBE values. Finally, skin and BFO equivalent dose values were calculated as a function of Al shielding thickness following exposure to two intense SPEs.

Table 1
NASA limits for non-cancer effects (NASA 2022-01-05).

	30–day limit (Gy-Eq)	1-year limit (Gy-Eq)	career limit (Gy-Eq)
Skin	1.5	3.0	6.0
Eye	1.0	2.0	4.0
BFO	0.25	0.5	Not Applicable
Heart	0.25	0.5	1.0
CNS	0.5	1.0	1.5

Table 2
ESA and RSA limits for non-cancer effects (Cucinotta, 2010).

	30-day limit (Sv)	1-year limit (Sv)	career limit (Sv)
Skin	1.5	3.0	6.0 *(RSA only)*
Eye	0.5	1.0	2.0 *(RSA only)*
BFO	0.25	0.5	Not Applicable

Table 3
NCRP recommended RBE values for non-cancer effects to be used for skin and BFO (NCRP 2000).

Radiation Type	Recommended RBE	Range
1 to 5 MeV neutrons	6.0	4–8
5 to 50 MeV neutrons	3.5	2–5
Heavy ions	2.5	1–4
Protons > 2 MeV	1.5	–

2. Materials and methods

2.1. RBE calculation by the bianca biophysical model

BIANCA is a biophysical model, implemented as a Monte Carlo code, that initially was specifically developed for chromosome aberrations (A. Ottolenghi and Merzagora, 1999; A.Ottolenghi and Biaggi, 2001, Ballarini et al., 2002; Ballarini and Ottolenghi, 2004; Ballarini and Ottolenghi, 2005), but now simulates the induction of cell death and chromosome aberrations following cell irradiation by photons or by different monochromatic ion beams, that is with different ion types and different energy values. The assumptions and parameters of the model, as well as the main simulation steps to obtain (simulated) dose-response curves for chromosome aberrations or cell death, have been discussed in detail in several publications. Herein, we will just mention that BIANCA relies on the idea that ionizing radiation induces in the cell nucleus a certain yield of DNA "critical lesions", which interrupt the continuity of the chromatin fiber thus producing independent chromatin fragments. These fragments either remain un-rejoined, or undergo distance-dependent incorrect rejoining (i.e., rejoining with a partner fragment different than the original one), giving rise to different types of chromosome aberrations. Finally, some aberration types (dicentric chromosomes, rings and deletions) are assumed to lead to (clonogenic) cell death.

With the goal of predicting cell survival curves for different cell types as a function of radiation type and energy, as a first step a radiobiological database describing the survival of V79 cells (chosen as a reference) as a function of dose, ion type and energy has been produced (Carante et al., 2018), and then an algorithm has been developed to predict survival curves for other cell types (Carante et al., 2019).

More specifically, as explained in (Carante et al., 2019), to construct the V79-cell database we adjusted our two model parameters to many experimental survival curves (that is, for many different particle types and energy values); afterwards, for any other cell line of interest each (simulated) survival curve for a given ion type and energy, and thus the corresponding RBEs, is a full prediction based on: 1) the response of V79 cells to that ion type and energy; 2) the response of the cell line of interest to photons.

First, such work has been performed for ions with Z between 1 (protons) and 8 (Oxygen) (Carante et al., 2018; Carante et al., 2019), thus allowing for applications in the field of cancer hadrontherapy (Carante et al., 2019; Carante et al., 2020; Carante et al., 2021; Embriaco et al., 2021; Kozlowska et al., 2022). More recently, heavier ions up to Fe have been implemented (Ricardo L. Ramos et al., 2022), thus making it possible to perform calculations for space radiation (Ramos et al., 2023; Ricardo L. Ramos et al., 2022; Ricardo Ramos et al., 2022)).

The construction of the human skin fibroblast (HSF) database applied in the present work has been described in detail elsewhere (Ricardo L. Ramos et al., 2022). Herein, it is sufficient to mention that such database consists of a table that, for each ion type and LET, reports the linear and quadratic coefficients (called α and β, respectively) characterizing the well-known equation that is usually adopted to describe cell survival dose-response:

$$S(D) = e^{-\left(\alpha D + \beta D^2\right)} \tag{1}$$

In eq. (1), S(D) is the fraction of surviving cells after receiving an absorbed dose D.

In particular, the photon coefficients were $\alpha = 0.17\ Gy^{-1}$ and $\beta = 0.045\ Gy^{-2}$; the highest value for the linear coefficient was $2.71\ Gy^{-1}$ (for 175 keV/μm Carbon ions). In this framework it is worth mentioning that very low energy particles were assumed to deposit their energy locally, and the highest coefficients available from the BIANCA tables were associated to those particles. While this may not reflect the underlying radiobiological mechanisms, because phenomena like 'overkilling' occur at high LET, this conservative approach was adopted to avoid the risk of underestimating the biological effectiveness of very low energy particles.

In this work, the HSF database was used both for skin and for Blood Forming Organs (BFO). Of course, hematopoietic stem cells (HSC) may be a better choice to model BFO damage; however, the use of HSF cells was a pragmatic choice mainly related to the fact that more systematic data sets, for many different particles and particle energies, are available in the literature for human skin fibroblasts than for hematopoietic stem cells. More generally, different alpha/beta ratios for different in vivo tissue reactions have been reported: while for early responding tissues (skin, colon etc.) such ratio is around 10 Gy, early responding tissues (spinal cord, kidney, lung etc.) tend to show values of about 2 Gy (Hall and Giaccia, 2012). In this respect, the value of 3.8 Gy resulting from the alpha and beta coefficients applied in this work ($\alpha = 0.17\ Gy^{-1}$, $\beta = 0.045\ Gy^{-2}$) is intermediate between these two groups.

In principle, the tables containing the linear and quadratic coefficients produced by BIANCA can be read by any radiation transport code; in this work they were read by FLUKA, exploiting a pre-existing interface between FLUKA and BIANCA. Specifically, whenever according to FLUKA a certain amount of energy (and thus a certain dose, D_i) was deposited in a target voxel by a given radiation type *i* (where "radiation type" means a given particle of given energy, and thus given LET), FLUKA read from the tables provided by BIANCA the corresponding cell-survival coefficients (called α_i and β_i) and used them to calculate the dose-averaged coefficients (called α and β) describing cell survival due to the mixed radiation field in that voxel:

$$\alpha = \frac{\sum_{i=1}^{n} \alpha_i D_i}{\sum_{i=1}^{n} D_i} \tag{2}$$

$$\sqrt{\beta} = \frac{\sum_{i=1}^{n} \sqrt{\beta_i} D_i}{\sum_{i=1}^{n} D_i} \tag{3}$$

This approach is based on the Theory of Dual Radiation action (TDRA) initially proposed by Kellerer and Rossi (Kellerer and Rossi, 1978), according to which a biological system exposed to more than one radiation type shows synergism, implying that the total number of lesions is larger than the sum of the lesions produced by each particle, due to interactions between sub-lesions produced by different components. This method has been applied in several previous works, mainly in the framework of cancer hadron therapy, in which FLUKA has been coupled either with the Local Effect Model e.g. (Mairani et al., 2010) or with BIANCA (Carante et al., 2019; Carante et al., 2020; Carante et al., 2021; Embriaco et al., 2021; Kozlowska et al., 2022).

Following calculation of the dose-averaged coefficients, the RBE in each voxel was calculated as D_X/D, where D is the total absorbed dose in the voxel, whereas D_X is the photon dose necessary to obtain the same biological effect, i.e. the same level of cell survival. The value of D_X was calculated according to eq. (4):

$$D_x = \frac{-\alpha_x + \sqrt{\alpha_x^2 - 4\beta_x \ln S(D)}}{2\beta_x} \tag{4}$$

In principle, the RBE values for deterministic effects may be obtained at doses corresponding to the threshold level for individual effects. However, this task is complex because there are different RBE values in different tissues for different endpoints; moreover, the threshold doses vary among individuals, and are not always easily determined. Therefore, ICRP Publication no. 58, 1990 (ICRP 1990), recommends reference to the low-dose limit of RBE for deterministic effects, although this implies extrapolation to doses at which the responses to both radiation types (the considered radiation and the reference radiation) were below the threshold. To overcome such limitations, in this work we adopted a new approach: in each voxel, the absorbed dose in the voxel, D, was multiplied by a RBE value obtained as D_x/D, where D_X is the photon dose calculated following eq. (4).

2.2. FLUKA simulations

Analogous to our previous GCR study (Ramos et al., 2023), the astronaut's exposure to a SPE inside a spacecraft in deep space was modeled by irradiating with FLUKA a spherical water phantom with radius 15 cm, placed into a cylindrical Aluminium shielding with radius 38 cm, height 180 cm and variable thickness. The selected values for the Al thickness varied from 0.3 g/cm^2 (light spacesuit) up to 30 g/cm^2, to simulate the necessary shielding in case of a very intense SPE (see below). The space between the shielding and the water phantom was filled with air. An isotropic spherical source of 200 cm radius was implemented in the simulations. Two spectra were considered, one from the October 2003 event, which is the most intense SPE of solar cycle 23, and one from the January 2005 event, which is less intense but "harder", since it involves higher energy particles. Fig. 1 shows the H, He and O particle fluence for these two events. The figure was produced by directly plotting the files "sep28oct2003.spc" and "sep20jan2005.spc" embedded in FLUKA, which report the particle fluence as a function of energy for H- He- and O-ions.

It is worth outlining that, although most primary particles are protons, the contribution of heavier ions in terms of biological effects may be not negligible, since the latter have higher LET and thus higher RBE.

Thanks to the interface between BIANCA and FLUKA, in addition to the absorbed dose we calculated the corresponding RBE values and thus the equivalent doses. For the RBE calculations, we considered Human Skin Fibroblast (HSF) cells, for which in a previous work (Ricardo L. Ramos et al., 2022) we have generated a radiobiological database describing cell survival as a function of ion type ($1 \leq Z \leq 26$) and LET, as well as absorbed dose. In this work, the RBE values calculated for HSF

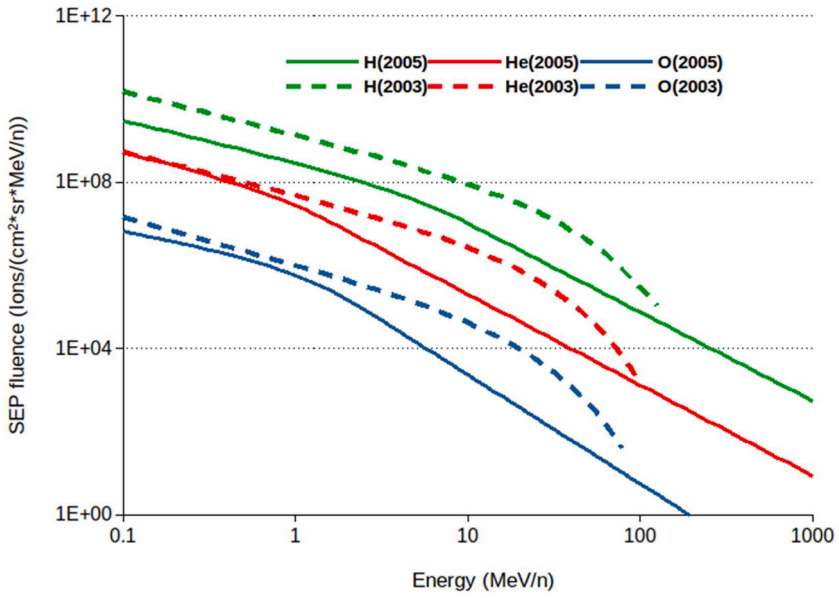

Fig. 1. H, He and O particle fluence from the two considered SPEs.

cell survival were used to predict the equivalent dose (in Gy-Eq) for deterministic effects, since these effects are strongly related to cell killing; this is not applicable for cataract induction (ICRP 1990).

As shown in Fig. 2, the skin dose was calculated considering the 1.5 mm superficial layer of the spherical phantom, whereas the BFO dose was calculated in a 5 mm layer located 2.5 cm under the phantom surface. Concerning the skin thickness, ICRP recommends to use a 0.07 mm value for dose calculations related to stochastic effects; however, since SPE exposure is mainly related to deterministic effects, which also occur in deeper skin layers, in this work we preferred to use a 1.5 mm value, which is intermediate between the 1.6 mm value for male and the 1.3 value for female reported in ICRP publication 110 (ICRP 2009). Concerning BFO, the 2.5 cm depth was chosen according to Dobynde et al., (2021).

The predicted equivalent doses were then compared with the recommended astronauts' dose limits.

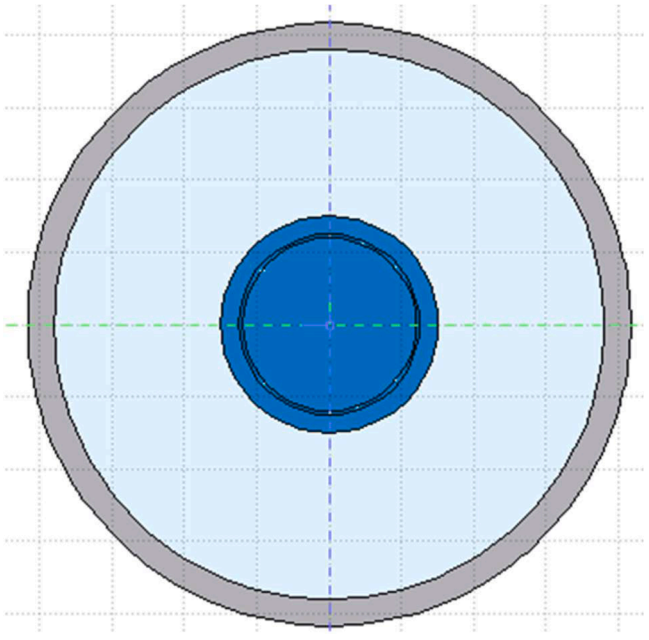

Fig. 2. 2D top view of the spherical water phantom (in blue) placed into the cylindrical Aluminum shielding (in grey).

3. Results and discussion

3.1. RBE values

Fig. 3 shows the RBE values for skin and BFO as a function of the Al shield thickness (SPE 2003 in the upper panel, SPE 2005 in the lower panel), calculated in this work based on the BIANCA HSF cell survival database as described in the methods. The statistical error is smaller than 1 % for all values.

For the 2003 event, the RBE behind thick shielding is higher than that behind thin shielding. In principle, this can be due to two main reasons: 1) with increasing shielding, the primary particles reaching the considered tissue/organ have lower energy and thus higher LET and RBE; 2) with increasing shielding, the absorbed dose in the considered tissue/organ becomes smaller, and it is known from radiobiology that at low doses the RBE tends to be higher than at higher doses. While for skin the RBE increases continuously from 0 to 30 g/cm^2, for BFO the RBE starts increasing only after 5 g/cm^2. This may be related to the so-called body "self-shielding", i.e. the presence of other tissues/organs before the tissue/organ of interest.

The behavior of the RBE for the 2005 event is more complex, most likely due to the presence of higher-energy (primary) particles that cause nuclear interactions in the shield and in the human body. In particular, protons can cause target fragmentation giving rise to slow, heavy particles that have higher LET and thus higher RBE. This may contribute to the RBE peak found for skin between 0 and 0.3 g/cm^2. On the contrary the RBE increase found for very thick shielding may be related to the decrease of the absorbed doses and/or the energy of the primary particles.

From a quantitative point of view, the RBE values obtained in this work were between 1.3 (2003 event, skin without shielding) and 2.2 (2003 event, skin after maximum shielding). The largest RBE variations with increasing shielding were found for the 2003 event (especially for skin, which is not affected by self-shielding), which is characterized by a spectrum consisting of lower-energy particles. On the contrary for the 2005 event, which consists of higher-energy particles, the RBE values tend to stay close to 1.5 (except for skin behind small shielding, as discussed above), which is the constant value recommended for protons by NCRP.

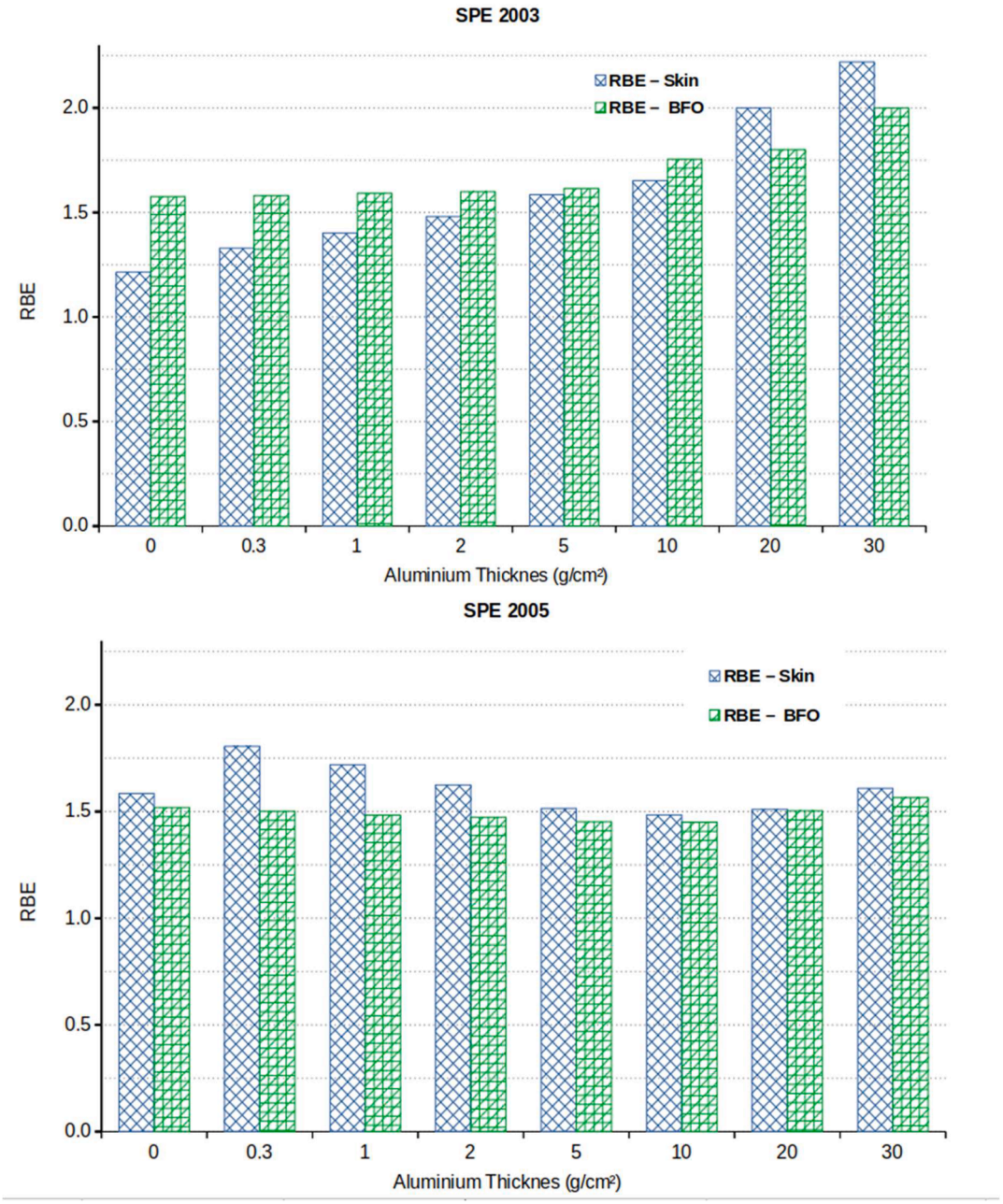

Fig. 3. RBE values for skin and BFO calculated in this work as a function of the Al shielding thickness (SPE 2003 in the upper panel, SPE 2005 in the lower panel).

A comparison with the RBE values recommended by ICRP and NCRP, reported in Table 3, is not straightforward, because the numbers calculated in this work and shown in Fig. 3 refer to the mixed radiation field resulting from the various SPE spectrum components (as well as their nuclear reaction products), whereas those reported in Table 3 refer to specific (primary) particle types. To help discussing this issue, Fig. 4 reports examples of the RBE values used as input in this work, for the case of 10 % cell survival or 50 % cell survival. However, any quantitative comparison must be taken with caution, because the RBE values calculated and applied in this work depend not only on particle type, but also on particle energy and dose.

In particular, the RBE for Ne ions results to be lower than that for Fe ions, which was not expected. This may be related to the fact that, according to our approach described in Section 2.2, possible fluctuations and/or inter-variability between different datasets affecting the V79 experimental data, considered as a reference, can influence the predictions done for other cell lines, which may represent a limitation for this approach. In any case it is worth mentioning that the contribution of ions with $8 < Z < 16$ to the considered SPE fluences is small (less than 0.1 %), and thus it is not likely that a possible underestimation of RBE for Ne ions has a significant impact on the results reported in this paper.

3.2. *Absorbed and equivalent doses and comparison with the dose limits*

Figs. 5a and 5b show the skin and BFO absorbed doses (in Gy) and equivalent doses (in Gy-Eq) calculated for the two SPEs considered in this work, again as a function of the Al shield thickness (skin in Fig. 5a, BFO in Fig. 5b). As described in the methods, in each irradiated tissue the equivalent dose was obtained by multiplying the absorbed dose by an RBE value that, in turn, was calculated based on the HSF cell survival database provided by BIANCA.

The calculations were performed for values of Al shield thickness in the range 0–30 g/cm^2. As expected, both the absorbed and the equivalent dose decreased with increasing shielding, and the decrease was

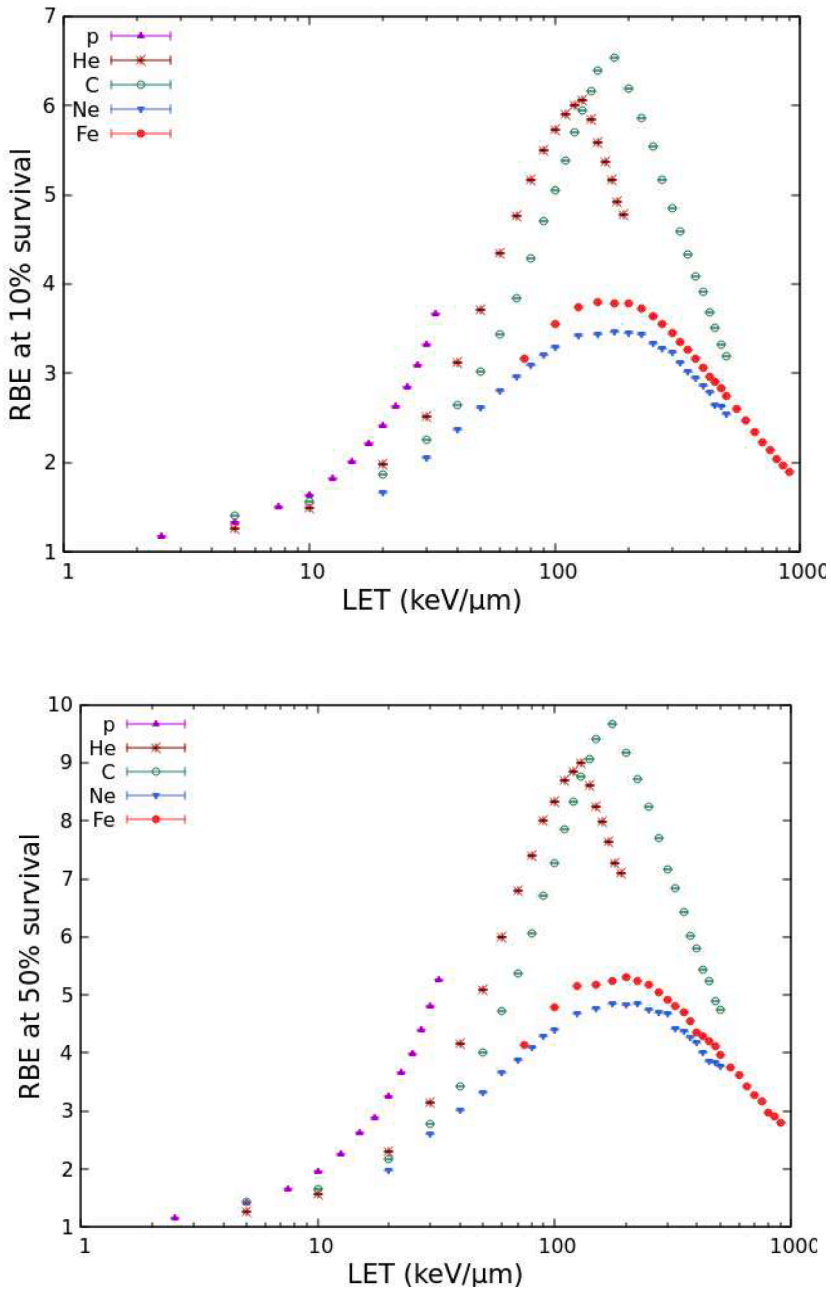

Fig. 4. examples of particle- and LET-dependent RBE values used in this work, for the case of 10 % cell survival (upper panel) or 50 % cell survival (lower panel).

much more pronounced for skin than for BFO. The latter issue may be related to the so-called "self-shielding", i.e. the shielding provided by the body itself, which is absent for the skin but plays an important role for BFO, which even at zero shielding receives an absorbed dose that can be more than ten times lower than the skin dose. In the absence of shielding, the latter is extremely high: more than 70 Gy (about 90 Gy-Eq) for the October 2003 event, and more than 10 Gy (about 17.3 Gy-Eq) for the January 2005 event. However, according to the calculations performed in this work, a 5 g/cm^2 Al shield was found to be sufficient to respect the skin 30-day limit (1.5 Gy-Eq) for the 2003 event, and 1 g/cm^2 Al was sufficient for the 2005 event. The scenario is different for BFO, for which the 30-day limit is 0.25 Gy-Eq. A shielding of 5 g/cm^2 Al was found to be sufficient for the 2003 event, whereas for the 2005 event the limit was respected even without shielding.

Of course it has to be considered that these numbers also depend on the specific methods adopted in this work, and that different quantitative conclusions may be derived by making different choices, such as using a fixed RBE rather than variable RBE values, or using RBE values for tissue reactions rather than in vitro cell survival, or even using in vitro cell survival RBE values derived from a cell line with different radiosensitivity with respect to HSF cells considered in this work. Another source of possible differences is given by the fact that, in this work, also primary ions heavier than protons were considered in the SPE spectra, and the role of these particles may be not negligible: for instance, in case of a 5 g/cm^2 Al shielding the contribution of ions heavier than protons to the equivalent dose was found to be 9 % for skin and 8 % for BFO, which are not negligible if one considers that the statistical error in the calculations is smaller than 1 %.

At the same time, it is interesting to mention that other authors, although adopting different methods (for instance, the fixed RBE values recommended by NCRP), found the same kind of result, i.e. that an Al shield of 5 g/cm^2 allows respecting the skin and BFO limits for the October 2003 event (Schwadron et al., 2010).

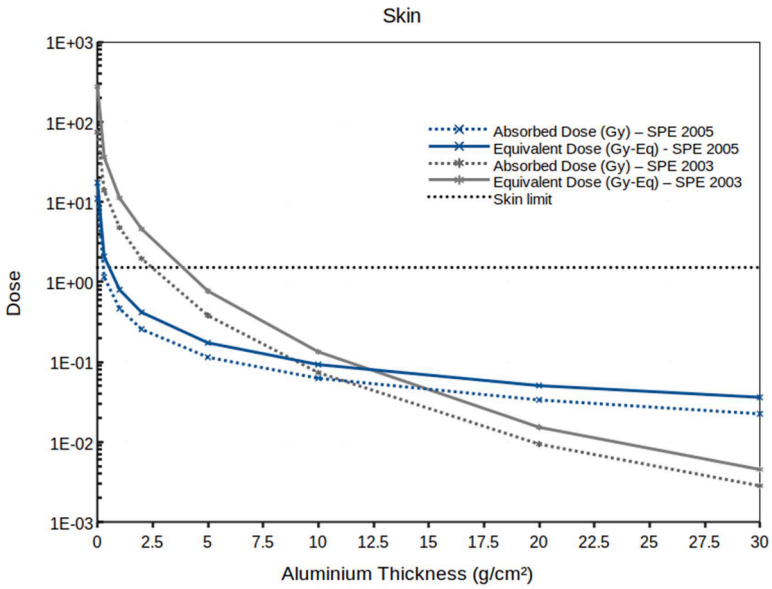

Fig. 5a. skin absorbed and equivalent doses for the two considered SPEs. The horizontal line represents the skin dose limit for 30-days missions (1.5 Gy-Eq).

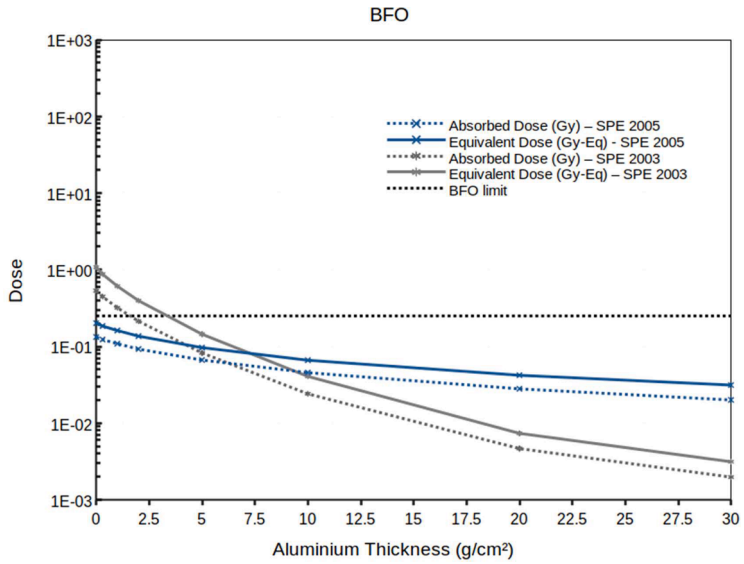

Fig. 5b. BFO absorbed and equivalent doses for the two considered SPEs. The horizontal line represents the BFO dose limit for 30-days missions (0.25 Gy-Eq).

4. Conclusions

In the framework of astronauts' protection from Solar Particle Events, thanks to an interface between the FLUKA transport code and the BIANCA biophysical model we developed a new approach to calculate equivalent-dose values, which allows taking into account the RBE dependence on particle energy and dose in addition to particle type. This approach was applied to the October 2003 and the January 2005 SPE; for the October 2003 event, our calculations suggested that a 5 g/cm^2 Al shield may be sufficient to respect the 30-day limits for skin and BFO equivalent doses, whereas a smaller shield value may be sufficient for the 2005 event, which was characterized by a harder spectrum but lower fluences and thus lower doses.

More generally, this work showed that the BIANCA model, when interfaced to a radiation transport code, can be used to calculate the RBE values associated to Solar Particle Events, also emphasizing the importance of taking into account the RBE dependence on particle energy and dose in addition to the dependence on particle type. Furthermore, it is worth outlining that the dose contribution from particles heavier than protons was also taken into account, considering that also low fluxes of these particle can cause non-negligible biological damage due to their high biological effectiveness (A.Campa et al., 2009) and, possibly, by low-dose-specific phenomena such as bystander effects e.g. (F. Ballarini et al., 2006). As a future development, we intend to reproduce the irradiation scenario in a more realistic way by using an anthropomorphic phantom instead of a sphere, and we will perform experiments in order to validate our model using a new innovative ion source (Leonardi et al., 2023).

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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