radiation

MDPI

Review

A Bibliometric Analysis of Research Examining How Space Radiation Affects Human and Rodent Cognition, 1990–2023

Pilar Simmons [1,2,3], Chase Swinton [1,2], Simeon Simmons [4], Taylor McElroy [5] and Antiño R Allen [1,2,3,*]

[1] Division of Radiation Health, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA; pgsimmons@uams.edu (P.S.); cswinton@stanford.edu (C.S.)
[2] Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA
[3] Department of Neurobiology & Developmental Sciences, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA
[4] Department of Physics & Astronomy, University of Central Arkansas, Conway, AR 72035, USA; simeonacklin@gmail.com
[5] Department of Aging, University of Florida, Gainesville, FL 32603, USA; t.mcelroy@ufl.edu
* Correspondence: arallen@uams.edu; Tel.: +1-501-686-7553

Simple Summary: The hazards associated with the space environment will likely impact many organs/systems. Specifically in the central nervous system, exposure to such radiation may directly affect its structure and function. The goal of the current bibliometric review is to evaluate the existing publications on human and rodent space radiation studies, with a focus on human cognition. Using bibliometric analysis, we categorize what journals, authors, and research papers have had the greatest influence on space central nervous system research. We also evaluate the most productive output by authors, institutions, countries, and journals from 1990 to 2023.

Abstract: The pursuit of exploring the outer space environment for biological research has been a topic of interest for nearly 60 years. The success of the next phase of space exploration depends on the ability to increase crew safety by identifying ways to mitigate these threats. Using a universal scientific citation indexing tool, we extracted data on literature production in terms of the most prolific key terms, authors, countries, institutions, and journals for two distinct topic sets related to space radiation research published from 1 January 1990 to 31 December 2023. The focus of space radiation research in relation to its effects on human health has fluctuated over time, as reflected in the term maps that were generated for each decade. Our bibliometric analysis provides insight into the trends in the top producers in the space radiation research field over the years, as well as into how the focus of such studies has evolved throughout the decades.

Keywords: space radiation; risk; exposure; bibliometric analysis

check for updates

Academic Editor: Gabriele Multhoff

Received: 6 September 2024
Revised: 12 November 2024
Accepted: 19 November 2024
Published: 28 December 2024

Citation: Simmons, P.; Swinton, C.; Simmons, S.; McElroy, T.; Allen, A.R. A Bibliometric Analysis of Research Examining How Space Radiation Affects Human and Rodent Cognition, 1990–2023. *Radiation* **2025**, *5*, 1. https://doi.org/10.3390/radiation5010001

1. Introduction

The pursuit of exploring the outer space environment for biological research has been a topic of interest for nearly 60 years [1]. Space provides a unique environment of stressors that organisms have never experienced on Earth, such as weightlessness and constant exposure to high doses of radiation [1]. Understanding how exposure to this hostile environment affects the human cardiovascular, neurological, and immunological systems, as well as understanding possible mitigations of these hazards, has been widely studied [2]. Since the late 1950s, space agencies have been developing spacecrafts for transporting terrestrial life into low Earth orbit (LEO) to examine responses to selected conditions of space, and much has been learned from space-based research in LEO and short lunar missions [3]. Currently, the National Aeronautics and Space Administration (NASA) is preparing for crewed missions to Mars over the next several decades [4]. Such missions will require long-duration spaceflight, which introduces new challenges, such as living in confined environments, prolonged exposure to radiation, and continuous exposure to microgravity, that pose significant risk of injury and illness [4]. The success of the next phase of space exploration is dependent on the ability to increase crew safety by identifying ways to mitigate these threats.

Between 1961 and June 2018, a total of 561 individuals from more than 40 countries went to outer space, on more than 1230 spaceflights, with a total of 46,947 person-days in space [5]. India is hoping to become the fourth nation in the world to launch their own crewed spacecraft [5]. Space exploration has advanced substantially in recent decades and plans to increase the duration of deep-space missions are in preparation [6]. NASA is aiming for a round-trip human mission to Mars in the 2030s, anticipated to last roughly three years [7]. Impending plans for travel to Mars make it critical to understand how spaceflight affects the human brain, behavior, and cognition [8].

As NASA prepares for long-duration deep-space missions, it is essential to consider the inevitable challenges to human health that are a part of the space environment. Astronauts will encounter a multitude of threats in a deep-space environment. On a mission to Mars, astronauts would be exposed to galactic cosmic rays (GCRs) for up to three years [9]. GCRs are the principal source of radiation in space and consist of high-energy ions of elements that have had all their electrons stripped away, with protons being the most abundant type [9]. Protection from the Earth's magnetosphere is lost as a spacecraft enters deep space, and exposure to GCRs increases about threefold [9]. A prevalent concern is the risk of exposure to space radiation [10], and the primary health concern is the potential damage to the central nervous system (CNS), resulting in a loss of cognitive abilities and function [11]. Several studies have shown how the harmful effects of ionizing radiation impact the CNS of astronauts engaged in deep-space travel [12]. Several mitigative and protective countermeasures have been developed; however, the range of irradiation paradigms are narrow, and few are translatable from animal models to humans [12]. For the proper assessment and management of human health in space, a promising research direction would be to continue studying the effects of radiation on the CNS to improve current countermeasures and discover novel therapeutics [6,12]. We evaluated the existing publications on human and rodent space radiation studies, with a focus on cognition, by performing a bibliometric analysis that examined (1) the most common terms mentioned in space radiation-, Mars-, or galactic cosmic ray-related articles and (2) the most productive output by authors, institutions, countries, and journals from 1990 to 2023.

2. Methods

2.1. Data Search Analysis

We extracted data on literature production from 1 January 1990 to 31 December 2023 of the most prolific key terms, authors, countries, institutions, and journals for two distinct topics sets related to space radiation. For our search, we used the Web of Science online database (Clarivate Analytics, Philadelphia, PA, USA), which is the world's most prominent scientific citation search and analytical information platform used as a research tool for data-intensive studies [13]. The topic sets of search terms were analyzed separately in "advanced search", and the document types selected were articles and reviews. The field tag topic set (TS) was selected and includes titles, abstracts, and keywords. The key search terms were categorized into the following two topic sets:

1. Topic set 1 = (((space radiation) or mars or (galactic cosmic rays)) and cognition) and (humans).
2. Topic set 2 = (((space radiation) or mars or (galactic cosmic rays)) and cognition) and (mice or rats).

The "custom year range" time span from 1990 to 2023 was applied to both topic sets. To construct bibliometric maps of the most prolific key terms, the timespan was divided into four time periods (1990s, 2000s, 2010s, and 2020–2023) for each topic set. Book chapters, proceedings papers, and retracted publications were excluded from the results of both topic sets. The data extracted from the Web of Science searches were downloaded as full records and as cited references and were saved in a tab-delimited file format. The citation analysis included data on publication by institution, country, author, and journal. Web of Science uses the authors' last names and takes collaborations into account toward publication count.

2.2. Data Analysis

VOSviewer version 1.6.20 was used to create the bibliometric network map of the key terms extracted from the citation research of both topic sets. VOSviewer is an effective science-mapping software that provides visualization tools to describe bibliometric research [14]. The term maps generated for software analysis were selected with the following specifications: "create a map based on bibliographic data", "read data from bibliographic database files", "type of analysis: co-occurrence", "unit of analysis: all keywords", and "counting method: full counting", "minimum number of occurrences of a keyword: 5". In VOSviewer, a keyword is a term that can be extracted from the title, abstract, or keyword list of a publication. The size of the knot indicates the popularity of the keyword, and the lines between the knots show how often keywords are used together. After filtering through all the keywords for each network, a thesaurus was created to merge terms, correct spelling differences, or exclude general terms. These settings allow the software to recognize words in the titles and abstracts of publications as they relate to papers in which they occur together. For example, the terms *spaceflight*, *space-flight,* and *space flight* were added to the list so their occurrences would not be counted separately in the networks. The key terms are constructed into a network of color-coded bubbles with interconnected links. Each link has a strength represented by a positive numerical value, with stronger links having a higher value [15]. The total link strength indicates the number of publications in which two keywords occur together [15]. VOSviewer uses a preset algorithm for color clusters. Colors indicate a cluster of closely related key terms and co-occurrences. Bubbles represent a single key term, and colors correspond with a cluster of related key terms. Each cluster contains at least 10% of the key terms generated from the data set. The size of the bubble indicates the number of occurrences in the publications. An increase in the size of the bubble is a representation of a high number of occurrences. A term might appear multiple times within a single publication, but it is counted as only one occurrence in the data analysis. The co-occurrences of terms in publications are related to the distance between each bubble—bubbles that are close in distance have a high number of co-occurrences reflected in the color-coded clusters. Data extracted from the tab-delimited files for publication output for countries were exported to Microsoft Excel and organized into tables by decade using Microsoft Word. Data extracted from tab-delimited files for publication output for authors and institutions were exported to Excel and organized into bar graphs and pie charts for all four decades. Data extracted from the tab-delimited files for overall publication output for both topic sets were exported to Excel and organized into trend tables. Key term data extracted from the tab-delimited files from publications 1990–2023 (5660 total) in topic sets 1 and 2, respectively, were exported to Excel and organized into tables by decade using Word.

3. Results

3.1. Evolution of Bibliographic Terms for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Humans from 1990 to 1999

The results from the 1990s comprise three clusters with a total of 91 terms, 969 links, and a total link strength of 1697. The top five most occurring terms were *cells*, *nuclear matrix*, *sites*, *genes*, and *proteins*. The term *cells* occurred 39 times, with 65 links and a total link strength of 162. *Nuclear matrix*, *sites*, and *genes* appeared 27 times, with link values of 46, 43, and 49 to include total link strengths of 144, 126, and 113, respectively. The term *proteins* occurred 26 times, with 46 links and a total link strength of 85. *Identification* and *radiation* have 24 occurrences, although *identification* has a higher link value (43 < 25) and total link strength (92 > 48) (Table 1).

Table 1. Top occurring terms in topic set 1, 1990–1999.

Rank	Keyword	Occurrences	Links	Total Link Strength
1	Cells	39	65	162
2	Nuclear matrix	27	46	144
3	Sites	27	43	126
4	Genes	27	49	113
5	Proteins	26	46	85
6	Identification	24	43	92
7	Radiation	24	25	48
8	DNA	23	50	93
9	Expression	21	44	84
10	Murine model	20	39	59

3.2. Evolution of Bibliographic Terms for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Humans from 2000 to 2009

The 2000s network consists of more than double the amount of key terms compared to the previous decade (Table 2). VOSviewer generated six clusters of 286 terms, 4141 links, and a total link strength of 6464. Terms with some of the greatest number of occurrences include *radiation*, *Mars*, *expression*, *gene expression*, *ionizing radiation*, *spaceflight*, and *murine model*. The term *radiation* had 94 occurrences, with 140 links and a total link strength of 361. *Mars* had 65 occurrences, with 83 links and a total link strength of 165. The term *expression* occurred 60 times, with 103 links and a total link strength of 255. *Gene expression* appeared 54 times in the network, with 102 links and a total link strength of 257. *Ionizing radiation* had 49 occurrences, with 97 links and a total link strength of 259. The term *spaceflight* occurred 43 times, with 76 links and a total link strength of 148. Finally, *murine model* (i.e., rat, rat model, mouse, mouse model, etc.) had 42 occurrences, 95 links, and a total link strength of 161.

Table 2. Top occurring terms in topic set 1, 2000–2009.

Rank	Keyword	Occurrences	Links	Total Link Strength
1	Radiation	94	140	361
2	Cells	76	126	357
3	Mars	65	83	165
4	Expression	60	103	255
5	Proteins	59	89	189
6	Gene expression	54	102	257
7	Ionizing radiation	49	97	259
8	Nuclear matrix	44	60	191
9	Spaceflight	43	76	148
10	Murine model	42	95	161

3.3. Evolution of Bibliographic Terms for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Humans from 2010 to 2019

Similar to the previous decade, the terms for the 2010s more than doubled compared to the 2000s, with six clusters of 582 terms, 12,497 links, and a total link strength of 20,570. *Radiation* continued to be a top occurring term, with 200 occurrences, 324 links, and a total link strength of 979. *Model*, *space radiation*, and *microgravity* were top occurring terms in this decade, with 112, 101, and 92 occurrences, 248, 185, and 181 links, and total link strengths of 470, 624, and 518, respectively. The terms *space* and *exposure* appeared for the first time this decade. *Space* had 92 occurrences, a link value of 194, and a total link strength of 477 (Table 3). *Exposure* occurred 85 times with 212 links and a total link strength of 476 (Figure 1).

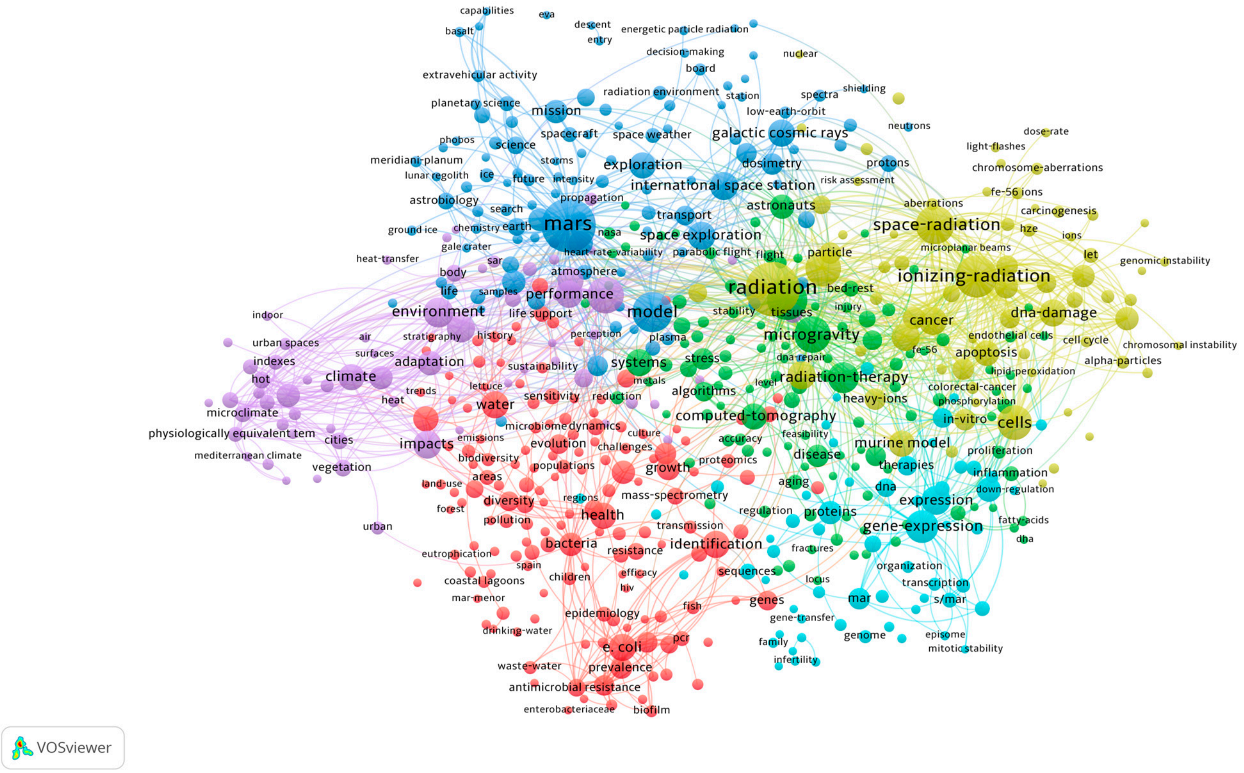


Figure 1. Topic set 1 term map for 2010–2019. Cluster 1 is represented by the red region, with 154 terms. Cluster 2 is the green region, with 119 terms. Cluster 3 is the blue region, with 112 terms. Cluster 4 is the yellow region, with 73 terms. Cluster 5 is the purple region, with 64 terms. Cluster 6 is represented by the teal region, with 60 terms.

Table 3. Top occurring terms in topic set 1, 2010–2019.

Rank	Keyword	Occurrences	Links	Total Link Strength
1	Radiation	200	324	979
2	Mars	199	271	862
3	Ionizing radiation	123	203	717
4	Model	112	248	470
5	Spaceflight	109	202	574
6	Space radiation	101	185	624
7	Microgravity	92	181	518
8	Space	92	194	477
9	Exposure	85	212	476
10	Cells	84	158	451

3.4. Evolution of Bibliographic Terms for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Humans from 2020 to 2023

For publications between 2020 and 2023, the network consists of six clusters of 552 terms, 12,1719 links, and a total link strength of 19,163. The term *Mars* continued to be a top occurring term, with 202 occurrences, 291 links, and a total link strength of 932. It was followed by *radiation*, appearing 187 times, with 327 links and a total link strength of 937. *Microgravity*, the third most occurring key term, had 116 occurrences, 221 links, and a total link strength of 724. *Risks* is a new top occurring term in the 2020s, with 74 occurrences, 190 links, and a total link strength of 364 (Table 4).

Table 4. Top occurring terms in topic set 1, 2020–2023.

Rank	Keyword	Occurrences	Links	Total Link Strength
1	Mars	202	291	932
2	Radiation	187	327	937
3	Microgravity	116	221	724
4	Spaceflight	106	195	601
5	Space radiation	94	184	535
6	Space	94	230	532
7	Exposure	80	192	470
8	Ionizing radiation	78	171	484
9	Model	78	187	365
10	Risks	74	190	364

3.5. Evolution of Bibliographic Terms for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Mice or Rats from 1990 to 1999

The results from the 1990s produced four clusters with a total of 76 terms, 792 links, and a total link strength of 1355. The terms with the most occurrences include *murine model*, *cells*, *expression*, *radiation*, and *transgenic mice*. *Murine model* occurred 69 times, with 61 links and a total link strength of 165 (Table 5). The term *cells* appeared 40 times, with 54 links and a total link strength of 115. *Expression* had 31 occurrences, with 43 links and a total link strength of 119. *Radiation* appeared 30 times, with 23 links and a total link strength of 47. Lastly, the term *transgenic mice* occurred 27 times, with 37 links and a total link strength of 133 (Figure 2).

Table 5. Top occurring terms in topic set 2, 1990–1999.

Rank	Keyword	Occurrences	Links	Total Link Strength
1	Murine model	69	61	165
2	Cells	40	54	115
3	Expression	31	43	119
4	Radiation	30	23	47
5	Transgenic mice	27	37	133
6	MAR (matrix attachment region)	26	38	153
7	Nuclear matrix	23	34	116
8	Proteins	20	30	53
9	In vitro	18	33	49
10	mRNA	18	30	49

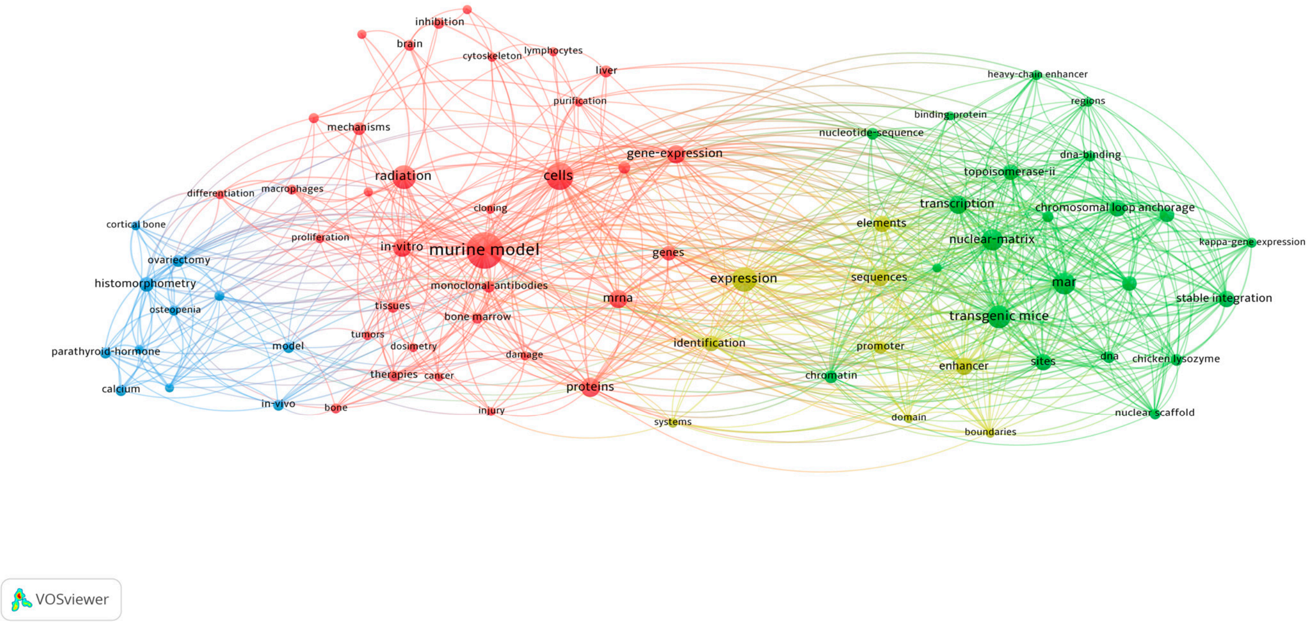


Figure 2. Topic set 2 term map for 1990–1999. Cluster 1 is represented by the red region, with 34 terms. Cluster 2 is the green region, with 22 terms. Cluster 3 is the blue region, with 11 terms. Cluster 4 is the yellow region, with 9 terms.

3.6. Evolution of Bibliographic Terms for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Mice or Rats from 2000 to 2009

The network from the 2000s we generated consists of four clusters of 165 terms, 2550 links, and a total link strength of 4558—more than double the number for each parameter from the previous decade. Akin to the 1990s, *murine model* was the top occurring term, with 165 occurrences, 156 links, and a total link strength of 662. *Gene expression*, *ionizing radiation*, *oxidative stress*, and *spaceflight* were also some of the top occurring terms of the decade. *Gene expression* occurred 39 times, with 78 links and a total link strength of 178. The *term ionizing radiation* appeared 32 times and had 63 links with a total link strength of 165. *Oxidative stress* and *spaceflight* both occurred 27 times, with 48 and 53 links and total link strengths of 124 and 159, respectively (Table 6).

Table 6. Top occurring terms in topic set 2, 2000–2009.

Rank	Keyword	Occurrences	Links	Total Link Strength
1	Murine model	165	156	662
2	Radiation	54	94	217
3	Cells	51	106	247
4	Expression	39	79	163
5	Gene expression	39	78	178
6	Nuclear matrix	36	48	160
7	In vivo	35	70	130
8	Ionizing radiation	32	63	165
9	Oxidative stress	27	48	124
10	Spaceflight	27	53	159

3.7. Evolution of Bibliographic Terms for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Mice or Rats from 2010 to 2019

The terms for the 2010s yielded five clusters of 265 terms, 5923 links, and a total link strength of 10,689. *Murine model* continued to be the top occurring term, with 200 occurrences, 237 links, and a total link strength of 1011. The term *space radiation* became a top occurring term this decade, with 77 occurrences, 153 links, and a total link strength of 524. The occurrences of the term *radiation* nearly tripled compared to the previous decade, with 167 appearances, 225 links, and a total link strength of 964. *Spaceflight* occurred 54 times, double the number of occurrences from the 2000s, with 110 links and a total link strength of 322 (Table 7). Other top occurring terms included *expression*, *cells*, and *in vivo*. *Expression* occurred 80 times, with 180 links and a total link strength of 442. The term *cells* had 71 occurrences, 156 links, and a total link strength of 379. Lastly, *in vivo* occurred 69 times, with 138 links and a total link strength of 307 (Figure 3).

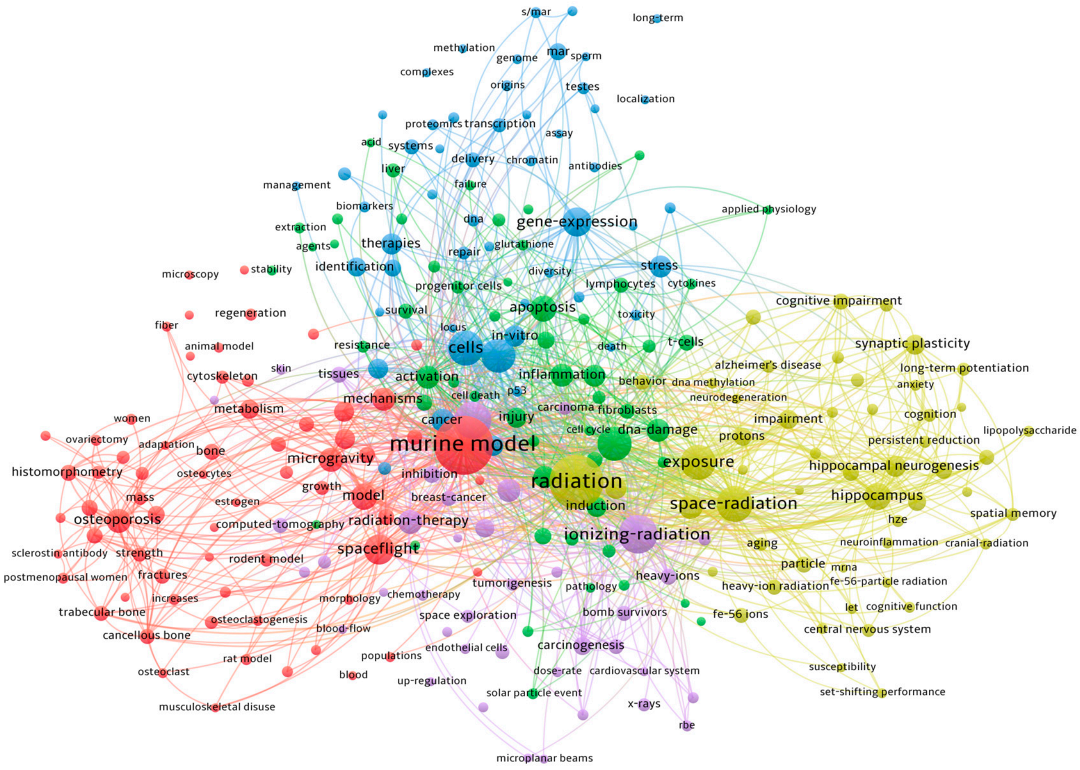


Figure 3. Topic set 2 term map for 2010–2019. Cluster 1 is represented by the red region, with 29 terms. Cluster 2 is the green region, with 28 terms. Cluster 3 is the blue region, with 24 terms. Cluster 4 is the yellow region, with 320 terms. Cluster 5 is the purple region, with 20 terms.

Table 7. Top occurring terms in topic set 2, 2010–2019.

Rank	Keyword	Occurrences	Links	Total Link Strength
1	Murine model	200	237	1011
2	Radiation	167	225	964
3	Ionizing radiation	88	169	552
4	Expression	80	180	442
5	Space radiation	77	153	524
6	Cells	71	156	379
7	Exposure	70	150	445
8	In vivo	69	138	307
9	Oxidative stress	66	160	439
10	Spaceflight	54	110	322

3.8. Evolution of Bibliographic Terms for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Mice or Rats from 2020 to 2023

Publications from 2020 to 2023 produced a term map with five clusters, 147 items, 2572 links, and a total link strength of 4623 (Figure 4). The term *murine model* remains the top occurring term, with 103 occurrences, 127 links, and a total link strength of 423. *Inflammation* is a top occurring term not seen in previous decades, with 24 occurrences, 55 links, and a total link strength of 78. *Radiation*, *space radiation*, and *ionizing radiation* continue to be top occurring terms as well (Table 8).

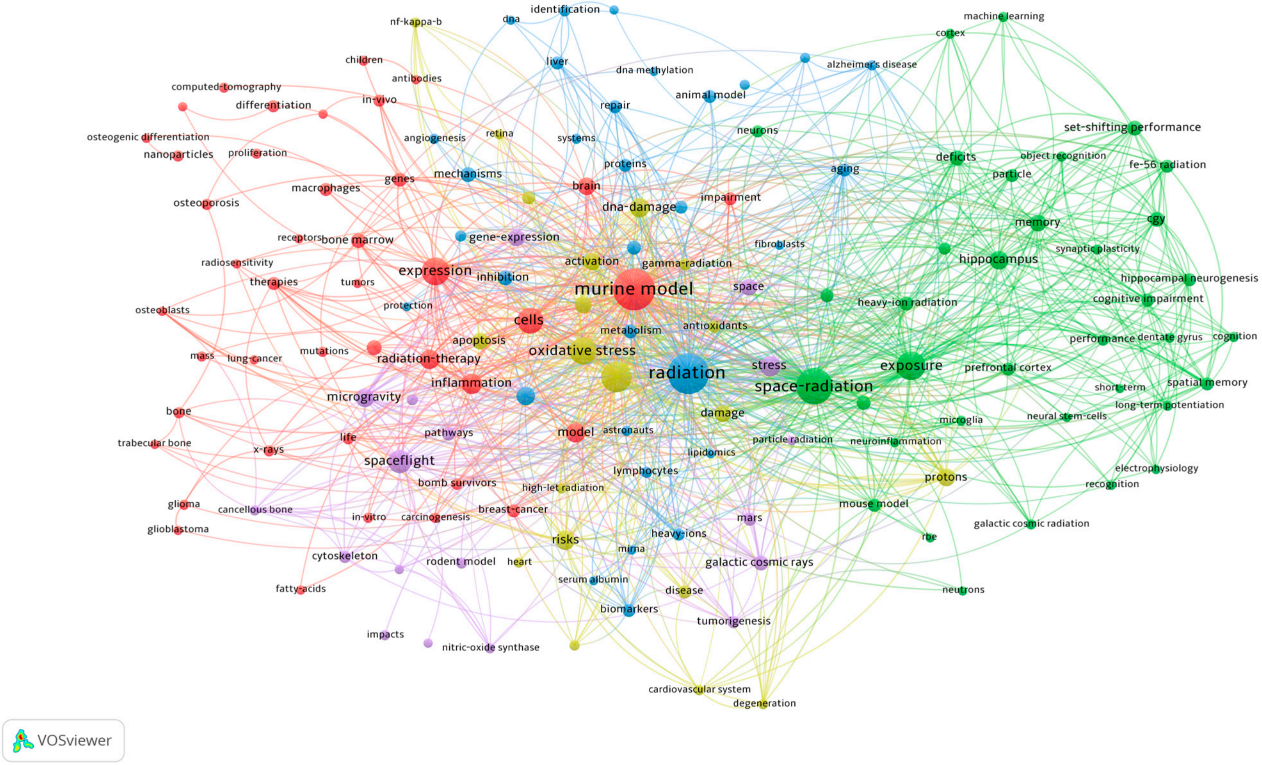


Figure 4. Topic set 2 term map for 2020–2023. Cluster 1 is represented by the red region, with 42 terms. Cluster 2 is the green region, with 36 terms. Cluster 3 is the blue region, with 31 terms. Cluster 4 is the yellow region, with 20 terms. Cluster 5 is the purple region, with 18 terms.

Table 8. Top occurring terms in topic set 2, 2020–2023.

Rank	Keyword	Occurrences	Links	Total Link Strength
1	Murine model	103	127	423
2	Radiation	96	128	496
3	Space radiation	75	116	433
4	Ionizing radiation	56	100	303
5	Exposure	48	97	300
6	Expression	46	88	199
7	Oxidative stress	42	94	237
8	Cells	41	84	175
9	Spaceflight	33	67	153
10	Inflammation	24	55	78

3.9. Evolution of Publication Output for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Humans in Relation to Countries of Origin from 1990 to 2023

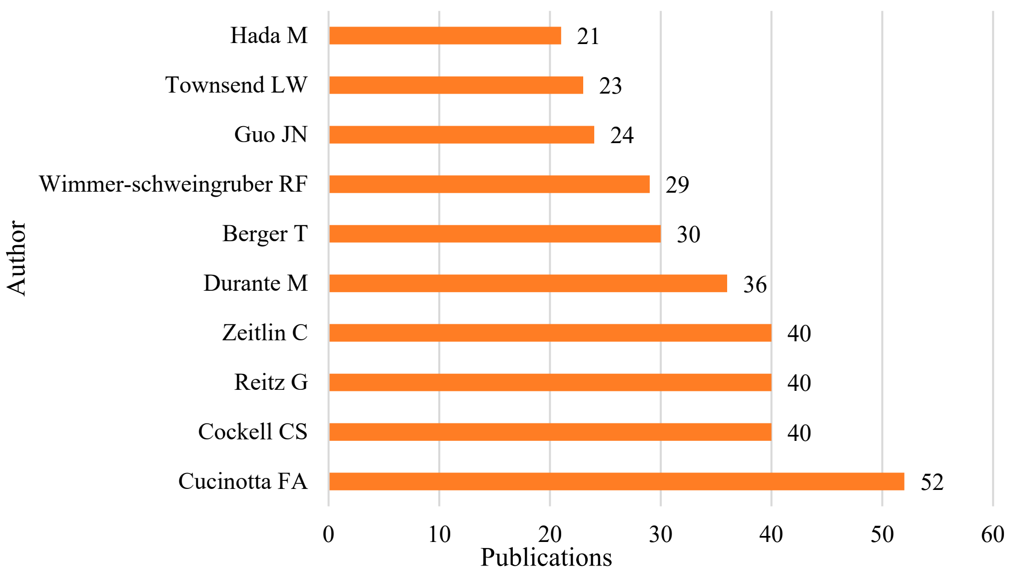
In the 1990s, the USA was the leading country for publication output, accumulating 200 total publications and nearly 13,000 citations from said publications. Germany ranked second, with 47 total publications, followed by France (36 publications), England (30 publications), and Japan (26 publications). The USA more than doubled their total publication and citation output in the 2000s, with 506 total publications and circa 29,500 citations. England superseded Germany for second most publications this decade, with 121 and 118 publications, respectively. Notably, Italy became a top publication-producing country during the 2000s, generating 67 publications. This decade marks Japan's last time in the top five producing countries for the topic set. In the 2010s, the USA continued to be the primary producer, with 923 publications. However, despite the nearly 75% increase in publication production since the 2000s, there was only an approximate 3% increase in times cited. China appeared as a top producing country for the first time, with 229 publications, ranking third overall of the 2010s. Three years into the 2020s, the USA remains the top producing country for topic set 1, with 657 publications thus far. China, Italy, and England have already surpassed their publication output from the previous decade, with 337 (vs. 229), 179 (vs. 150), and 149 (vs. 129) publications, respectively.

3.10. Evolution of Publication Output for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Mice or Rats in Relation to Countries of Origin from 1990 to 2023

From 1990 to 1999, the publications related to topic set 2 were mainly produced in the USA, with 136 total publications and 8024 citations from said publications. Japan was the second top producing country during the 1990s with 33 publications, followed by Germany with 29 publications. England and France were also top producing countries during this decade. In the 2000s, the USA continued to be the only country with production output in the triple digits with 250 total publications. Japan continued to rank second with 73 publications and Germany continued to rank third with 43 publications. Although France was no longer a top producing country during this decade, Italy joined the rankings with 28 publications. The USA continued to be the top producing country into the 2010s, with a publication count of 411 and 13,076 citing articles. The USA generated almost 65% more publications in this decade than the last, but there was virtually no difference in times cited. During this decade China emerged as the second rank producer and second country to break triple-digit publication output with 105 publications and 2066 citing articles. Japan, England, and Germany also stayed in the top five producing countries with total publications of 44, 40, and 39 respectively. From 2020 to 2023, the USA persists as the top producing country for topic set 2 with over 200 publications. No other country in the top five has yet produce over 100 publications, with China being second rank at 85 publications. France has re-entered the rankings, positioned at fifth with 24 publications thus far.

3.11. Profile of the Most Productive and Most Cited Authors for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Humans from 1990 to 2023

From 1990 to 2023, Cucinotta was the top producer of studies in topic set 1, with 52 publications (Table 5), 3362 times cited (TCs), and an average times cited per publication (ACP) of 69.85 (Table S1). Cucinotta generated 16% of all studies amongst the top ten authors in topic set 1 (Figure 5b). Cockell, Reitz, and Zeitlin followed with 40 publications, each producing 12% of publications. Durante has the third most publications (36) and the third highest ACP (48.17). Both Berger and Wimmer-Schweingruber produced 9%, although Wimmer-Schweingruber has the second highest ACP (57.45) overall (Table S1). Guo and Townsend, the eighth- and ninth-ranking authors, respectively, each generated 7% of publications amongst the top ten authors. Lastly, Hada published 6% of the studies, with 21 publications that resulted in 658 TCs and 31.33 ACP.


a. Topic Set 1: Publications per Author

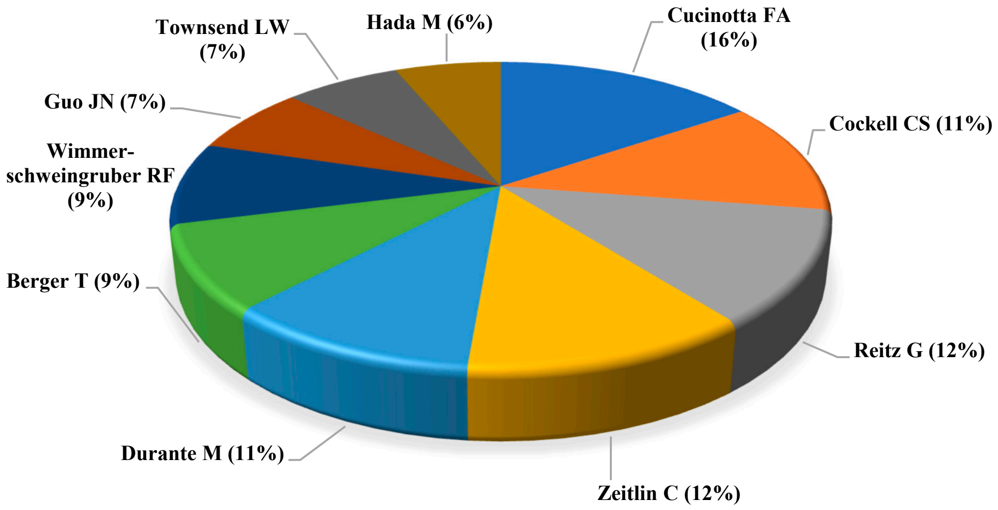
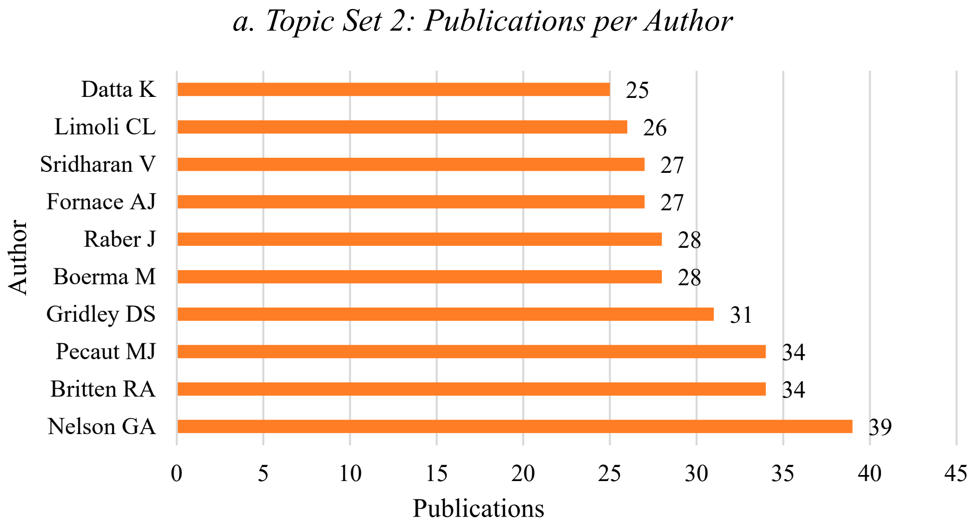

b. Topic Set 1: Percentage of Publications per Author

Figure 5. Clustered bar graph of the top ten most productive authors of topic set 1 from 1990 to 2023 showing how many articles each author has published (**a**). Pie chart of the top ten most productive authors of topic set 1 from 1990 to 2023 shows the percentage of studies each author has produced amongst their peers (**b**).

3.12. Profile of the Most Productive and Most Cited Authors for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Mice or Rats from 1990 to 2023

From 1990 to 2023, Nelson was the top producing author of papers related to topic set 2, with 39 publications (Figure 6a), 1535 times cited (TCs), and an average times cited per publication (ACP) of 39.36 (Table S2). Nelson produced 13% of all studies amongst the top ten authors in topic set 2. Britten and Pecaut both produced 34 publications (11%), although Pecaut yielded a higher ACP (31.24 > 24.41) (Figure 6b; Table S2). Third ranking was Gridley, who published 31 articles (10%), with just over 1000 TCs and an ACP of 32.94. Boerma, Raber, Fornace and Sridharanall produced circa 9% of studies in topic set 2. However, Limoli had 1430 TCs and 55 ACP, boasting the second highest TCs and highest ACP overall

(Table S2). Datta was the tenth ranking author in topic set 2, with 25 publications, yielding 8% of studies published amongst the top ten most productive authors.



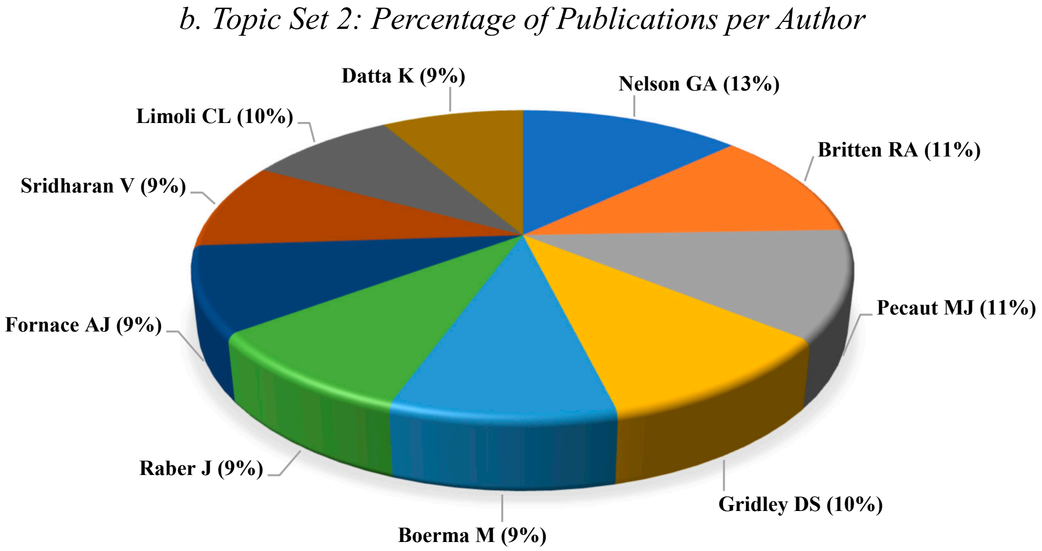
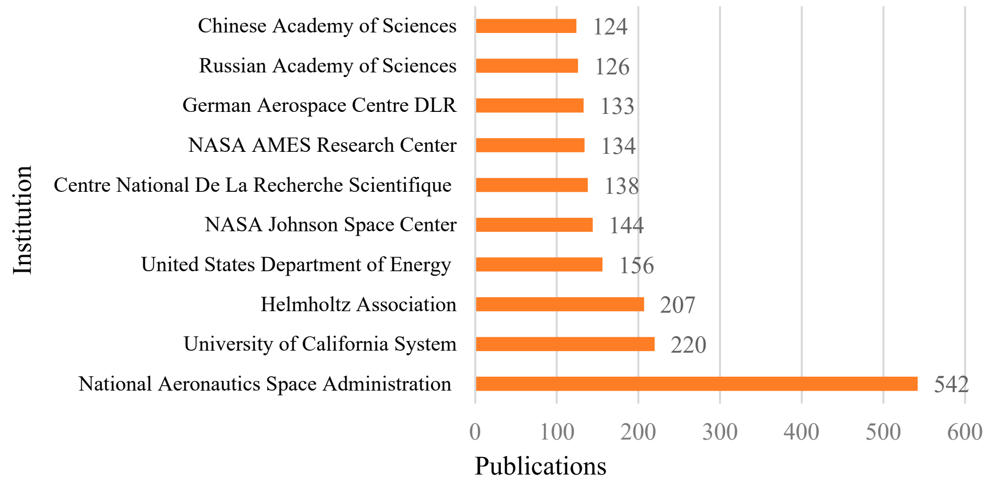


Figure 6. Clustered bar graph of the top ten most productive authors of topic set 2 from 1990 to 2023 showing how many articles each author has published (**a**). Pie chart of the top ten most productive authors of topic set 2 from 1990 to 2023 showing the percentage of studies each author has produced amongst their peers (**b**).

3.13. Profile of the Most Productive and Most Cited Institutions for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Humans from 1990 to 2023

From 1990 to 2023, NASA produced 542 publications (Table 7) which resulted in 18,275 times cited (TCs) and an average times cited per publication (ACP) of 33.72 (Table S3). NASA generated 28% of studies in topic set 1 amongst the top ten institutions (Figure 7b). The University of California System, with the highest ACP of 46.77, and the Helmholtz Association in Germany produced circa 11% of studies. Following these, the DOE published 156 articles that comprise 8% of the total. The NASA Johnson Space Center (JSC), Centre National De La Recherche Scientifique, German Aerospace Center DLR, and the Russian Academy of Sciences each contributed 7%. However, both the NASA JSC and the Centre National De La Recherche Scientifique had a TC over 4000 and an ACP over 40, unlike their institutional peers (Table S3). Notably, Web of Science distinguishes between NASA, NASA Johnson Space Center, and NASA Ames Research Center for publication output. Lastly, the Chinese Academy of Sciences was the tenth ranking producer of studies for topic set 1, with 124 publications that comprise 6% of the total.

a. Topic Set 1: Publications per Institution



b. Topic Set 1: Percentage of Publications per Institution

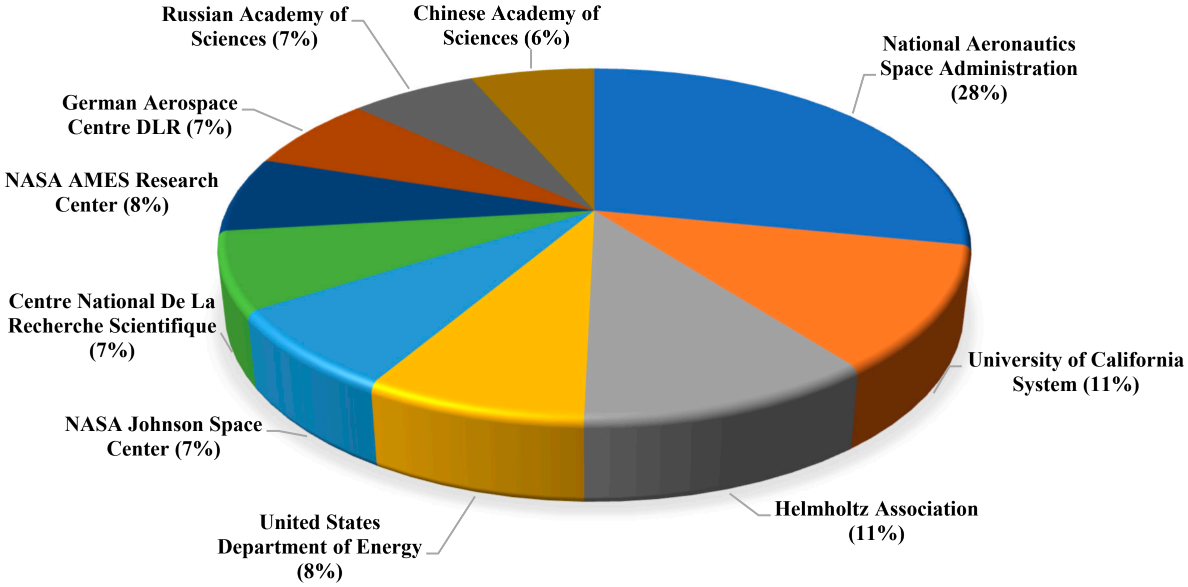


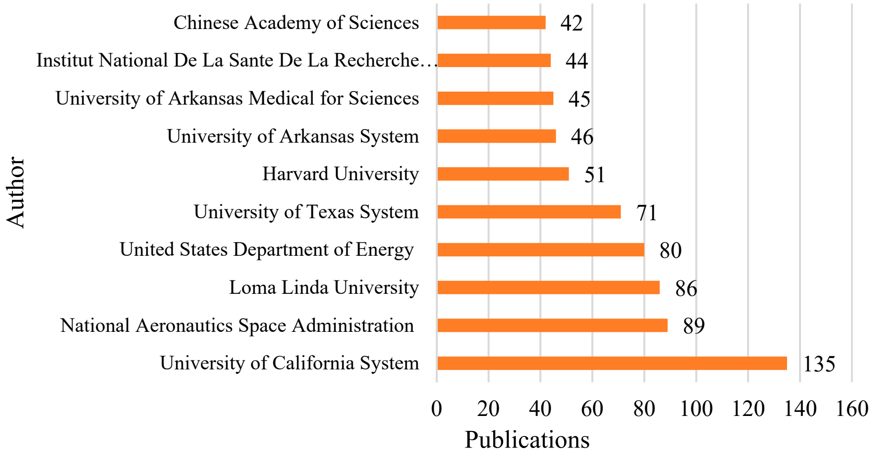
Figure 7. Clustered bar graph of the top ten most productive institutions of topic set 1 from 1990 to 2023 showing how many articles each institution has published (**a**). Pie chart of the top ten most productive institutions of topic set 1 from 1990 to 2023 showing the percentage of studies each institution has produced amongst their peers (**b**).

3.14. Profile of the Most Productive and Most Cited Institutions for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Mice or Rats from 1990 to 2023

From 1990 to 2023, the University of California System was the top-ranking producer of studies for topic set 2, with 135 publications (Figure 8a), nearly 6000 times cited (TCs), and the average times cited per publication of 44.02 (ACP) (Table S4). The University of California System generated 20% of all publications amongst the top ten institutions of topic set 2. Ranking second was NASA, producing 13% with 89 publications (Figure 8a,b). Both

Loma Linda University and the DOE produced 12% of studies. Loma Linda University had a slightly higher publication output than the DOE (86 > 80), but the DOE had a higher TC and ACP (3202 > 2973; 40.03 > 34.57) (Table S4). The University of Texas System followed closely behind, producing 10% with 71 publications and 1733 times cited. Harvard University had a total publication output of 51 articles (7%) but had one of the highest ACPs, at 41.06, preceded only by the University of California System (44.02) and the Institut National De La Sante De La Recherche Medicale (47.41) (Table S4). Both the University of Arkansas System and the University of Arkansas for Medical Sciences produced 7% of studies amongst the top ten institutions, with 832 TCs and 812 TCs, respectively (Table S4). Lastly, the Chinese Academy of Sciences was the tenth ranking producer of studies for topic set 2, with 42 publications that comprise 6% of the total (Figure 8b).

a. Topic Set 2: Publications per Insitiution



b. Topic Set 2: Percentage of Publications per Institution

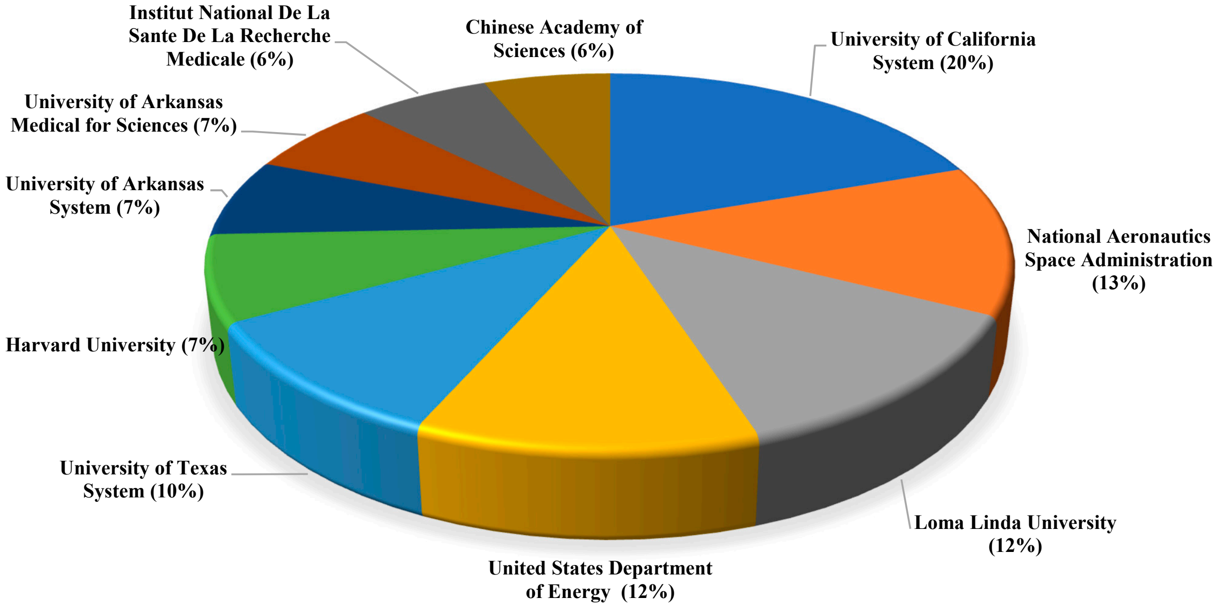


Figure 8. Clustered bar graph of the top ten most productive institutions of topic set 2 from 1990 to 2023 showing how many articles each institution has published (**a**). Pie chart of the top ten most productive institutions of topic set 2 from 1990 to 2023 showing the percentage of studies each institution has produced amongst their peers (**b**).

3.15. Analysis of Growth Trends in Publications for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Humans from 1990 to 2023

From 1990 to 2004, there were fewer than 100 publications published per year among the studies relating to topic set 1. In 2005, 110 articles were published. The number of publications increased nearly every year, except for 2008, 2010, 2015, and 2022. Each completed decade has more than doubled its output from beginning to end. In 1990, there were only two publications for topic set 1. By 1999, there were 60 publications. The following year, there were 71 articles published. By 2009, 169 articles had been published. Moving into the 2010s, there were 165 publications, while 2019 saw 337 publications for topic set 1. Although publication output has only been recorded for three years of the 2020s, there is an increase in publications since the beginning of the current decade (Figure 9).

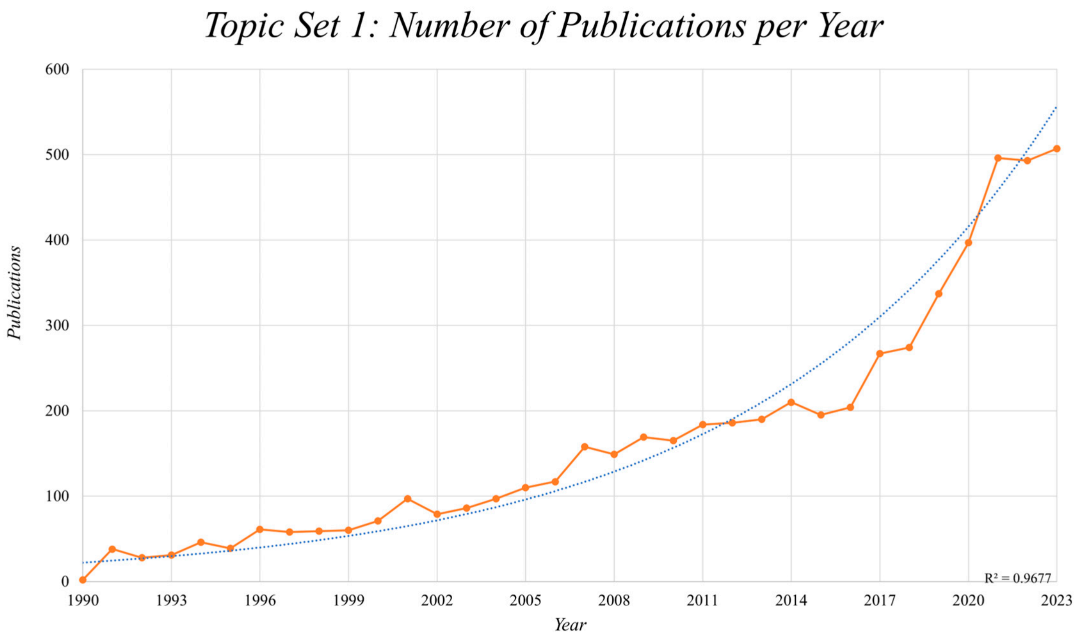


Figure 9. Line graph that shows the exponential growth trend in publication output per year for topic set 1 from 1990 to 2023. Orange line: Data Points of Publication for Each Year. Blue line: Line of Best Fit, represented by R^2 equation.

Radiation is the only key term to appear in every decade, being the most frequent term for two consecutive decades (2000s, 2010s) and the most occurring term overall. The terms *Mars* and *spaceflight* first appeared in the 2000s and have increased in rank every decade; they are the second and third most occurring terms overall, respectively. *Ionizing radiation* also appeared every decade since the 2000s, ranking seventh (2000s), third (2010s), and then eighth (2020s). *Space radiation* has ranked higher than *ionizing radiation* in the 2020s so far (Table 9).

Microgravity, *space*, and *exposure* follow a similar trend. These terms first appeared in the 2010s as the seventh, eighth, and ninth most occurring key terms and subsequently became the third, sixth, and seventh most occurring in the early 2020s, respectively. The term *model* was ranked fourth in the 2010s but fell to rank nine in the 2020s, although it remains the seventh most occurring term overall. Many of the key terms of the 1990s and 2000s, such as *nuclear matrix*, *proteins*, and *expression*, did not appear as top-occurring terms in the 2010s and onward. Conversely, *risks* is a new top key term, first appearing in the top ten during the 2020s (Table 9). The term *cells* was a highly ranked key term in the 1990s (first) and 2000s (second), but it became less frequently occurring moving into the 2010s (tenth), although *cells* is the overall fifth-ranking term. As *cells* decreased in frequency, the term *radiation* increased in frequency after the 1990s and is the most occurring term overall.

Table 9. The top ten most-occurring key terms organized by decade and top key terms from 1990 to 2023 for topic set 1.

Rank	1990–1999	2000–2009	2010–2019	2020–2023	1990–2023
1	Cells	Radiation	Radiation	Mars	Radiation
2	Nuclear matrix	Cells	Mars	Radiation	Mars
3	Sites	Mars	Ionizing radiation	Microgravity	Spaceflight
4	Genes	Expression	Model	Spaceflight	Ionizing radiation
5	Proteins	Proteins	Spaceflight	Space radiation	Cells
6	Identification	Gene expression	Space radiation	Space	Microgravity
7	Radiation	Ionizing radiation	Microgravity	Exposure	Model
8	DNA	Nuclear matrix	Space	Ionizing radiation	Space
9	Expression	Spaceflight	Exposure	Model	Space radiation
10	Murine model	Murine model	Cells	Risks	Exposure

3.16. Analysis of Growth Trends in Publications for Space Radiation, Mars, Galactic Cosmic Rays, Cognition, and Mice or Rats from 1990 to 2023

In 2020, more than 100 publications relating to topic set 2 were produced for the first time. The 1990s was the only decade to see a doubled production output, from two publications in 1990 to forty-two publications in 1999. The 2000s saw a nearly 15% increase, as there were 53 publications in 2000 and 61 in 2009. The year 2010 saw 62 publications, while 2019 saw 94 publications, boasting around a 50% increase in output. Since 2020, more than 100 articles have been published every year. Although the number of publications did not increase every year, there is still a positive trend in publication output for research studies related to topic set 2 (Figure 10).

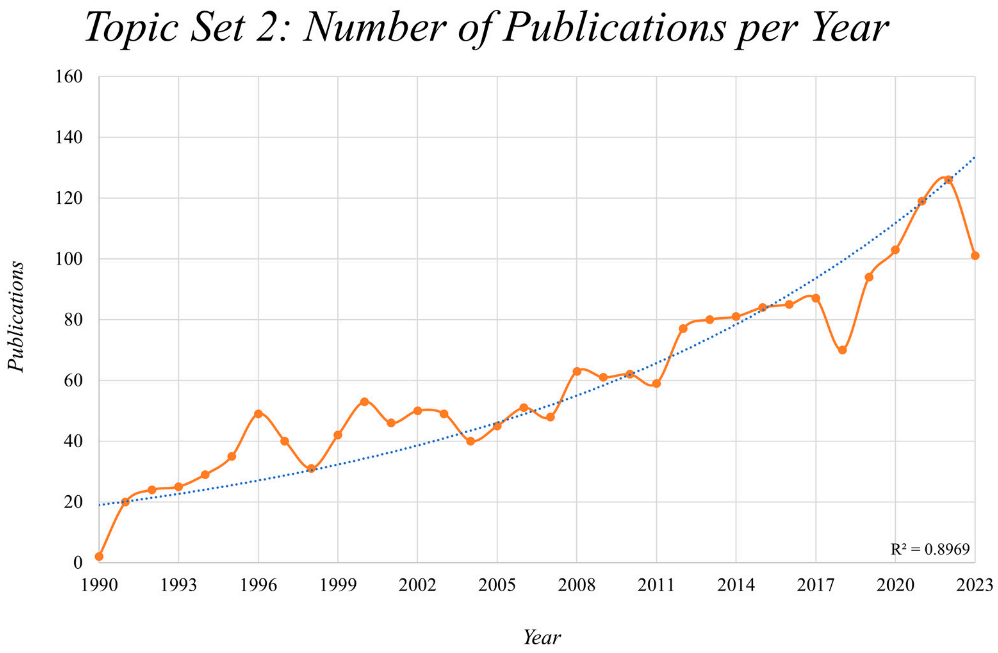


Figure 10. Line graph that shows the exponential growth trend in publication output per year for topic set 2 from 1990 to 2023. Orange line: Data Points of Publication for Each Year. Blue line: Line of Best Fit, represented by R^2 equation.

4. Discussion

4.1. A Comparison Between Trips to Space and Publication Output from the Respective Country

The first module of the International Space Station (ISS), the Russian Zarya, was launched in 1998 [16]. Space agencies from the USA (NASA), Russia (RSA, now Roscosmos), Canada (CSA), Japan (NASDA, now JAXA), and Europe (ESA) were significantly involved in the early stages of the construction and development of the ISS [17]. This activity coincides with the countries that produced the most articles for topic set 1 (i.e., USA, Germany, Frace, England, and Japan; Table 10) and topic set 2 (i.e., USA, Japan, Germany, England, and France; Table 11) during the 1990s. Although Canada did not show up in the top five countries in terms of publication output, it was in the top ten for both topic sets for the 90s (Tables S5 and S6). This could be due to Canada's close partnership with the ESA since the 1970s. Similarly, Russia was not a top five-ranking country but was also in the top ten. This is perhaps because most Russian missions heavily involve international partners [18]. Notably, Russia created a system of countermeasures that aimed to alleviate the effects of microgravity on cosmonauts while on long-duration spaceflight missions. Exercise, diet, and pharmacological components were tested on the Russian-manned Salyut (1971–1986) and Mir (1986–1996) orbital stations [19]. These countermeasures were later successfully implemented by the ISS, allowing for 280 people across 23 countries to visit the ISS to date [20].

Table 10. Top five most productive countries for articles in topic set 1 from 1990 to 2023, organized by decade.

Rank	Country	Publications	Times Cited
1990–1999			
1	USA	200	12,895
2	Germany	47	4866
3	France	36	1990
4	England	30	1399
5	Japan	26	913
2000–2009			
1	USA	506	29,436
2	England	121	8335
3	Germany	118	7841
4	Japan	86	3224
5	Italy	67	2871
2010–2019			
1	USA	923	30,349
2	Germany	244	9661
3	China	229	7083
4	Italy	150	4257
5	England	129	5792
2020–2023			
1	USA	657	6179
2	China	337	4077
3	Germany	215	2155
4	Italy	179	1360
5	England	149	1443

This trend continued into the 2000s and 2010s, with slight fluctuations in European country rankings. The ESA is composed of 22 countries: Austria, Belgium, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, the Netherlands, Norway, Poland, Portugal, Romania, Spain, Sweden, Switzerland, and the United Kingdom. The larger countries that have adequate resources to take part in substantial space projects have played a significant role in space radiation research. This is noticeable in the consistent shifts amongst Germany, Italy, France, and England for the top producing European countries for topic sets 1 and 2 within each decade.

Table 11. Top five most productive countries for articles in topic set 2 for 1990 through 2023, organized by decade.

Rank	Country	Publications	Times Cited
1990–1999			
1	USA	136	8024
2	Japan	33	840
3	Germany	29	1800
4	England	25	1264
5	France	17	671
2000–2009			
1	USA	250	13,008
2	Japan	73	2687
3	Germany	43	2380
4	England	35	1278
5	Italy	28	1242
2010–2019			
1	USA	411	13,076
2	China	105	2066
3	Japan	44	1162
4	England	40	1957
5	Germany	39	2224
2020–2023			
1	USA	227	1462
2	China	85	477
3	Japan	37	227
4	England	28	218
5	France	24	201

In 2011, China launched its first prototype space laboratory, Tiangong-1, into orbit. Then, in 2016, it launched its second, Tiangong-2, to provide a platform for Chinese scientists to conduct a series of space experiments [21]. These stations were deorbited towards the end of the 2010s, in 2018 and 2019, respectively. Accordingly, these advances are reflected in the first appearance of China as a top five producing country for both topic sets 1 and 2 during the 2010s (Tables 9 and 10).

Moving into the early 2020s, China continues to be one of the top countries producing space radiation research—ranking second overall in both topic sets after the USA. In 2021, the China Manned Space Agency launched Tianhe, the core module of the China Space Station (CSS). The following year, the Wentian and Mengtian laboratory cabin modules (LCMs) were orbited in space to complete the CSS, also known as the Tiangong Space Station [22]. The completion of the CSS marks the third multi-modular space station following Mir (1986–2001) and the ISS (1998-present).

4.2. Advancements in Technology and Accelerator-Based Research in Relation to Publication Output

Particle accelerator technologies were designed decades ago to provide a realistic representation of the space environment [23]. The consistent progression of accelerator-based and ground-based research in the field of space radiation has been a point of interest for many space agencies across the globe.

The first cyclotron, a cyclical accelerator that accelerates charged particles in a spiral pattern, was invented in 1930 by Ernest Lawrence at the University of California, Berkeley, in the USA [24]. Lawrence's invention led to the eventual commission of the 88-Inch Cyclotron in what is now the Lawrence Berkeley National Laboratory (LBNL) in 1962.

The LBNL is seated and managed by the University of California, Berkeley, and overseen by the United States Department of Energy (DOE). The Berkeley Accelerator Space for Effects Facility (BASE), operated by the 88-Inch Cyclotron, provides proton, heavy-ion, and neutron particle radiation that can simulate the space environment [25]. The first tests of Single-Event Effects (SEEs), when a changed particle strikes an electrical circuit and a pressing concern for long-duration spaceflight, were conducted at the BASE [26,27].

Built in 1966, the University of California, Davis (USA), houses the Crocker Nuclear Laboratory (CNL). The 76-inch cyclotron provides lower-energy proton beams which allow for accurate testing of the effects of space radiation on electronic equipment housed in spacecrafts by agencies such as NASA [28].

The first hospital-based proton facility in the world was established in the USA in 1990 at Loma Linda University Medical Center (LLUMC) [29]. The Proton Treatment & Research Center at LLUMC is in partnership with the NASA Space Radiation Health Program [30]. In the early 2000s, the radiation shielding properties of American and Russian extravehicular activity (EVA) space suits to be worn to the ISS were evaluated. The American Extravehicular Mobility Unit (EMU) suit and the Russian Orlan-M suit were irradiated at varying doses and organ sites at the Proton Treatment Center to determine their radioprotective properties in a simulated LEO environment [31].

In 2003, the NASA Space Radiation Laboratory (NSRL), located at Brookhaven National Laboratory, was created to provide heavy-ion radiotherapy research to measure the risks and ameliorate the effects of radiation in space [32]. Notably, the NSRL was the first heavy-ion accelerator complex established explicitly for space radiation research [29]. The NSRL facility has accelerator technology that has allowed the USA to conduct a significant amount of ground-based research relevant to spaceflight [33]. The majority of ground-based research on space radiation-induced health risks have been studied using single-particle simulations [34]. However, the NASA Space Radiation Laboratory has recently developed a GCR simulator (GCRsim) that can generate a spectrum of ion beams that closely mimics the space radiation environment [34]. This technological advancement is crucial in improving the safety of space missions and provides the means to expand our understanding of simulated GCR effects on the CNS. The USA remained the top producing country for articles in both topic sets throughout all four decades (Tables S5 and S6), in part due to their numerous particle accelerator complexes across the country.

Built in 1992, the Proton Irradiation Facility (PIF), located in Switzerland, was designed and constructed by both the ESA and the Paul Scherrer Institute (PSI). The PIF simulates the proton spectra that are found in the space environment and encountered by spaceflight. Hence, the PIF's principal focus is to investigate the radiobiological effects of proton radiation for manned space missions [35]. Although Switzerland is not a top ten-ranked country for either topic set, many countries in the ESA, such as Germany, England, France, and Italy, are (Tables S5 and S6).

In Canada, a top ten producer of research studies for both topic sets 1 and 2 (Tables S5 and S6), the TRI University Meson Facility (TRIUMF) was established in the late 1960s. In the 1990s, TRIUMF developed beamlines that could simulate proton space radiation, which has allowed researchers to effectively study the effects of space radiation on space technology. Notably, TRIUMF is the world's largest cyclotron [36]. TRIUMF's neutron and proton beamlines have been used to measure parameters such as SEEs and shielding effects, as well as testing on GCR spectra and at ground level [37].

The Institute of Radiological Sciences was built in Japan [38]. From 2002 to 2005, JAXA, RSA, ESA, and NASA were all a part of the HIMAC Inter-Comparison of Cosmic Rays with Heavy Ion Beams (ICCHIBAN) project. ICCHIBAN was the first ground-based research project that measured the intercomparison of passive and active space dosimeters. The objective of the project was to mitigate the discrepancies between space radiation detectors across global space agencies. This was accomplished by testing space detectors with varying doses of heavy ions found in the GCR spectrum within the space environment [39]. Then, in 2009, Japan completed the construction of a high-intensity proton accelerator facility, the Japan Proton Accelerator Research Complex (J-PARC), which provides state-of-the-art technology for radiation research [40]. Japan has been a second- or third-ranking producer of research studies for topic set 2 and a top ten-ranking country overall for topic set 1 since the 2000s.

In Darmstadt, Germany, the Facility for Antiproton and Ion Research in Europe (FAIR) is being constructed as of 2017. FAIR is an expansion of the GSI Helmholtz Centre for Heavy Ion Research [41]. Russia and several members of the ESA, including Czechia, Germany, Finland, France, Poland, Romania, Sweden, and the United Kingdom, are affiliated with the FAIR. Notably, India is a shareholder in the FAIR and is tied with Canada for the place of eighth-ranking producer of research studies for topic set 2 in the 2010s (Table S6).

A heavy-ion particle accelerator, the Rare Isotope Accelerator Complex for ON-line Experiments (RAON), is being developed in South Korea as of 2014 and is expected to be completed circa 2025 [42]. Coincidentally, South Korea appeared as a top ten producing country for topic set 2 in the 2010s (Table S6).

The countries that have developed these types of facilities have consistently appeared among the top producing countries for publications in both topic sets throughout the decades. Researchers will be able to further develop countermeasures that prevent or mitigate CNS damage and cognitive deficits given the immense progress of accelerator radiation technology.

4.3. Institutional Analysis for Topic Sets 1 and 2 as They Correspond with Top Producing Countries

As previously noted, the USA was the top producing country with the most articles in both topic sets across all four decades. Moreover, these results for topic set 1 are consistent with institutions located in this country, such as NASA, the University of California System, and the DOE (Figure 7a). From the 1990s to the early 2020s, Germany had consistent growth of publication output. This is reflected in the fact that the Helmholtz Association and the German Aerospace Centre DLR are among the top producing institutions for topic set 1. China became a top producer of research studies in the 2010s and has sustained its production output going into the 2020s, consistent with the Chinese Academy of Sciences being one of the top producing institutions. The Russian Academy of Sciences appeared as a top producing institution for topic set 1, as did the Centre National De La Recherche Scientifique in France (Figure 7b). Although Russia did not appear in the results for top five producing countries, its space agency is part of the ISS, and it has become increasingly collaborative over the years. France did not appear in the top five rankings either but did appear in the top ten rankings of topic set 1 for all four decades. Notably, the ESA headquarters is located in Paris, France. This may suggest that collaborative efforts amongst other European countries such as Germany, England, and Italy could account for France's lower ranking.

The Institut National De La Sante De La Recherche Medicale in France and the Chinese Academy of Sciences were the only institutions not located in the USA for topic set 2 (Figure 8a). France has consistently been in the top ten producing countries for topic set 2 for all four decades. China did not become a top producer until the 2000s and was subsequently propelled to second rank in the 2010s and the 2020s thus far (Table S6).

Across all four decades, the USA has produced the most research studies for topic set 2. The LBNL, seated at the University of California, Berkeley, often collaborates with NASA and is overseen by the DOE. NASA also collaborates with the University of California, Davis, via the Crocker Nuclear Laboratory. C.L. Limoli, a principal investigator at the University of California, Irvine, is a top ten producer of studies in topic set 2 (Figure 6). These numerous affiliations correspond to the University of California System being the top producer overall in topic set 2 (Figure 7a). The third-ranking institution Loma Linda University and NASA have a partnership supported by the Proton Treatment & Research Center at LLUMC[73]. Additionally, Loma Linda University is home to three of the top ten-ranking researchers of topic set 2: G.A. Nelson, M.J. Pecaut, and D.S. Gridley (Emeritus) (Table S2).

4.4. Highlights of Research by Top Authors by Publication Output in Topic Sets 1 and 2

The results for most of the top producing authors in both topic sets correlated with top producing countries and institutions. F.A. Cucinotta was the most productive author for topic set 1 (Figure 5a). In the 1990s, Cucinotta's research focused on models and assessments of risks for astronauts in space from exposures such as solar particle events, GCRs, geomagnetic-trapped radiation, and onboard nuclear propulsion engines [43]. The author's studies also focused on modifying the space environment by providing structures to shield astronauts' bodies [44]. In the 2000s, more studies began to focus their attention on the new challenges imposed by the adverse effects of long-term exposure to the space environment, as opposed to the brief exposures experienced by astronauts [45]. Cucinotta's studies also continued to focus on designing materials to provide adequate shielding to protect astronauts from space radiation, as well as shielding materials for vehicle construction [46]. Understanding the oncogenic potential of GCRs became an area of great interest for Cucinotta [47]. Research continued to investigate experimental models with the hopes of creating testable theories that could lead to accurate projections of astronaut risk [48].

During the 2000s, great uncertainty surrounded GCR risk projections due to limited radiobiology data and knowledge of GCR heavy ions [49], and studies focused on developing risk models to mitigate these uncertainties. In the 2010s, projecting cancer risks due to space radiation exposure to astronauts was a primary focus. Cucinotta's work also placed a significant emphasis on studying the cognitive detriments that may occur during exposure to heavy-ion radiation that have been linked to changes in neuronal morphology and plasticity [50]. Developing experimental models that use ground-based GCR simulators were a high priority for space radiobiology research [51].

Moving into the 2020s, cancer risks remained a principal focus in Cucinotta's work, with particular attention to high LET radiation. A study in January 2020 investigated the risks of cancer and circulatory disease for private space flight to Mars [52], which is of growing public interest with the boom of companies such as SpaceX, Blue Origin, and Virgin Galactic. Cucinotta et al. found that exposure to high LET radiation in the space environment led to a cancer morbidity risk of circa 21% and 13% in 20-year-old females and males, respectively, within a 95% confidence interval. There was a higher chance of cancer morbidity for younger people (>40) [52]. Another study conducted by Cucinotta in 2020 looked at how uncertainties in parameters such as dose rate modifiers, non-targeted effects (NTEs), or tumor lethality may affect how GCR exposure corresponds to space-related cancer risks [53]. NTEs are a phenomenon in which irradiation causes damage to non-irradiated tissues. This occurs when the non-irradiated cells have descended from the irradiated cells and engendered genomic instability or because there was cellular communication between the non-irradiated and irradiated tissues [54]. NTEs, as they relate to space radiation-induced tissue damage, have also been a focal point in some of Cucinotta's work.

In 2022, Cucinotta and Sanganti proposed the first predictions of space radiation cancer risks, independent of age, for four racial demographics in the USA: Asian/Pacific

Islander (API), Black, Hispanic (White and Black), and White (non-Hispanic) [55]. The study found that Black males and females have comparable cancer risk to their White counterparts, although Black people have a lower life expectancy. Hispanic people and API males have the lowest cancer risk; White females have the highest cancer risk. This study is groundbreaking as it paves the way for further research that considers differences in both ethnicity and sex and how these parameters interact with the space environment. Notably, Sanganti is a principal investigator from Prairie View A&M University, a historically Black university.

G.A. Nelson was the most productive author for topic set 2 (Figure 6a) and has collaborated with seven other highly ranked authors (viz., R.A. Britten, M.J. Pecaut, D.S. Gridley, M. Boerma, J. Raber, V. Sridharan, and C.L. Lomoli) between 1990 and 2023. During the 1990s, Nelson had several publications that used a subset of *Caenorhabditis elegans* nematodes for radiobiological studies to assess the biological effects of HZE radiation during long-duration spaceflight [56]. In the 2000s, Nelson published studies that examined the long-term effects of space-like proton exposures on immune system status. The data from one study indicated that whole-body exposure to proton radiation at doses of the order of large solar particle events may have long-term effects on immune status [57]. Nelson also published a few studies that examined the effects of space radiation on skeletal muscle, bone architecture, cortical bone, and trabecular bone. One publication used an animal model to study the causes of radiation-induced osteoporosis, and the results revealed significant losses in trabecular bone volume fraction after exposure to all radiation species [58]. In the latter part of the decade, Nelson published a few studies that explored ^{56}Fe particle radiation exposure on the CNS. Results from one particular study showed a dose-related decrease in hippocampal neurogenesis and a dose-related increase in newly born activated microglia [59].

In the 2010s, there was growing interest in estimating cardiovascular disease risk from exposure to space radiation. This increase in concern was due to studies that suggested the heart may be injured by lower doses of ionizing radiation than previously thought [60]. In one particular publication, Nelson highlighted the current models used to address cardiovascular effects of space radiation, as well as potential pharmacological countermeasures against its adverse effects [61]. In the later part of the decade, a few of Nelson's publications evaluated the potential health risks associated with neuronal exposure. Data from one study confirmed that irradiation with ^{28}Si particles at relatively low doses alters the properties of the hippocampal network, which can lead to limitations in connections with other brain centers [62].

This work was continued into 2020, when a study found that low doses ($\leq$15 cGy) of ^{28}Si radiation to male rats resulted in increased long-term neuronal depression in the pre-frontal cortex and impaired cognitive flexibility. These findings also suggested that space radiation-induced impairments may not be the sole cause of such deficits [63]. Nelson also published two articles that explored how proton and oxygen ion irradiation affects the cardiovascular system in rabbits and rats [64,65]. Both studies found that low doses of whole-body ^{16}O or proton irradiation induced mild changes in vascular function and an increase in CD68, a marker for macrophages which can signify tissue inflammation [66].

4.5. The Evolution of Bibliographic Terms for Topic Sets 1 and 2 over Each Corresponding Decade

The interest in space radiation research has followed a consistently upward trend, as shown in the steady increase in publication output over the last three decades. However, the focus of space radiation research in relation to its effects on human health has fluctuated over time, as reflected in the term maps that were generated for each decade. Most of the key terms during the 1990s related to topics on a cellular level, with terms such as *cells nuclear matrix*, *DNA*, *expression* and *murine model* (Figure 11). During this time period, research seemed to focus on how radiation might affect the physical structure and molecular interactions of cells. The use of in vitro cell cultures to gain a deeper knowledge about the biological effects of space radiation and about cellular repair mechanisms to mediate the risks of space radiation played a key role in research during this decade [67]. This trend was similar for studies of mice or rats (i.e., topic set 2), with key terms such as *cells*, *nuclear matrix*, *gene expression*, *protein*, and *nucleotide sequence*. However, some degree of bone-related research was indicated by the cluster of key terms such as *cortical bone*, *histomorphometry*, *parathyroid hormone*, and *calcium*. During the 1990s, a large emphasis was placed on the damage a mission to Mars could have on bone loss. Calcium metabolism was considered one of two key physiologic and medical challenges during a trip to Mars [68]. These same key terms that relate to bone research appear in the network maps for human research (i.e., topic set 1) in the 2000s. They also include terms such as *osteoporosis*, *mineral density*, *oxidative stress*, *carcinoma*, *p53*, *apoptosis*, *cancer*, and *chemoprevention* (Figure 12).

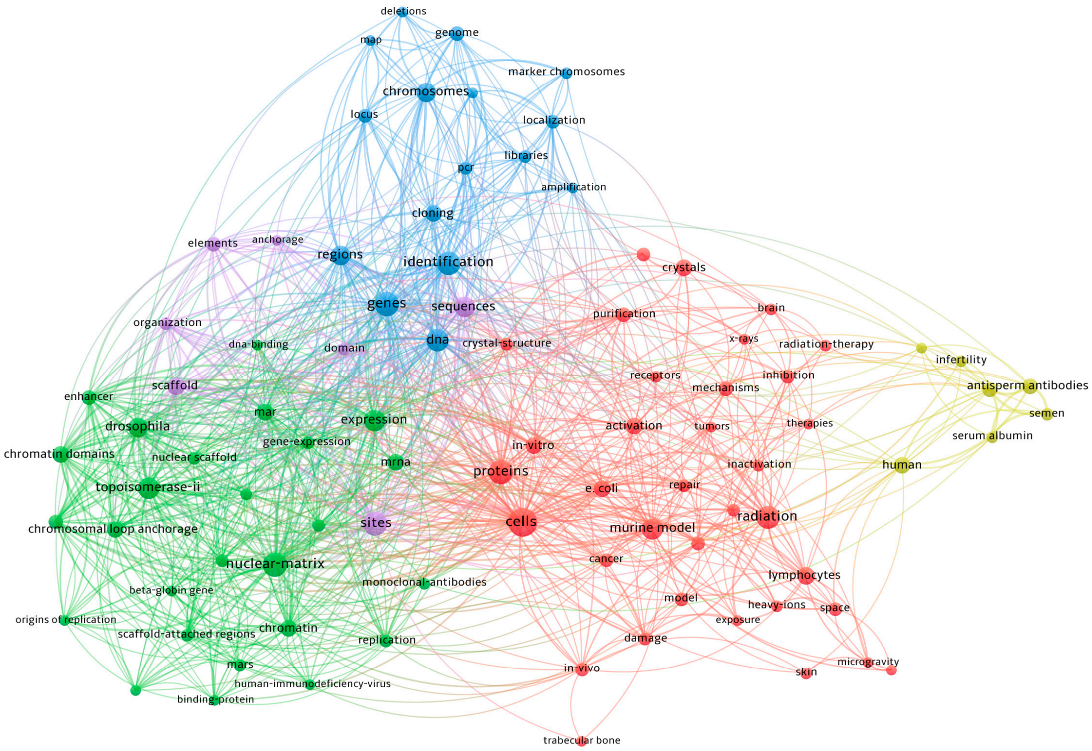


Figure 11. Topic set 1 term map from 1990 to 1999. Cluster 1 is represented by the red region, with 42 terms. Cluster 2 is the green region, with 33 terms. Cluster 3 is the blue region, with 16 terms.

In addition to radiation exposure, there was a major concern over exposure to microgravity, which also appears as a term in the network map during the 2000s (Figure 13). A number of publications reported how these exposures would contribute to the loss of bone mass among astronauts. One particular study looked at how oxidative stress mediates radiation-induced bone loss in cancellous tissue [69]. Another large area of focus during this decade was research on projecting cancer risks from exposure to space radiation. Cancer risk projections were considered challenging to assess and highly uncertain because of the absence of data for humans and the limited radiobiology data available for estimating the late effects of the high-energy heavy ions (HZE particles) present in GCRs [70]. Throughout the 2000s, cancer induction in astronauts continued to appear in publications as a primary concern due to the minimal amount of data and the many uncertainties [71].

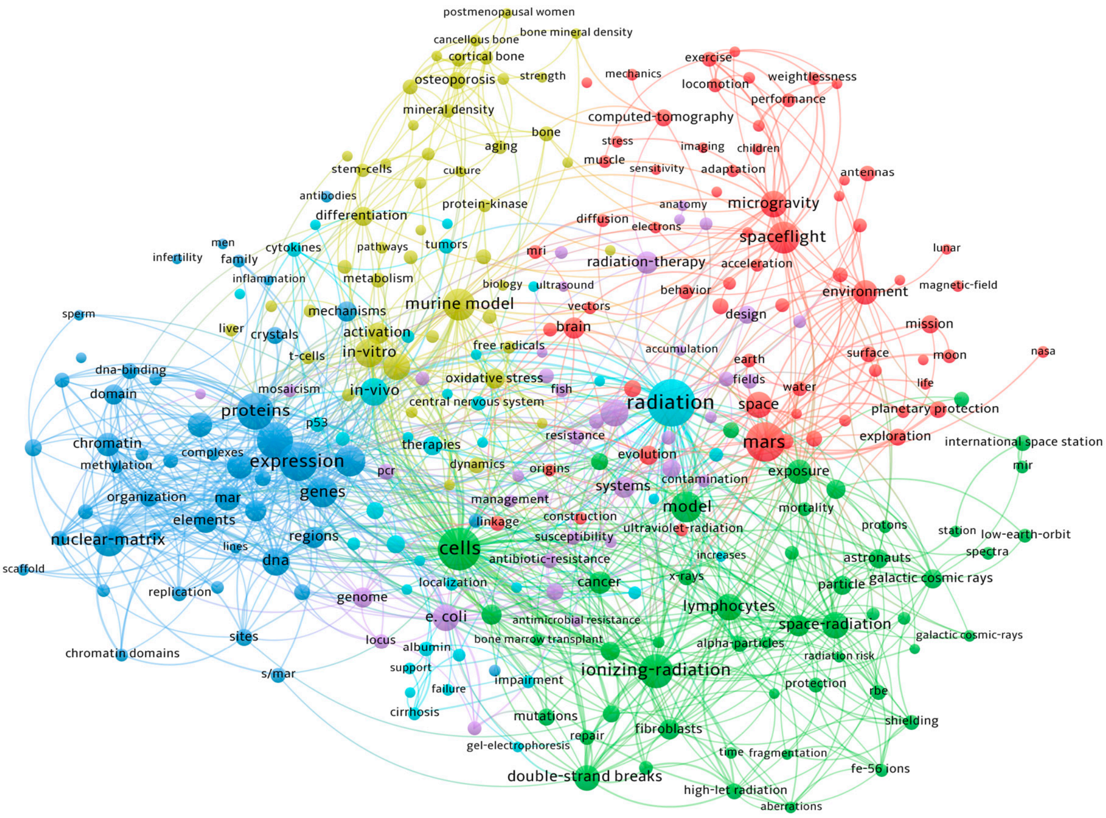


Figure 12. Topic set 1 term map for 2000–2009. Cluster 1 is represented by the red region, with 65 terms. Cluster 2 is the green region, with 50 terms. Both cluster 3 and 4, blue and yellow, respectively, have 48 terms. Cluster 5 is represented by the purple region, with 38 terms. Cluster 6 is the teal region, with 37 terms.

In the network map for the topic set related to mice or rats, the key term *brain* appears for the first time. Publications focused on how exposure to radiation might disturb the CNS began to increase and to particularly target how brain damage can influence cognitive function. Research on rats and mice throughout the decade suggested potential significant CNS effects of long-term spaceflight on astronauts that may produce behavioral changes during the mission or sometime after the return [72]. Most of these studies used whole-body irradiation composed of a single dose of GCR-relevant HZE particles. A notable study looked at how exposure influenced neurogenesis, synaptic plasticity, and learning deficits. Their findings suggested that GCR exposure can persistently alter brain health and cognitive function during and after long-duration travel in deep space [73].

In the 2020s, the size of the *Mars* bubble term in the network map increased in size, along with an expansion of a cluster of intertwining key terms such as *microbiome*, *memory deficits*, *cancer risk*, *aretemis*, *behavior*, *cranial irradiation*, *countermeasure*, *exercise*, *cognitive function*, *anxiety*, and ^{56}*Fe-particles* (Figure 14). Key terms related to bone were still present in this time span, as were key terms that are associated with cellular and molecular interactions. However, very few key terms were related to cancer research, as evident in the previous decade. There is a large shift in a more detailed focus toward researching the brain, particularly the hippocampal region. The hippocampus is the part of the CNS that is most sensitive to radiation, and damage can modify the higher integrative brain functions, leading to cognitive disorders [74]. During the early 2010s, it was clear that ionizing radiation had a significant impact on hippocampal neurogenesis and function, but there was considerable uncertainty about the mechanisms underlying these effects [75].

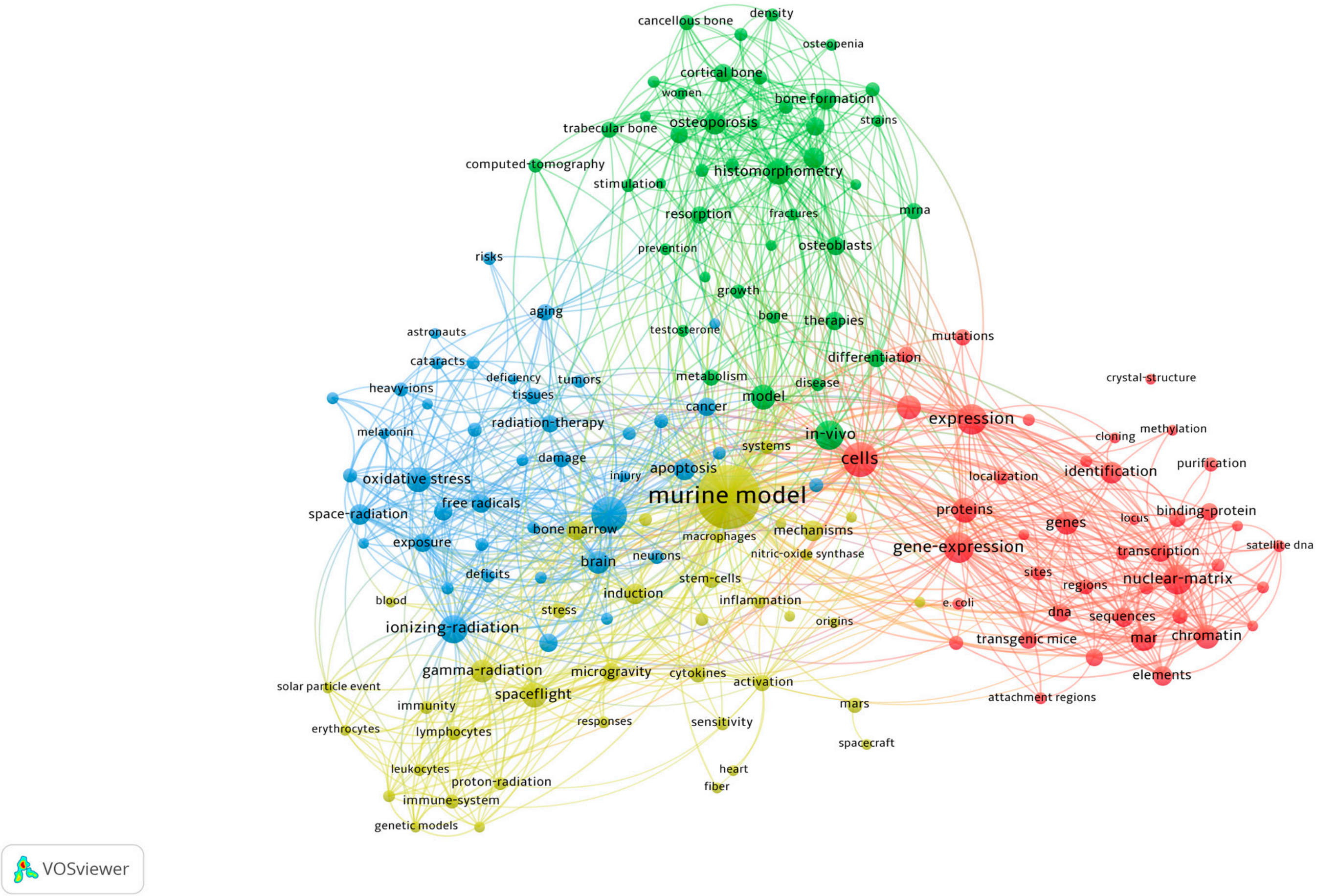


Figure 13. Topic set 2 term map for 2000–2009. Clusters 1, 2, and 3, represented by the red, green, and blue regions, respectively, have 42 terms each. Cluster 4 is the yellow region, with 39 terms.

In addition to a focus on the hippocampal region of the brain, there was also a significant amount of research that studied the prefrontal cortex (PFC). Chronic cognitive impairments associated with GCRs in rodent model systems were identified in both of these regions [76]. Although the PFC did not appear in any of the term maps, it was noteworthy in most publications that studied cognitive dysfunction. In the early 2000s, a series of studies conducted by Britten et al. proposed the idea that neurocognitive tasks regulated by the PFC could be impaired from low-dose HZE particles, which could lead to deficits in complex executive functions [63]. In studies of rats, mission-relevant doses of ^{56}Fe particles resulted in the loss of functionality in several regions of the cortex. This raises the possibility that astronauts on prolonged space missions could consequently develop deficits in executive function [77]. Another study exposed rodents to cosmic radiation and observed correlations between decrements in cortical-based performance and alterations in morphology of PFC neurons [78]. Data from studies on how exposure to space radiation affects the PFC consistently indicated reductions in neuronal structure and increases in cognitive impairment. Throughout the latter years of the decade, research focused on gaining new mechanistic insights and on potential countermeasures to these deleterious effects.

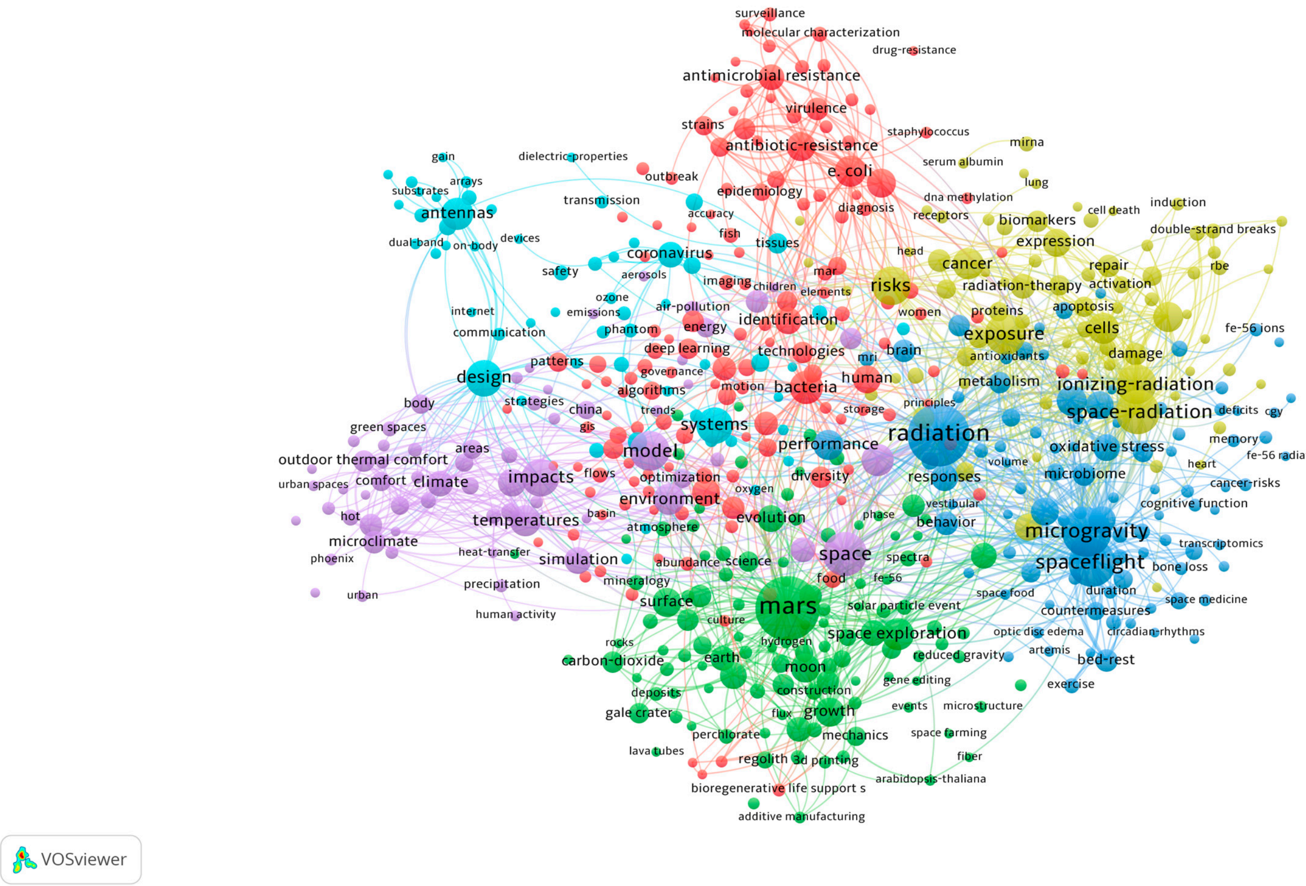


Figure 14. Topic set 1 term map for 2020–2023. Cluster 1 is represented by the red region, with 146 terms. Cluster 2 is the green region, with 112 terms. Cluster 3 is the blue region, with 95 terms. Cluster 4 is the yellow region, with 77 terms. Cluster 5 is the purple region, with 64 terms. Cluster 6 is represented by the teal region, with 58 terms.

5. Conclusions

Bibliometrics is a useful tool to gather information on scientific outcomes for a specific topic or field over a period of time. Our bibliometric analysis provides insight into the trends, from 1990 to 2023, in the top producers in the field of space radiation research and illustrates how the focus of this field has evolved. We selected the search terms to analyze any trends in research on the effects of space radiation on cognition in human and rodent models over the last three decades. However, there are limitations to a bibliometric analysis. For instance, an author may produce fewer publications, yet their small body of work may be influential within their field and have a tremendous impact that is not accounted for in a standardized h-index.

Space radiation is made up of particles trapped within the Earth's magnetosphere from Van Allen belts, solar particle events (SPEs) from sporadic solar flares, and high-energy protons and heavy ions from GCRs [34]. Beyond Earth's protective magnetosphere, astronauts are at significant risk to the dangerous and penetrative properties of SPE and GCR exposure. When NASA ventures out for long-duration missions to Mars, astronauts will endure higher levels of radiation due to SPEs and GCRs. GCRs are a continuous source of radiation that is unavoidable during deep-space missions [79]. However, there are a limited number of individuals who have endured GCRs in deep-space travel; therefore, research depends on animal models to understand simulated GCR exposure. In addition, relatively few studies have incorporated ^{4}He into behavioral studies, even though it is the second most prevalent radiation type in GCRs, comprising 14% of GCRs [80]. It is estimated that during deep-space missions, each cell in the body will be traversed by a helium ion approximately once every three weeks [81,82]. However, studies investigating the effects of whole-body exposure to ^{4}He on hippocampus-dependent behavior have shown deficits in hippocampus-dependent behaviors [83].

Astronauts will need to maintain high levels of cognitive performance in order to carry out a successful exploration of Mars. One of the primary risks of concern includes central nervous system (CNS) effects resulting in potential cognitive or behavioral impairments and late neurological disorders [84]. NASA's ultimate goal is to enable human space exploration within acceptable risks from exposure. There is a vast amount of research studies indicating the anti-inflammatory effects of many vitamins and phytochemicals in plants that could be promising candidates for therapeutic applications [85,86]. NASA is currently funding research to understand how radiation risks in space will affect astronauts and to find potential antioxidant and inflammatory countermeasures to mitigate those risks.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/radiation5010001/s1. Table S1 shows the most productive and cited authors of articles in topic set 1 from 1990 to 2023. Table S2 shows the most productive and cited authors of articles in topic set 2 from 1990 to 2023. Table S3 shows the most productive and cited institutions for articles in topic set 1 from 1990 to 2023. Table S4 shows the most productive and cited institutions for articles in topic set 2 from 1990 to 2023. Table S5 shows the top ten most productive countries for topic set 1, organized by decade. Table S6 shows the top ten most productive countries for topic set 2, organized by decade.

Author Contributions: Conceptualization, A.R.A. and P.S.; methodology, P.S. and C.S.; validation, A.R.A., P.S. and C.S.; formal analysis, A.R.A., P.S. and C.S.; investigation, P.S., C.S., S.S. and T.M.; resources, A.R.A.; data curation, C.S.; writing of the original draft preparation, A.R.A., P.S., S.S. and T.M.; writing and review of editing, A.R.A. and C.S.; visualization, P.S. and C.S.; supervision, A.R.A., project administration, A.R.A.; funding acquisition, A.R.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Translational Research Institute through NASA cooperative agreements NNX16AO69A and NIH R25GM083247 (A.R.A.).

Acknowledgments: We thank Kerry Evans from the UAMS Science Communication Group for grammatical editing of this manuscript.

Conflicts of Interest: The authors declare no conflicts of interest. The funders had no role in the design of this study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. Prasad, B.; Richter, P.; Vadakedath, N.; Mancinelli, R.; Kruger, M.; Strauch, S.M.; Grimm, D.; Darriet, P.; Chapel, J.P.; Cohen, J.; et al. Exploration of space to achieve scientific breakthroughs. *Biotechnol. Adv.* **2020**, *43*, 107572. [CrossRef] [PubMed]
2. Chancellor, J.C.; Blue, R.S.; Cengel, K.A.; Aunon-Chancellor, S.M.; Rubins, K.H.; Katzgraber, H.G.; Kennedy, A.R. Limitations in predicting the space radiation health risk for exploration astronauts. *NPJ Microgravity* **2018**, *4*, 8. [CrossRef] [PubMed]
3. Aglietti, G.S. Current Challenges and Opportunities for Space Technologies. *Front. Space Technol.* **2020**, *1*, 1. [CrossRef]
4. Pendergraft, J.G.; Carter, D.R.; Tseng, S.; Landon, L.B.; Slack, K.J.; Shuffler, M.L. Learning From the Past to Advance the Future: The Adaptation and Resilience of NASA's Spaceflight Multiteam Systems Across Four Eras of Spaceflight. *Front. Psychol.* **2019**, *10*, 1633. [CrossRef]
5. Ganapathy, K.; da Rosa, M.; Russomano, T. Neurological changes in outer space. *Neurol. India* **2019**, *67*, 37–43. [CrossRef]
6. Furukawa, S.; Nagamatsu, A.; Nenoi, M.; Fujimori, A.; Kakinuma, S.; Katsube, T.; Wang, B.; Tsuruoka, C.; Shirai, T.; Nakamura, A.J.; et al. Space Radiation Biology for "Living in Space". *Biomed. Res. Int.* **2020**, *2020*, 4703286. [CrossRef]
7. Axpe, E.; Chan, D.; Abegaz, M.F.; Schreurs, A.S.; Alwood, J.S.; Globus, R.K.; Appel, E.A. A human mission to Mars: Predicting the bone mineral density loss of astronauts. *PLoS ONE* **2020**, *15*, e0226434. [CrossRef]

8. Hupfeld, K.E.; McGregor, H.R.; Reuter-Lorenz, P.A.; Seidler, R.D. Microgravity effects on the human brain and behavior: Dysfunction and adaptive plasticity. *Neurosci. Biobehav. Rev.* **2021**, *122*, 176–189. [CrossRef]
9. Sobel, A.; Duncan, R. Aerospace Environmental Health: Considerations and Countermeasures to Sustain Crew Health Through Vastly Reduced Transit Time to/From Mars. *Front. Public Health* **2020**, *8*, 327. [CrossRef]
10. Chancellor, J.C.; Scott, G.B.; Sutton, J.P. Space Radiation: The Number One Risk to Astronaut Health beyond Low Earth Orbit. *Life* **2014**, *4*, 491–510. [CrossRef]
11. Kokhan, V.S.; Matveeva, M.I.; Mukhametov, A.; Shtemberg, A.S. Risk of defeats in the central nervous system during deep space missions. *Neurosci. Biobehav. Rev.* **2016**, *71*, 621–632. [CrossRef]
12. Pariset, E.; Malkani, S.; Cekanaviciute, E.; Costes, S.V. Ionizing radiation-induced risks to the central nervous system and countermeasures in cellular and rodent models. *Int. J. Radiat. Biol.* **2021**, *97*, S132–S150. [CrossRef] [PubMed]
13. Li, K.; Rollins, J.; Yan, E. Web of Science use in published research and review papers 1997–2017: A selective, dynamic, cross-domain, content-based analysis. *Scientometrics* **2018**, *115*, 1–20. [CrossRef] [PubMed]
14. Yang, W.; Zhang, J.; Ma, R. The Prediction of Infectious Diseases: A Bibliometric Analysis. *Int. J. Environ. Res. Public Health* **2020**, *17*, 6218. [CrossRef]
15. Guo, Y.-M.; Huang, Z.-L.; Guo, J.; Li, H.; Guo, X.-R.; Nkeli, M.J. Bibliometric Analysis on Smart Cities Research. *Sustainability* **2019**, *11*, 3606. [CrossRef]
16. Novikova, N.; De Boever, P.; Poddubko, S.; Deshevaya, E.; Polikarpov, N.; Rakova, N.; Coninx, I.; Mergeay, M. Survey of environmental biocontamination on board the International Space Station. *Res. Microbiol.* **2006**, *157*, 5–12. [CrossRef] [PubMed]
17. Neubert, T.; Østgaard, N.; Reglero, V.; Blanc, E.; Chanrion, O.; Oxborrow, C.A.; Orr, A.; Tacconi, M.; Hartnack, O.; Bhanderi, D.D.V. The ASIM Mission on the International Space Station. *Space Sci. Rev.* **2019**, *215*, 26. [CrossRef]
18. Galeev, A.A. Russian program of planetary missions. *Acta Astronaut.* **1996**, *39*, 9–14. [CrossRef]
19. Kozlovskaya, I.B.; Yarmanova, E.N.; Yegorov, A.D.; Stepantsov, V.I.; Fomina, E.V.; Tomilovaskaya, E.S. Russian Countermeasure Systems for Adverse Effects of Microgravity on Long-Duration ISS Flights. *Aerosp. Med. Hum. Perform.* **2015**, *86*, A24–A31. [CrossRef]
20. Graf, A. International Space Station Visitors by Country. Available online: https://www.nasa.gov/international-space-station/space-station-visitors-by-country/ (accessed on 18 November 2024).
21. Pei, W.; Hu, W.; Chai, Z.; Zhou, G. Current status of space radiobiological studies in China. *Life Sci. Space Res.* **2019**, *22*, 1–7. [CrossRef]
22. Zhu, H. Scientific experiments on Tiangong-2, the predecessor of the China Space Station. *Natl. Sci. Rev.* **2022**, *9*, nwac189. [CrossRef] [PubMed]
23. Thariat, J.; Habrand, J.L.; Lesueur, P.; Chaikh, A.; Kammerer, E.; Lecomte, D.; Batalla, A.; Balosso, J.; Tessonnier, T. Why proton therapy? And how? *Bull. Cancer* **2018**, *105*, 315–326. [CrossRef] [PubMed]
24. Wagner, H.N., Jr. A brief history of positron emission tomography (PET). *Semin. Nucl. Med.* **1998**, *28*, 213–220. [CrossRef]
25. Johnson, M.B.; McMahan, M.A.; Gimpel, T.L.; Tiffany, W.S. Berkeley Accelerator Space Effects (BASE) Light Ion Facility Upgrade. In Proceedings of the 2006 IEEE Radiation Effects Data Workshop, Ponte Vedra Beach, FL, USA, 17–21 July 2006. [CrossRef]
26. Pearton, S.J.; Haque, A.; Khachatrian, A.; Ildefonso, A.; Chernyak, L.; Ren, F. Review—Opportunities in Single Event Effects in Radiation-Exposed SiC and GaN Power Electronics. *ECS J. Solid State Sci. Technol.* **2021**, *10*, 075004. [CrossRef]
27. Smith, K. 88-Inch Cyclotron/Berkeley Accelerator Space Effects Facility. Available online: https://www.nasa.gov/setmo/facilities/88-inch-cyclotron-berkeley-accelerator-space-effects-facility/ (accessed on 18 November 2024).
28. Castaneda, C.M. Crocker Nuclear Laboratory (CNL) Radiation Effects Measurement and Test Facility. In Proceedings of the 2001 IEEE Radiation Effects Data Workshop. NSREC 2001. Workshop Record. Held in conjunction with IEEE Nuclear and Space Radiation Effects Conference (Cat. No.01TH8588), Vancouver, BC, Canada, 16–20 July 2001. [CrossRef]
29. Slater, J.D. Development and operation of the Loma Linda University Medical Center proton facility. *Technol. Cancer Res. Treat.* **2007**, *6*, 67–72. [CrossRef]
30. Miller, J. Proton and heavy ion acceleration facilities for space radiation research. *Gravit. Space Biol. Bull.* **2003**, *16*, 19–28.
31. Benton, E.R.; Benton, E.V.; Frank, A.L. *Characterization of the Radiation Shelding Properties of US and Russian EVA Suits*; Eril Research, Inc.: San Rafael, CA, USA, 2001.
32. La Tessa, C.; Sivertz, M.; Chiang, I.H.; Lowenstein, D.; Rusek, A. Overview of the NASA space radiation laboratory. *Life Sci. Space Res.* **2016**, *11*, 18–23. [CrossRef]
33. Miller, J.; Zeitlin, C. Twenty years of space radiation physics at the BNL AGS and NASA Space Radiation Laboratory. *Life Sci. Space Res.* **2016**, *9*, 12–18. [CrossRef]
34. Simonsen, L.C.; Slaba, T.C.; Guida, P.; Rusek, A. NASA's first ground-based Galactic Cosmic Ray Simulator: Enabling a new era in space radiobiology research. *PLoS Biol.* **2020**, *18*, e3000669. [CrossRef]
35. Hajdas, W.; Adams, L.; Nickson, B.; Zehnder, A. The Proton Irradiation Facility at the Paul Scherrer Institute. *Nucl. Instrum. Methods Phys. Res. B* **1996**, *113*, 54–58. [CrossRef]

36. Craddock, M. 40 Years On—Reflections on the History of TRIUMF from Conception to the First Beam. *Phys. Can.* **2019**, *75*, 72–78.
37. Blackmore, E.; Trinczek, M.; Jiang, K.; Sachdev, M.; Wright, D. SRAM Dosimeter for Characterizing the TRIUMF Proton and Neutron Beams. *IEEE Trans. Nucl. Sci.* **2019**, *66*, 276–281. [CrossRef]
38. Iguchi, T.; Fukahori, T. *JAERI-Conf 96-008, Proceedings of the 1995 Symposium on Nuclear Data, Tokai, Japan, 16–17 November 1995*; Japan Atomic Energy Research Institute: Ibaraki, Japan, 1996.
39. Benton, E.R.; Berger, T.; Uchihori, Y.; Kitamura, H. Intercomparison of Radiation Detectors and Dosimeters for Use in Manned Space Flight. *Radioisotopes* **2019**, *68*, 411–418. [CrossRef]
40. Nagamiya, S. Introduction to J-PARC. *Prog. Theor. Exp. Phys.* **2012**, *2012*, 02B001. [CrossRef]
41. Schuy, C.; Weber, U.; Durante, M. Hybrid Active-Passive Space Radiation Simulation Concept for GSI and the Future FAIR Facility. *Front. Phys.* **2020**, *8*, 337. [CrossRef]
42. Hong, B. Status of the RAON project in Korea. *AAPPS Bull.* **2023**, *33*, 3. [CrossRef]
43. Cucinotta, F.A.; Wilson, J.W. Initiation-promotion model of tumor prevalence in mice from space radiation exposures. *Radiat. Environ. Biophys.* **1995**, *34*, 145–149. [CrossRef]
44. Wilson, J.W.; Thibeault, S.A.; Cucinotta, F.A.; Shinn, J.L.; Kim, M.; Kiefer, R.; Badavi, F.F. Issues in protection from galactic cosmic rays. *Radiat. Environ. Biophys.* **1995**, *34*, 217–222. [CrossRef]
45. Simonsen, L.C.; Wilson, J.W.; Kim, M.H.; Cucinotta, F.A. Radiation exposure for human Mars exploration. *Health Phys.* **2000**, *79*, 515–525. [CrossRef]
46. Wilson, J.W.; Cucinotta, F.A.; Miller, J.; Shinn, J.L.; Thibeault, S.A.; Singleterry, R.C.; Simonsen, L.C.; Kim, M.H. Approach and issues relating to shield material design to protect astronauts from space radiation. *Mater. Des.* **2001**, *22*, 541–554. [CrossRef]
47. Cucinotta, F.A.; Durante, M. Cancer risk from exposure to galactic cosmic rays: Implications for space exploration by human beings. *Lancet Oncol.* **2006**, *7*, 431–435. [CrossRef] [PubMed]
48. Cucinotta, F.A. Once we know all the radiobiology we need to know, how can we use it to predict space radiation risks and achieve fame and fortune? *Phys. Med.* **2001**, *17* (Suppl. S1), 5–12. [PubMed]
49. Cucinotta, F.A.; Schimmerling, W.; Wilson, J.W.; Peterson, L.E.; Saganti, P.B.; Dicello, J.F. Uncertainties in estimates of the risks of late effects from space radiation. *Adv. Space Res.* **2004**, *34*, 1383–1389. [CrossRef] [PubMed]
50. Alp, M.; Cucinotta, F.A. Biophysics Model of Heavy-Ion Degradation of Neuron Morphology in Mouse Hippocampal Granular Cell Layer Neurons. *Radiat. Res.* **2018**, *189*, 312–325. [CrossRef]
51. Kim, M.H.; Rusek, A.; Cucinotta, F.A. Issues for Simulation of Galactic Cosmic Ray Exposures for Radiobiological Research at Ground-Based Accelerators. *Front. Oncol.* **2015**, *5*, 122. [CrossRef]
52. Cucinotta, F.A.; Cacao, E.; Kim, M.-H.Y.; Saganti, P.B. Cancer and circulatory disease risks for a human mission to Mars: Private mission considerations. *Acta Astronaut.* **2020**, *166*, 529–536. [CrossRef]
53. Cucinotta, F.A.; Cacao, E.; Kim, M.Y.; Saganti, P.B. Benchmarking risk predictions and uncertainties in the NSCR model of GCR cancer risks with revised low let risk coefficients. *Life Sci. Space Res.* **2020**, *27*, 64–73. [CrossRef]
54. Wright, E.G. Manifestations and mechanisms of non-targeted effects of ionizing radiation. *Mutat. Res.* **2010**, *687*, 28–33. [CrossRef]
55. Cucinotta, F.A.; Saganti, P.B. Race and ethnic group dependent space radiation cancer risk predictions. *Sci. Rep.* **2022**, *12*, 2028. [CrossRef]
56. Nelson, G.A.; Schubert, W.W.; Marshall, T.M. Radiobiological studies with the nematode Caenorhabditis elegans. Genetic and developmental effects of high LET radiation. *Int. J. Rad. Appl. Instrum. D* **1992**, *20*, 227–232. [CrossRef]
57. Pecaut, M.J.; Gridley, D.S.; Nelson, G.A. Long-term effects of low-dose proton radiation on immunity in mice: Shielded vs. unshielded. *Aviat. Space Environ. Med.* **2003**, *74*, 115–124. [PubMed]
58. Hamilton, S.A.; Pecaut, M.J.; Gridley, D.S.; Travis, N.D.; Bandstra, E.R.; Willey, J.S.; Nelson, G.A.; Bateman, T.A. A murine model for bone loss from therapeutic and space-relevant sources of radiation. *J. Appl. Physiol.* **2006**, *101*, 789–793. [CrossRef]
59. Rola, R.; Fishman, K.; Baure, J.; Rosi, S.; Lamborn, K.R.; Obenaus, A.; Nelson, G.A.; Fike, J.R. Hippocampal neurogenesis and neuroinflammation after cranial irradiation with (56)Fe particles. *Radiat. Res.* **2008**, *169*, 626–632. [CrossRef]
60. Ramadan, S.S.; Sridharan, V.; Koturbash, I.; Miousse, I.R.; Hauer-Jensen, M.; Nelson, G.A.; Boerma, M. A priming dose of protons alters the early cardiac cellular and molecular response to (56)Fe irradiation. *Life Sci. Space Res.* **2016**, *8*, 8–13. [CrossRef] [PubMed]
61. Boerma, M.; Nelson, G.A.; Sridharan, V.; Mao, X.W.; Koturbash, I.; Hauer-Jensen, M. Space radiation and cardiovascular disease risk. *World J. Cardiol.* **2015**, *7*, 882–888. [CrossRef] [PubMed]
62. Rudobeck, E.; Nelson, G.A.; Sokolova, I.V.; Vlkolinsky, R. (28)silicon radiation impairs neuronal output in CA1 neurons of mouse ventral hippocampus without altering dendritic excitability. *Radiat. Res.* **2014**, *181*, 407–415. [CrossRef]
63. Britten, R.A.; Duncan, V.D.; Fesshaye, A.; Rudobeck, E.; Nelson, G.A.; Vlkolinsky, R. Altered Cognitive Flexibility and Synaptic Plasticity in the Rat Prefrontal Cortex after Exposure to Low ($\leq$15 cGy) Doses of (28)Si Radiation. *Radiat. Res.* **2020**, *193*, 223–235. [CrossRef]

64. Nemec-Bakk, A.S.; Sridharan, V.; Seawright, J.W.; Nelson, G.A.; Cao, M.; Singh, P.; Cheema, A.K.; Singh, B.; Li, Y.; Koturbash, I.; et al. Effects of proton and oxygen ion irradiation on cardiovascular function and structure in a rabbit model. *Life Sci. Space Res.* **2023**, *37*, 78–87. [CrossRef]
65. Sridharan, V.; Seawright, J.W.; Landes, R.D.; Cao, M.; Singh, P.; Davis, C.M.; Mao, X.W.; Singh, S.P.; Zhang, X.; Nelson, G.A.; et al. Effects of single-dose protons or oxygen ions on function and structure of the cardiovascular system in male Long Evans rats. *Life Sci. Space Res.* **2020**, *26*, 62–68. [CrossRef]
66. Chistiakov, D.A.; Killingsworth, M.C.; Myasoedova, V.A.; Orekhov, A.N.; Bobryshev, Y.V. CD68/macrosialin: Not just a histochemical marker. *Lab. Investig.* **2017**, *97*, 4–13. [CrossRef]
67. Meli, A.; Perrella, G.; Curcio, F.; Ambesi-Impiombato, F.S. In vitro cultured cells as probes for space radiation effects on biological systems. *Mutat. Res./Fundam. Mol. Mech. Mutagen.* **1999**, *430*, 229–234. [CrossRef] [PubMed]
68. Buckey, J.C. Preparing for Mars: The physiologic and medical challenges. *Eur. J. Med. Res.* **1999**, *4*, 353–356. [PubMed]
69. Kondo, H.; Yumoto, K.; Alwood, J.S.; Mojarrab, R.; Wang, A.; Almeida, E.A.; Searby, N.D.; Limoli, C.L.; Globus, R.K. Oxidative stress and gamma radiation-induced cancellous bone loss with musculoskeletal disuse. *J. Appl. Physiol.* **2010**, *108*, 152–161. [CrossRef]
70. Cucinotta, F.A.; Schimmerling, W.; Wilson, J.W.; Peterson, L.E.; Badhwar, G.D.; Saganti, P.B.; Dicello, J.F. Space radiation cancer risks and uncertainties for Mars missions. *Radiat. Res.* **2001**, *156*, 682–688. [CrossRef]
71. Hellweg, C.E.; Baumstark-Khan, C. Getting ready for the manned mission to Mars: The astronauts' risk from space radiation. *Naturwissenschaften* **2007**, *94*, 517–526. [CrossRef]
72. Joseph, J.A.; Shukitt-Hale, B.; McEwen, J.; Rabin, B.M. CNS-induced deficits of heavy particle irradiation in space: The aging connection. *Adv. Space Res.* **2000**, *25*, 2057–2064. [CrossRef]
73. Miry, O.; Zhang, X.L.; Vose, L.R.; Gopaul, K.R.; Subah, G.; Moncaster, J.A.; Wojnarowicz, M.W.; Fisher, A.M.; Tagge, C.A.; Goldstein, L.E.; et al. Life-long brain compensatory responses to galactic cosmic radiation exposure. *Sci. Rep.* **2021**, *11*, 4292. [CrossRef]
74. Grigor'ev, A.I.; Krasavin, E.A.; Ostrovskiĭ, M.A. Galactic heavy charged particles damaging effect on biological structures. *Ross. Fiziol. Zhurnal Im. I.M. Sechenova* **2013**, *99*, 273–280.
75. Kim, J.S.; Yang, M.; Kim, S.H.; Shin, T.; Moon, C. Neurobiological toxicity of radiation in hippocampal cells. *Histol. Histopathol.* **2013**, *28*, 301–310. [CrossRef]
76. Krukowski, K.; Jones, T.; Campbell-Beachler, M.; Nelson, G.; Rosi, S. Peripheral T cells as a biomarker for oxygen-ion-radiation-induced social impairments. *Radiat. Res.* **2018**, *190*, 186–193. [CrossRef]
77. Lonart, G.; Parris, B.; Johnson, A.M.; Miles, S.; Sanford, L.D.; Singletary, S.J.; Britten, R.A. Executive function in rats is impaired by low (20 cGy) doses of 1 GeV/u ^{56}Fe particles. *Radiat. Res.* **2012**, *178*, 289–294. [CrossRef] [PubMed]
78. Parihar, V.K.; Allen, B.D.; Caressi, C.; Kwok, S.; Chu, E.; Tran, K.K.; Chmielewski, N.N.; Giedzinski, E.; Acharya, M.M.; Britten, R.A.; et al. Cosmic radiation exposure and persistent cognitive dysfunction. *Sci. Rep.* **2016**, *6*, 34774. [CrossRef] [PubMed]
79. Whitman, K.; Norbury, J.W.; Lee, K.; Slaba, T.C.; Badavi, F.F. Comparison of space radiation GCR models to AMS heavy ion data. *Life Sci. Space Res.* **2019**, *22*, 76–88. [CrossRef] [PubMed]
80. Raber, J.; Torres, E.R.S.; Akinyeke, T.; Lee, J.; Weber Boutros, S.J.; Turker, M.S.; Kronenberg, A. Detrimental Effects of Helium Ion Irradiation on Cognitive Performance and Cortical Levels of MAP-2 in B6D2F1 Mice. *Int. J. Mol. Sci.* **2018**, *19*, 1247. [CrossRef]
81. Cucinotta, F.A. Space radiation risks for astronauts on multiple International Space Station missions. *PLoS ONE* **2014**, *9*, e96099. [CrossRef]
82. Nelson, G.A. Space Radiation and Human Exposures, A Primer. *Radiat. Res.* **2016**, *185*, 349–358. [CrossRef]
83. Krukowski, K.; Feng, X.; Paladini, M.S.; Chou, A.; Sacramento, K.; Grue, K.; Riparip, L.K.; Jones, T.; Campbell-Beachler, M.; Nelson, G.; et al. Temporary microglia-depletion after cosmic radiation modifies phagocytic activity and prevents cognitive deficits. *Sci. Rep.* **2018**, *8*, 785783.
84. Kiffer, F.; Boerma, M.; Allen, A. Behavioral effects of space radiation: A comprehensive review of animal studies. *Life Sci. Space Res.* **2019**, *21*, 1–21. [CrossRef]
85. Krukowski, K.; Grue, K.; Becker, M.; Elizarraras, E.; Frias, E.S.; Halvorsen, A.; Koenig-Zanoff, M.; Frattini, V.; Nimmagadda, H.; Feng, X.; et al. The impact of deep space radiation on cognitive performance: From biological sex to biomarkers to countermeasures. *Sci. Adv.* **2021**, *7*, eabg6702. [CrossRef]
86. Zwart, S.R.; Mulavara, A.P.; Williams, T.J.; George, K.; Smith, S.M. The role of nutrition in space exploration: Implications for sensorimotor, cognition, behavior and the cerebral changes due to the exposure to radiation, altered gravity, and isolation/confinement hazards of spaceflight. *Neurosci. Biobehav. Rev.* **2021**, *127*, 307–331. [CrossRef]