Kibo Utilization Scenario toward 2020 in the field of Space Medicine

The Kibo Utilization Promotion Committee
The Scenario Examination Working Group in Space Medicine

Table of Contents

1. Introduction

A decision made by the Strategic Headquarters for Space Policy in August 2010 has led to Japan's continued participation in the ISS Program beyond 2016. A report prepared by the Expert Examination Committee for Space Policy in August 2011 shows that "Results in fields such as life sciences and observation have been obtained. However, it is necessary to expand upon the research through the characteristics of manned missions and to achieve concrete results from this point forward". While considering certain political situations, such as the financial situation of Japan and the fourth term of the Science and Technology Basic Plan, the president of JAXA commissioned the ISS/Kibo Utilization Promotion Committee, an external consultative body chaired by Dr. Makoto Asashima, to prepare Kibo utilization scenarios toward 2020. Examination started in October 2010.

The Kibo utilization promotion committee has provided the following approaches as indicators of examination of the Kibo utilization scenarios toward 2020:

View point 1: Forefront scientific research only enabled by ISS/Kibo

1. Obtaining scientific knowledge in life sciences and material sciences over the long term (more than 5 years)
2. Creating such breakthrough technologies and making such findings in the short term (approximately 3 years) as those listed below:
   - Contributions to social problem solving, disaster recovery, etc., on the ground
   - Contributions to green/life innovation, creation of new industries, education, general use, etc.

View point 2: Fundamental research and development for the future space activities

Accumulating fundamental technology and knowledge in life sciences, space medicine, and technology development for Japan's lunar and planetary exploration and manned expeditions.

The range of research done in the ISS is wide, and includes human sciences, social science, space life sciences, materials science, and space and Earth science (Fig. 1). Space medicine, the foundation of humanity's advancement into space, and life sciences, which studies the science of living organisms, are treated as a common field as they both aid us in understanding the mechanisms of life.

Space medicine is an area of research that targets human abnormalities, and though it shares commonalities with life sciences, a separate space Medical Research scenario was created. The Space Medicine Scenario Workgroup, a subgroup of the ISS/Kibo Utilization Promotion Committee, checked past research scenarios and ISS research trends, debated prioritized goals and promotion policies, and created "Utilization of the ISS/Kibo for Space Medicine until 2020."

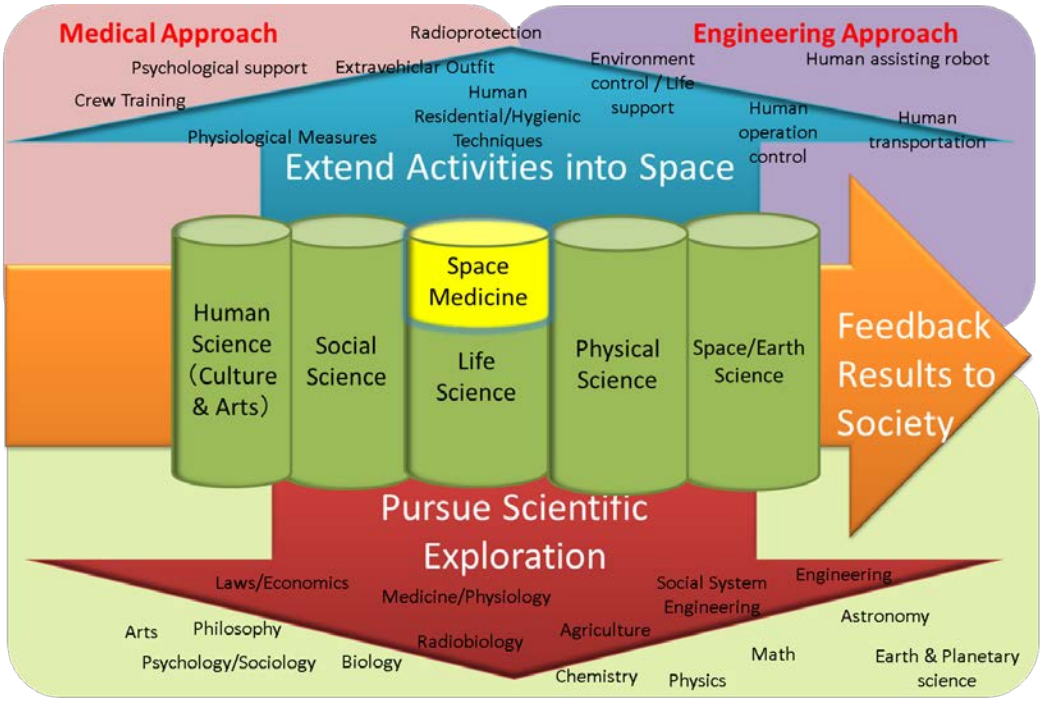

Fig.1 The range of research done in the ISS

2. Objectives of Space Medicine Research

When in space, astronauts live and work in a hostile environment that includes microgravity (μG), cosmic radiation, confinement, and isolation. The extreme nature of the space environment has been found to adversely affect the psychological and behavioral health of humans in space. During their first few days in space, astronauts experience conditions such as space motion sickness, fluid shift, and sensory deprivation. As the length of the stay increases, astronauts' health risks become more prominent. The physiological risks include bone mass loss resulting from calcium loss, muscle atrophy, disruption of biological rhythms, compromised immune system, and longer exposure to space radiation. Keys to successful human spaceflight are maintaining the psychological and behavioral health of astronauts, maximizing their work performance, and facilitating readaptation to Earth's gravity on their return. Space Medical Research plays a vital role in providing solutions to the critical health problems that place astronauts at risk and in developing new preventive methods for these problems.

Of the above-mentioned view points, we have chosen to promote View point 2:

View point 2: Fundamental research and development for the future space activities

Considering not only the microgravity environment of the ISS but also the low-gravity environment on the Moon (1/6 G) and Mars (1/3 G), it is essential to address the human health risks of spaceflight, elucidate their biological mechanisms, and identify promising methods of counteracting these effects. Emphasis has been placed on the management and recovery of astronauts' health in and post flight using the findings from rehabilitation science and exercise therapy. To expand the accumulated knowledge of the biological mechanisms underlying the human health risks associated with spaceflight, researchers should explore ways to employ the cutting-edge techniques needed to address in-flight medical issues and incorporate the findings from ground-based innovative scientific research on brain functions, regenerative medicine, genomics, medicinal chemistry, and the like.

Thus, space Medical Research has the following two goals:

- **Goal 1: Space Medicine Research to improve health care technologies of astronauts.**
- **Goal 2: Space Biomedical Research to elucidate fundamental mechanisms of the effects of space flight on humans and animals**

3. Status of Initial Utilization of Kibo

Initially, space Medical Research conducted in Kibo has been divided into two categories: research done by JAXA Space Biomedical Research Office and that done by researchers selected by Life Sciences International Public Announcements.

3.1 JAXA's Space Medicine Research

3.1.1 Areas of Study

JAXA's space medical biological research identifies critical problems and systematically advances research in five areas: physiological countermeasures, psychological support, healthcare against space radiation, space environmental medicine, and space telemedicine [1].

3.1.2 Critical Problems

The critical problems indentified in each of the five research areas consider medical risks, frequency of occurrence, impacts on crew and mission, and feasibility of research. Examples of critical problems in each area are as follow: bone loss and biological rhythm disruption (physiological countermeasures), methods of relaxation in space (psychological support), space radiation exposure measurement (healthcare against space radiation), environmental monitoring (space environmental medicine), and physiological function monitoring (space telemedicine).

3.1.3 Research Process of On-orbit Experiments

Space medicine experiments conducted on orbit must aim to achieve as many research results as possible under various restrictions, such as sample and device transportation, schedule arrangement, and remote operations. Before the results of research can be adapted for use in actual health care implementation, the following course of action must be followed:

① Draft a countermeasure that can be employed on orbit based on scientific knowledge of the prioritized research objective and develop a research plan

② Sufficiently validate the hypothesis in simulated space environments (bed-rest, closed environment experiments, etc.) prior to experimenting on orbit

③ Conduct on-orbit experiments after conducting scientific and ethical review of the space experiment, obtaining imformed consent from crew members, training, and making adjustments to avoid conflicts with other experiments

④ Confirm the validity of risk mitigation on orbit and consider the implementation into medical operation

The current process of on-orbit experiments for space Medical Research is shown in Fig. 2.

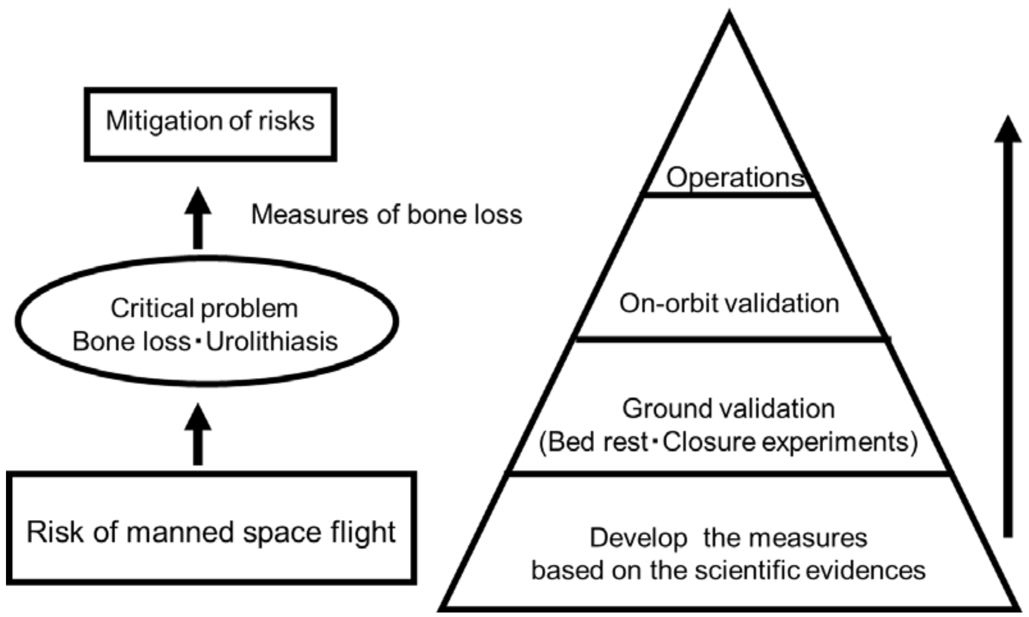

Fig.2 Research Process of Space Medicine

3.1.4 Ongoing Research Themes

JAXA's space Medical Research themes carried out to date are described below:

① Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss (Bisphosphonates) (*)

② The Effect of Long-term Microgravity Exposure on Cardiac Autonomic Function by Analyzing 24-hours Electrocardiogram (Biological Rhythms)

③ Mycological Evaluation of Crew Exposure to ISS Ambient Air (Myco)

④ Biomedical Analyses of Human Hair Exposed to a Long-term Space Flight (Hair)

⑤ Changes in Nutrient Contents in Space Food After Long-term Space Flight (Space Food Nutrient)

⑥ Evaluation of Onboard Diagnostic Kit (ODK)

*: Conducted by JAXA and NASA as international joint research and selected by a Life Sciences International Public Announcement.

The outline of each theme can be found at the following link:
http://iss.jaxa.jp/en/kiboexp/theme/first/

The research results gained so far are described below:

① Under microgravity bone resorption rises and bone mass decreases ten times faster than they do through osteoporosis on the ground. However, the combination of the prophylactic use of Bisphosphonate and physical exercise has proven to reduce bone loss and urinary tract stones.

② A regular life rhythm on orbit is important. According to an evaluation of heart autonomic nerve activity using a Halter electrocardiograph, the circadian rhythm of long-duration ISS mission crew changed immediately after the launch. However, a tendency to improve was seen in the second half of their mission.

③ Hair element and resident flora on the human body are currently being analyzed to determine the influence of the space environment on human body and microorganisms.

④ An electroencephalograph, electronic stethoscope, etc., are installed in Kibo to carry out verification of the medical on-board diagnosis, which shares acquired data between the terminal on orbit and the ground.

In addition to the themes described above, ground-based researches are underway on muscle atrophy, physical exercise, nutritional therapy, immune disorder, the biological effects of radiation, moon walking, lunar dust, an evaluation of environmental responses using medaka, etc., as basic space medical research[2)].

3.2 International Announcement of Opportunity of Life Science

3.2.1 Basic Policy

In the "Research Scenario in Space Medicine (4th edition)" created by the Space Medicine Advisory Committee of the Space Environment Utilization Research Committee[3)], the objectives of space Medical Research are described as "promotion of fundamental medical research using the space environment" and "clinical medicine research to elucidate the effect of space flight on human body and to validate countermeasure technology." The basic policy aims to devise research that sets Japan apart as a world leader, to overcome the medical challenges that stand in the way of human space travel, and to promote future manned space missions.

3.2.2 Selected Research Themes

The research themes selected by Life Sciences International Public Announcements are described below:

A) The 2004 International Announcement of opportunity of Life Science selected theme:

① Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss (Bisphosphonates) (*)

*: Conducted by JAXA and NASA as international joint research

B) The 2009 International Announcement of opportunity of Life Science selected themes:

① Effect of the Hybrid Training Method on the disuse atrophy of the musculoskeletal system of the astronauts staying in the International Space Station for a long term.

② Visual and Neck Proprioceptive Contributions to Perceived Head and Body Tilt during Long-term Space Life.

③ Human cerebral autoregulation during long-duration spaceflight.

④ Plastic alteration of vestibulo-cardiovascular reflex and its countermeasure.

⑤ Artificial gravity with ergometric exercise as the countermeasure for space deconditioning in humans (AGREE).

Preparation and coordination for on-orbit experiments are being performed for each of the 2009 selected themes. Themes that win flight experiment evaluation approval will be performed on orbit individually.

Space Medical Research performed in Kibo, research themes selected by International Announcement of opportunity of Life Science and in the preparation phase for flight experiment, and a future outlook are shown in Fig. 3.

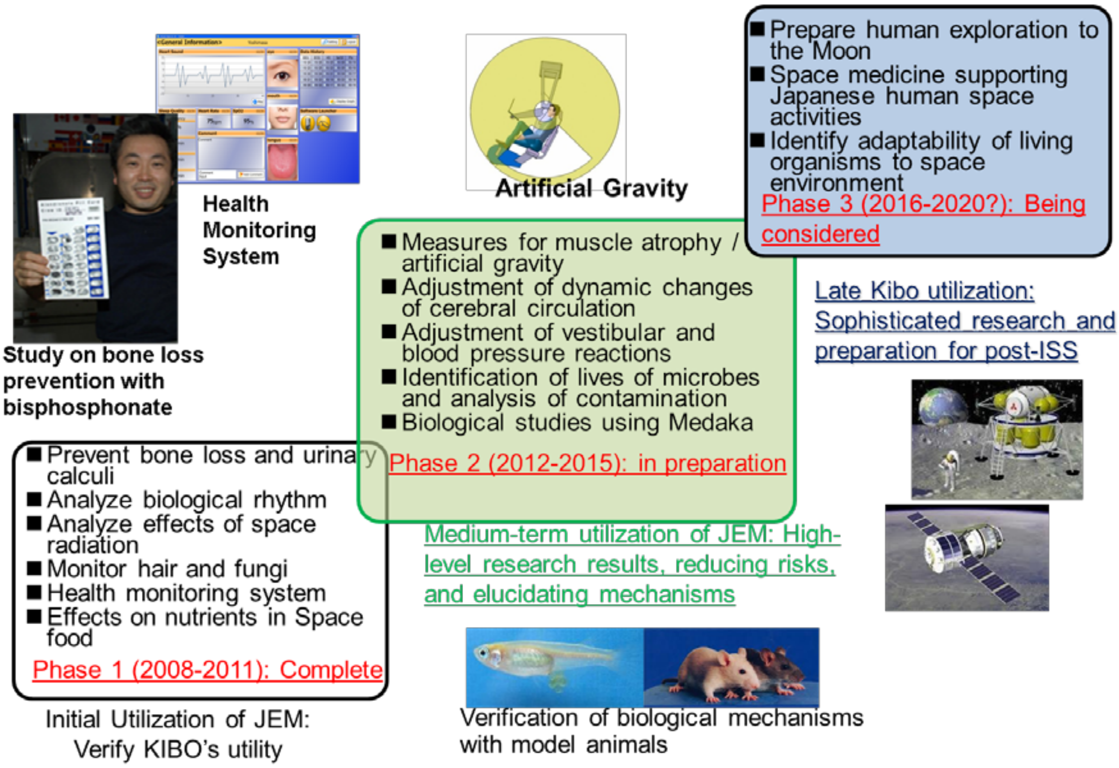

Fig.3 Current and Future outlook of Space Medical Research

4. International Trends and Long-term Perspective

4.1 International Trends

4.1.1 NASA's Direction

The National Aeronautics and Space Administration (NASA) is obtaining medical data from a long-duration mission on the ISS and carrying out technical verification needed for exploration of the Moon and Mars. They published the tasks of space Medical Research required for the ISS, Moon, or Mars mission on their web-based tool, the Human Research Roadmap, and have begun conducting experiments[4].

The U.S. National Academy of Sciences, by request of NASA, collected proposals from the scientific community on NASA's 10-year activity plan in life and physical sciences in space as a decadal survey. The National Research Council then published the survey as *Recapturing a Future for Space Exploration: Life and Physical Sciences Research for a New Era* in April 2011[5]. The main research tasks from the report relevant to this scenario are shown below.

- **Cross-Cutting Issues for Humans in the Space Environment**
  - Integrative, multisystem mechanisms of post-landing orthostatic intolerance;
  - Countermeasure testing of artificial gravity;
  - Food, nutrition, and energy balance in astronauts;
  - Continued studies of short- and long-term radiation effects in astronauts and animals; and
  - Cell studies of radiation toxicity endpoints.

- **Animal and Human Biology**
  - Studies of bone preservation and bone-loss reversibility factors and countermeasures, includingpharmaceutical therapies;
  - In-flight animal studies of bone loss and pharmaceutical countermeasures;
  - T cell activation and mechanisms of immune system changes during spaceflight;
  - Animal studies incorporating immunization challenges in space; and
  - Studies of multigenerational functional and structural changes in rodents in space.

The priority of a research task is set using evaluation criteria, such as how the research reduces space exploration risk and cost, whether the research can be done only by NASA, the synergistic effect with other organizations' needs, and whether use of the space environment is indispensable and effective.

The implementation system includes the Human Research Program[6], the National Space Biomedical Research Institute[7], and the Universities Space Research Association[8].

4.1.2 ESA's Direction

The European Space Agency (ESA) establishes the Programme for European Life and Physical Sciences in Space (ELIPS) every three years and promotes utilization of the ISS and ground-based research[9].

The European Science Foundation (ESF) has developed "Towards Human Exploration of Space: a European Strategy (THESEUS)", a roadmap of European life sciences research for manned exploration using funding from the EU[10].

4.2 Long-term Perspective

The long-term view of space Medical Research is shown in Fig. 4. In the initial space shuttle phase, evaluation of the impact on the human body, examination of diagnosis/treatment, preparations for ISS research, etc., were performed. In the practice phase (also known as the ISS/Kibo phase), verification and improvement of a crew's health care technology, post-ISS preparation research, are performed and results announcements are expected. In the future post-ISS phase, space Medical Research on flights to the Moon and Mars, as well as space Medical Research supporting Japan's original manned space activity, are planned (Fig. 4).

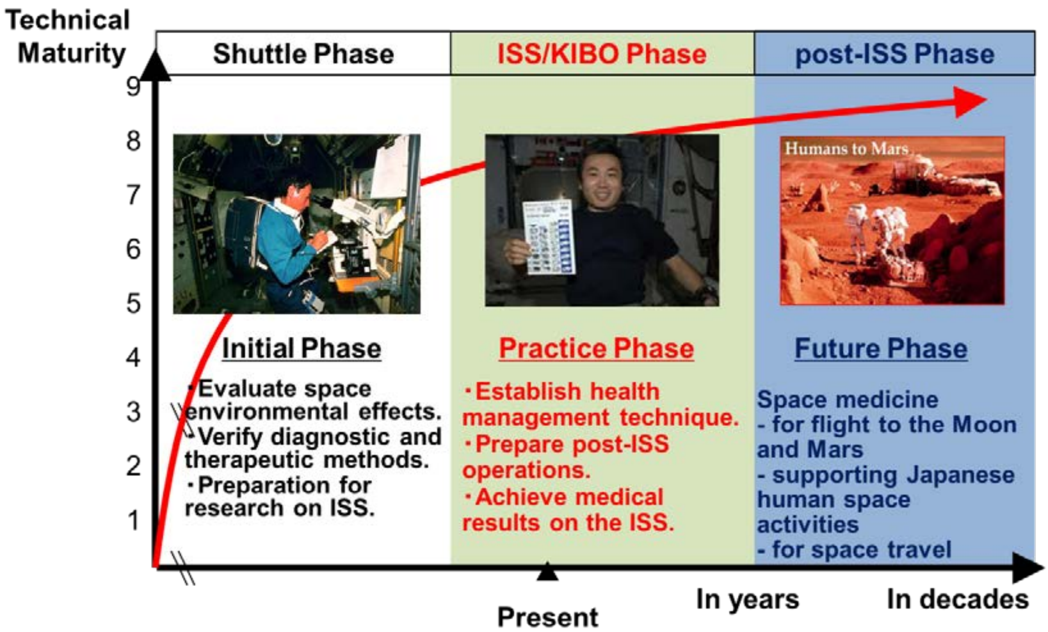

Fig.4 The long-term view of space Medical Research

5. Goals and Prioritized Research

5.1 Expectations of Space Medicine Research

What is needed most is space Medical Research that is useful in managing the health of astronauts and that proves the mitigation of risks to the human body in the microgravity environment, enclosed spaces, and space radiation.

High-quality clinical research outcomes using the space environment on the ISS/Kibo and simulated space environments on the ground (bed-rest research and experiments in enclosed space), as well as clarifying basic mechanisms of life using model animals, such as medaka, mice, rats, etc., are needed. Other countries have started medical research necessary to the development of original manned spacecraft for flights to the Moon and Mars as post-ISS preparation and are considering using the ISS as a test bed for these future flights.

Japan's contribution to space medical research has been expected among the international community. We have to endever to publish a scholarly treatise of its research results as well as to contribute to society in areas such as education and the promotion of health in the elderly.

5.2 Research in Various Areas

The Space Medicine Scenario WG examined JAXA's and NASA's past space Medical Research scenarios in addition to the space Medical Research themes conducted in Kibo by JAXA and other countries. The space Medical Research tasks are divided into the research areas.

5.3 Selection of Prioritized Research Topics

We evaluated and selected prioritized research topics from the 40 tasks based on evaluation criteria that considered applicability to long-duration space missions, emergency/necessity, feasibility, and JAXA's demands (originality, contribution to society, and investment-result performance). Objective 1: "Space Medical Research Should Contribute to Maintaining Astronauts' Health" and Objective 2: "Fundamental Space Medical Research Should Aim to Understand the Biological Mechanisms Underlying the Human Health Risks Associated with Spaceflight" were selected.

5.4 Goal 1: "Space Medicine Research to improve health care technologies of astronauts"

5.4.1 Physiological Countermeasures

- Countermeasures to prevent bone loss and metabolic disorder of bone mineral
- Monitoring and countermeasure to sleep and biological rhythms
- Evaluation and preventive countermeasure to muscle atrophy

5.4.2 Psychological Support

- Monitoring/ countermeasure of Stress/Fatigue

5.4.3 Health Care against Space Radiation

- Advanced space radiation dose monitoring technology

5.4.4 Space Environmental medicine

- Monitoring of water, air, microorganism, and noise and work environmental management.

5.4.5 Space Telemedicine

- Bio-monitoring and Disease prevention

Goal 1 aims to mitigate the remarkable risks accompanying spaceflight through prioritized research of bone loss/mineral metabolic disorder, sleep/biorhythm, and muscle atrophy (physiological countermeasures), and stress/fatigue (psychological support). Moreover, a technique to measure radiation exposure, onboard environment management technology, and remote medicine technology were selected as medical technology research required in the medicine on orbit.

5.5 Goal 2: "Space Biomedical Research to elucidate fundamental mechanisms of the effects of space flight on humans and animals"

5.5.1 Physiological Countermeasures

- Mechanism clarification & preventive measures to bone loss and muscle atrophy
- Space environmental stress responses in cardio-vascular, neuro-vestibular, and immune systems
- Multi-generation effects of space flight by use of model animals (medaka fish, mouse, rat)

5.5.2 Health Care against Space Radiation

- Dose assessment of low-dose, long-duration space radiation exposure & Development of bio-marker
- Prevention and protection of biological effects from space radiation exposure

Goal 2 aims to back up space Medical Research useful to health management. So 3 prioritized research tasks in Physiological Countermeasure(bone loss/muscle atrophy, the environmental response mechanisms of the circulatory/vestibular/immune systems and utilization of model animals) and 2 in Radiation Exposure (the influence of low doses of prolonged exposure, and protection against the effects of radiation) were selected.

These prioritized research tasks will be revised based on the progress of ground-based research and any environmental changes in the space experiments, and any changes will be reflected in a revised edition.

6. Promoting Space Medicine Research

In promoting space Medical Research, it is necessary to base new research upon the experiences obtained in the initial phases of research, and to produce results that exceed the investment put into each selected prioritized research task. JAXA plans to develop research themes, expand the views of researchers inside and outside of Japan who take part in space Medical Research, manage research projects (e.g., documentation of research plans/reports, cost management, etc.) and support research community as the keystone of its cooperation with the research community.

6.1 Demands from the Research Community

The research community has requested JAXA of periodical announcement opportunity of flight experiments, restart of public announcements for ground research, provision of international trends and space experiment technology, etc.

6.2 Public Announcements for Research Projects

Frontier joint research, public announcements of ground research, etc., and preparatory research of space medicine experiments have been conducted to promote the use of the space environment in research; however, because utilization of the ISS was planned to end by the end of 2015, public announcements of ground research were stopped. In recent years, only flight experiments have been recruited, and even then irregularly, so researchers, such as those in university, have been forced to gain external funding themselves to continue ground-based research.

Utilization of the ISS will now be extended until 2020 instead of 2015 and as a result public announcements for flight experiments will be performed yearly from now on. In addition to public announcements of conventional flight experiments, public announcements for ground-based research and project research plans are once again being taken into consideration.

6.3 Supporting the Research Community

JAXA has supported the research community through information on international trends and space experiment technology, symposiums/workshops/seminars, virtual institutes (grand design), and public announcements, e.g., for bed-rest and enclosed space experiments and international projects. However, these projects are not always utilized fully for the promotion of space Medical Research and they must be enriched with more substance and practicality.

6.4 Cooperation with International Agencies

JAXA plans to participate in international joint research, such as long-term bed-rest and enclosed space experiments, in cooperation with international space agencies, such as NASA, ESA, and IBMP.

6.5 Outreach/Promotion of Understanding/Development of Human Resources

The results of research in space medicine or space biology should not only be opened to the scientific society or published in scientific journals but also be explained simply to society so we may encourage younger generations to study science, promote healthy living among the general public, and develop future human resources.

7. References

1) Ucyuigakukennkyuunosuisumekata oyobi saijyuuyoukadai (Version.2) (JFX-2005035)(https://www.in-jaxa/fw/dfw/5a03/doc_web/pdf.jsp?ID=D0000127699)
2) J-SBRO Annual Report 2010 (ISSN 1349-113X) (http://repository.tksc.jaxa.jp/dr/prc/japan/contents/AA0065001000/65001000.pdf?IS_STYLE=jpn)
3) JAXA's Space biomedicine research scenarios (http://iss.jaxa.jp/utiliz/pdf/med4.pdf)
4) Human Research Roadmap (http://humanresearchroadmap.nasa.gov/)
5) Recapturing a Future for Space Exploration: Life and Physical Sciences Research for a New Era (http://www.nap.edu/openbook.php?record_id=13048&page=R1)
6) Human Research Program (http://www.nasa.gov/exploration/humanresearch/index.html)
7) National Space Biomedical Research Institute (http://www.nsbri.org/)
8) Universities Space Research Association (http://www.usra.edu/)
9) The Programme for European Life and Physical Sciences in Space (http://www.esa.int/esaHS/SEMFUZ4DHNF_iss_0.html)
10) Towards Human Exploration of Space – a European Strategy: THESEUS (http://www.theseus-eu.org/)