January 30, 2001

Ministry of Public Management, Home Affairs, Posts and Telecommunications

Interim Report by Committee to Promote Research on the Possible Biological Effects of Electromagnetic Fields

The Ministry of Public Management, Home Affairs, Posts and Telecommunication (MPHPT) (formerly The Ministry of Posts and Telecommunications) set up the Committee to Promote Research on the Possible Biological Effects of Electromagnetic fields (Chairman: Shoogo Ueno, Professor of the University of Tokyo)(hereafter abbreviated to "the Committee") in 1997. The Committee has since been organizing the research program to assess the possible health effects of radio waves on the human body.

The Committee has issued an interim report on research projects it has carried out to date, in response to increasing public concern about the effects of electromagnetic waves on human health.

- Summary of the interim report by the Committee -

1. Research into the effects of radio waves on the human body has been conducted for more than 50 years in countries around the world, including Japan. Based on voluminous findings from those studies, exposure guidelines including the Japanese guideline of the "Radio-Radiation Protection Guidelines for Human Exposure to Electromagnetic Fields" has been developed with a safety margin enough to protect human health from adverse effects of radio waves.

2. The rapid spread of mobile phones has raised public concern about the possible effects of radio waves on health, even though international expert organizations including those in Japan concur that there is no obvious evidence demonstrating any adverse effects of radio waves at intensities less than the guideline levels.

3. However, some reports state that low-level radio waves below guideline levels may cause some effects on the human body. Such research results should not be treated as evidence for health risks until their reproducibility is confirmed because many of those studies have been criticized in regard to the reliability of experimental methods and conditions. Lack of appropriate dissemination of precise information has created an obscure fear of radio waves among the public.

4. The Committee fairly and neutrally has coordinated a research program in accordance with the recommendation of the International EMF Project of the World Health Organization (WHO). The projects of the research program have been performed in close cooperation of medical and biological experts and engineers with expertise of dosimetry. The results obtained from the Committee's projects to date indicate that radio waves emitted from base stations and mobile phone devices have no adverse effect on human health. In addition, the replication studies of previous studies suggesting existence of health effects have not been successful in the replication studies this program using advanced and improved medical/engineering techniques.

5. Thus, the Committee currently considers that there is no firm evidence of the adverse effects of radio waves at intensities not exceeding the level defined in the Radio-Radiation Protection Guideline for Human Exposure to Electromagnetic Fields.

6. The Committee recognizes that there is an opinion that the guideline levels should be decreased to even lower levels than current guideline levels in consideration of the "precautionary principle." It should be noted that it is different from scientific-based guidelines. The Committee believes that the current guidelines do not need to be revised at present because the guideline levels for the general environment adopted by most countries including Japan have already included a substantial safety margin (1/50) to the threshold for the effects confirmed by animal experiments, thus offering sufficient prevention.

7. The Committee will continue its activities to promote researches for assessing the safety of radio waves aimed at improving the reliability of scientific basis for the Radio-Radiation Protection Guideline for

Human Exposure to Electromagnetic Fields. The Committee would otherwise recommend the revision of the Radio-Radiation Protection Guideline for Human Exposure to Electromagnetic Fields level if necessary. The Committee believes that continuation of reviewing the scientific basis for the guidelines will contribute to the development of a sound radio-wave environment where people can benefit from radio wave technology without any undue fear concerning health risks.

Attachment is abstracts and so forth for the research and experiments conducted performed to date.

Future schedule

The Committee plans to successively conduct (1) experiments based on a two-year exposure (corresponding to a rat's average life span) of rats' heads to radio wave, and (2) epidemiological studies to clarify the relationship between the use of mobile phones and brain cancer in collaboration with the international study managed by IARC, and so on.

Contact us;

Electromagnetic Environment Division,
Radio Department,
Telecommunications Bureau,

Ministry of Public Management, Home Affairs,
Posts and Telecommunications (MPHPT)

Tel: +81-3-5253-5907
Fax: +81-3-5253-5914

Attachment

Summary of previous research and experiments

1. Terms of reference for the Committee

With the rapid spread of mobile phones, concerns about the effects of radio waves on health have grown. International experts consider that, provided the guidelines for protection against radio waves are observed, then unfavorable effects on the human body will not occur. However, it is important to scientifically clarify the effects of radio waves on human health. Therefore, in 1997, the Ministry of Posts and Telecommunications set up a committee to conduct research into the electromagnetic environment surrounding the human body, in cooperation of medical and engineering researchers from related ministries, agencies and universities (Chairman: Shoogo Ueno, Graduate School of Medicine, the University of Tokyo). This Committee has promoted researches into assessing the safety of radio waves from both medical and engineering viewpoints.

(1) Scope

(i) Establishment of the research program and evaluation of the research results related to the assessment of the effects of radio waves on the human body

(ii) Evaluation of foreign research results concerning assessment of the safety of radio waves on the human body

(2) Selection of research subjects

The Committee chose the research issues from among those presented in the 1997 report issued by the Telecommunications Technology Council, “the Radio-Radiation Protection Guideline for Human Exposure to Electromagnetic Fields,” in line with the research subjects suggested by the WHO International EMF Project. The recommended priority was taken into account while the feasibility in terms of available resources was also considered.

The Committee performs fair, neutral research in close cooperation with medical and biological experts and engineers, who provide precise evaluations of exposure conditions.

2. Present state of research

(1) Summary of 1997 research (omit Appendix 1)

The research performed in 1997 focused on the effect of microwaves on the brain. The brain is one of the most important organs in the human body and is subject to highest local exposure from mobile phones. Some reports have described an increase in incidence of diseases such as brain tumor and epilepsy, so the effects of exposure of microwaves on the brain must first be clarified. Therefore, an experiment on exposing rats’ brains to microwaves was performed in 1997 and confirmed that short-term exposure (*2) to a general environmental standard (*1) with guidelines for partial-body specific absorption rates had no effect that could possibly damage the blood-brain barrier (*3).

(*1) Intensity of microwaves as laid down in the guideline for protection against microwaves emitted by mobile phones. Partial-body SAR: 2 W/kg. The actual intensity of microwaves emitted by mobile phone or PHS devices is lower than this standard level.

(*2) 1 hour per day, for 2 weeks and 4 weeks

(*3) BBB: Blood-Brain Barrier: This is a general term for the structure that exists between the cerebral capillary vessels and tissue, which prevents the entry of toxic substances into the brain by limiting the permeation of high polymers and water-soluble molecules and which maintains the cellular environment (osmolarity, pH, electrolytes, particularly potassium concentration) surrounding the nerve cells. Heat stimulation, trauma, acute hypertension, cerebral ischemia, convulsion, etc. have been confirmed to increase the permeability. Thus, if the permeability of the BBB is increased by exposure to microwaves, the development of brain tumors due to the invasion of carcinogens into the brain, epilepsy or convulsions could be caused.

(2) Summary of 1998 research (omit Appendix 2)

In 1998, following a report claiming that the BBB was affected by more intense microwave exposure

(*4), an experiment using almost the same intensity of microwaves was performed. At a microwave intensity that causes no thermal effects, damage to the BBB was not confirmed.

(*4) Fritze et al. in Germany reported, in 1997, that the permeability of the BBB was increased by an average SAR of 7.5 W/kg in the brain.

(3) Summary of 1999 research (omit Appendix 3)

To investigate the effect of radio waves on memory learning, a learning experiment using rats in a T-shaped maze was performed. This experiment did not reveal any effect on the subjects' ability to learn under conditions causing no thermal effects in rats even if the radio wave exposure level of the brain greatly exceeded that in Radio-Radiation Protection Guideline for Human Exposure to Electromagnetic Fields for mobile phones (Partial-body absorption guidelines).

In addition, an experiment for evaluating local exposure effects on the hemodynamics of cerebral microcirculation was carried out using a chronic implanted type of cranial window, by which microcirculation in the pia can be intravital-microscopically observed (repeated continuous observation can be performed in vivo). This window was surgically implanted into rats' cranial regions, to evaluate the biological effects of radio wave emissions on hemodynamic parameters (vessel diameter, blood flow rate, blood flow volume), the behavior of blood cells (erythrocytes, leukocytes, platelets) and vascular permeability (BBB function). None of the hemodynamic parameters, the behavior of blood cells or vascular permeability showed any changes under acute (at Brain averaged SAR: 1, 4, 8 W/kg for 10 minutes) or chronic (Brain averaged SAR 4W/kg for 4-week) radio wave exposure.

The long-term, large-scale animal exposure experiment in which adverse effect of electromagnetic field (EMF) on rat brain tumor development will be investigated is top priority in the Japanese part of the WHO's EMF project. A preliminary study has been performed prior to the main experiment in order to check whether all procedure and apparatus would work properly.

An epidemiological study is planned as an international collaborative study under the coordination of the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO). In this study, an association between the use of mobile phone and the risk of brain tumors is examined by a case-control study, the protocol of which has been developed by the IARC. A preliminary study (feasibility study) was undertaken in 1999.

(4) Research from 2000 (omit Appendix 4)

The long-term exposure experiment has started. Pregnant F344 rats were intravenously injected with ethylnitrosourea for the initiation of brain tumorigenesis in the fetus and after birth, exposure of EMF to rat brain has been performing. The exposure will be continued for 2 years at two different EMF levels until 2002. In addition, a 2-year epidemiological study has started as well.

In addition, a maze learning experiment to examine the effects of radio wave emissions on memory register and recall ability continued, as well as an experiment to evaluate cerebral microcirculation in comparison with the experiment performed in 1999, but using new equipment that more localized emits electromagnetic waves into the rat's head.

3. International collaboration/ cooperation

The biological effects of radio waves should be studied through international collaboration. Therefore, international exchanges have been promoted since 1997 by holding expert panel meetings from Korea and Japan. In 1999, dialog with the EU was initiated based on an agreement made through the 10th Japan/EU Bilateral Meeting in 1998. The following meetings have been held:

(1) The Japan-Korea Joint Meeting on EMF human hazard issues
These were held in Tokyo in 1996 and in Seoul in 1997.

(2) The first Japan-Korea-EU workshop on EMF human hazard issues
These were held in Tokyo in 1999.

In these expert panel meetings and workshops, the latest results of research on the biological effects of radio waves were presented by experts and administrators from Korea and the EU as part of the

international effort, and views were exchanged with Japanese experts and administrators.

4. Overseas trends

(1) The World Health Organization (WHO) (omit Appendix 5-1)

The WHO published a fact sheet Number 193 entitled “Electromagnetic Fields and Public Health: Mobile Telephones and Their Base Station” revised in June 2000.

This fact sheet was updated based on the reviews of the Independent Expert Group on Mobile Phones (IEGMP) in the UK and the Royal Society of Canada, and states the following.

Current scientific evidence indicates that exposure to RF fields, such as those emitted by mobile phones and their base stations, is unlikely to induce or promote cancers. And scientists have reported other effects of using mobile phones including changes in brain activity, reaction times, and sleep patterns. These effects are small and have no apparent health significance.

In order to analyze the scientific evidence relating to the possible effects of the electromagnetic environment on human health, the WHO set up its International Electromagnetic Fields Project, reviewed the results of scientific studies and health risk assessments, and encourage the development of an international exposure standard for harmonizing exposure limits of RF fields world widely. In addition, the International Agency for Research on Cancer (IARC), a research institute of the WHO, is coordinating a large-scale epidemiological study involving more than 10 countries to investigate the relationship between mobile phones and the development of cancers of the head and neck; this study is due to be completed in 2003.

In summary, the recent reviews have found no adverse effects on health through exposure to radio waves from mobile phones and their base stations, but because of public concerns, the WHO have facilitates to conduct further studies for better health risk assessment which will take about 3 to 4 years. And present scientific information does not indicate the need for any special precautions for use of mobile phones.

(2) International Commission on Non-Ionizing Radiation Protection (ICNIRP)

ICNIRP was established in 1992 for promoting the non-ionizing radiation protection. ICNIRP is non-governmental organization authorized by WHO and ILO. ICNIRP is independent and neutral, international commission. ICNIRP published Guidelines for Limiting Exposure to Time-Varying Electric, Magnetic, and Electromagnetic fields (up to 300GHz), this guidelines are adopted in European countries.

ICNIRP published the statement, Health Issues Related to the Use of Hand-held Radiotelephones and Base Transmitters, in 1996, noted that there is no substantial evidence that health effects, including cancer, can occur in people exposed to levels at or below the ICNIRP guidelines on this time. After 1996, ICNIRP has contributed to WHO EMF project as cooperative organization.

(3) EU

COST244bis covers the biomedical effects of electromagnetic fields, and is a part of COST, a system for collaboration in scientific research managed by the EC. The report found no clear evidence of the adverse effects of mobile phones on health. COST244bis was completed on November 19, 2000 and new studies into electromagnetic fields and advanced technologies will be started in the future.

(4) USA

The Federal Communication Committee of the USA released a report entitled ”Information on human exposure to radiofrequency fields from cellular and PCS radio transmitters” in January 1998. According to the report, the FCC reported that radio waves from base stations, mobile phones, car phones, etc. were of significantly lower intensity than the figure in the NCRP guideline, and stated that research should be continued through the working group in collaboration with the relevant ministries on the possible effects of radio wave exposure on health.

The US Food and Drug Administration released a report entitled “Latest consumer information on mobile phones” in October 1999. The report states that there is no firm evidence for the adverse effect of radio waves from mobile phones on human health, and states that research in cooperation with ministries, industry, and academic organizations will be continued.

(5) Canada

The Health Canada decided to review Safety Code 6 (Limits of human exposure to radiofrequency electromagnetic fields in the frequency range from 3kHz to 300GHz) and requested that an expert panel be set up to review this code based on recent scientific literature. The Royal Society therefore

established an expert panel, performed investigations and compiled a report entitled “Investigation on the possible health risk of radio frequencies from radio communication equipment” in March 1999.

The report stated that the research results obtained so far indicate no correlation between radio wave exposure and carcinogenesis, DNA damage, epilepsy, sleep disorders, reproductive difficulty, congenital anomaly, headaches, etc., and stated that the present Safety Code 6 did not need to be revised, considering cases without thermal effect. However, it recommended that part of the code be revised due to the omission of provisions for radio wave workers.

(6) Australia

The Agency for Radiological Protection and Nuclear Safety of Australia released a report entitled “The mobile phone system and health effects” on its web site, stating that the Australian government is promoting research by investing 450 million dollars, although so far there has been no positive evidence of harmful health effects.

(7) United Kingdom

The British government established the IEGMP (Independent Expert Group on Mobile Phones) to examine the effects of mobile phones on health. In April 2000, the IEGMP compiled and published a report entitled “Mobile phones and health.”

According to the report, the results of investigations conducted so far suggested no adverse effects of radio wave exposure at lower than the level defined in the guideline but that the investigation should be continued for another 3 years. In the United Kingdom, where the guideline prepared by the National Radiological Protection Board (NRPB) is used as the guideline, the report recommended adopting the guideline prepared by the International Commission on Non-Ionizing Radiation Protection (ICNIRP), in line with other EU countries, and stated that it believes that the widespread use of mobile phones by children for non-essential should be discouraged as precautionary approach.

5. Conclusion

Research into the effects of radio waves on the human health have been conducted for over 50 years in several counties including Japan, and exposure guidelines including the Japanese guideline of the “Radio-Radiation Protection Guidelines for Human Exposure to Electromagnetic Fields” have been established to promote the safe use of radio waves based on huge findings from those studies.

Recently, the rapid spread of mobile phones has raised public concern about the possible effects of radio waves from mobile phones and base stations on health. However, international expert organizations including those in Japan have not been able to find obvious evidence linking radio waves at intensities less than the guideline levels from mobile phones and base stations with adverse effects on health, and recognize that it is not appropriate to impose controls on the use of mobile phones immediately.

However, some studies state that low-level radio waves below the guideline levels may cause some effects on the human health. Such results frequently contradict previous research, and so the results should be interpreted carefully. Such research results should not be treated as scientific evidence for health risks until their reproducibility is confirmed many of those studies have been criticized in regard to the reliability of experimental methods and conditions. Lack of appropriate dissemination of precise information has caused obscure fear to radio waves in the public.

The Committee to Promote Research on the Possible Biological Effects of Electromagnetic fields has conducted biological and medical experiments to directly evaluate the health effects of radio waves emitting from mobile phones, etc. The Committee fairly and neutrally has coordinated a research program in accordance with the recommendation of the International EMF Project of the World Health Organization (WHO). The projects of the research program have been performed in close cooperation of medical and biological experts and engineers with expertise of dosimetry.

The results obtained from the Committee’s projects to date indicate that radio waves emitted from base stations and mobile phones devices have no adverse effect on the human health. In addition, the replication studies of previous studies suggesting existence of health effects have not been successful in the replication studies this program using advanced and improved medical/engineering techniques. Thus, the Committee currently considers that there is no firm evidence for the adverse effects of radio waves at intensities not exceeding the level defined in the Radio-Radiation Protection Guideline for Human

Exposure to Electromagnetic Fields.

Furthermore, the committee recognizes that there is an opinion that the guideline levels should be decreased to even lower levels than current guideline levels in consideration of the “Precautionary Principle” or “Precautionary Measurement”. It should be noted that it is different from scientific-based guidelines. The Committee believes that the current guidelines do not need to be revised at present because the guideline levels for the general environment adopted by most countries including Japan have already included a substantial safety margin to the threshold for the effects confirmed by animal experiments, thus offering sufficient prevention. This is similar to the opinions reported by the WHO and the governmental views in many countries.

The Committee will continue it’s the activities to promote researches for the assessment of the safety of radio waves in order to improve the reliability of scientific basis for the Radio-Radiation Protection Guideline for Human Exposure to Electromagnetic Fields. The Committee would otherwise recommend the revision of the Radio-Radiation Protection Guideline for Human Exposure to Electromagnetic Fields level if necessary. The Committee believes that continuation of reviewing the scientific basis for the guidelines will contribute to the development of sound radio-wave environment where people can receive benefits of radio wave technology without any unnecessary fear from health risks.

Studies in 1997

1. Development of exposure setups for biological studies

(1) Objective

In order to investigate the health effects of localized exposure of the human head during the use of cellular telephones, localized exposure setups for laboratory animals were developed based on the exposure setup used in the previous studies by Fritze et al. The local exposure conditions under non-thermal conditions were improved such that the elevation of the rectal temperature due to whole-body power absorption could be avoided.

(2) Improvements and modifications of the new exposure setup

- Whereas Wister rats, 250-300 g in weight, were used in the previous studies, we used large Sprague-Dawley (SD) rats, over 700 g in weight, because the whole-body SAR, the measure of the thermal effects of whole-body power absorption, could be decreased if larger rats were used.

- A higher frequency band (1.5 GHz) was used because the power absorption could be more superficial, whereas the 900-MHz band was used in the previous studies.

- By replacing the dipole antenna with a monopole antenna, the space needed for the exposure setup was reduced.

- Eight rats were positioned around the antenna because of the advantage of symmetrical positioning in numerical simulations, whereas ten rats were used in the previous studies.

- PDC (TDMA system used in Japanese digital cellular telephones) signal was used, whereas the GSM signal was used by Fritze et al.

(3) Dosimetry

Numerical simulations using realistic rat models based on the MRI data and experimental evaluation using solid phantom models of the same shape with the numerical model were performed. Good agreement between the calculation and the experiment was obtained. The local SAR distribution in the rats was evaluated in detail by numerical simulation.

(4) Exposure Conditions for in vivo studies.

- In the case that eight rats weighing 720 g were positioned in the exposure setup, the peak SAR of 2 W/kg in the brain corresponded to the antenna input power of 0.91 W.

- The whole-body-averaged SAR was about 1/9 of the peak SAR in the brain tissue. The thermal effects by whole-body power absorption could be ignored because the whole-body-averaged SAR was much less than the threshold of thermal effect (1-4 W/kg).

2. Short-term exposure of microwaves

(1) Objective

To clarify the effects of microwaves on living organisms, especially on the brain.

(2) Exposure conditions

Eight rats were simultaneously exposed to microwaves at a brain average SAR of 2 W/kg as defined in the safety guidelines for exposure to microwaves emitted by mobile phones. Twenty-four male Sprague Dawley (S.D.) rats (over 30 weeks old) were divided into three groups consisting of eight rats each; exposed group, sham control group (placement in the exposure system, without exposure), and cage control group (without exposure). The rats were exposed to microwaves for 1 hour per day, 5 days per week for 2 weeks or 4 weeks.

(3) Results

The effect on Blood Brain Barrier (BBB) permeability

An increase of the BBB permeability was not found in the brains of the exposed group (2 weeks and 4 weeks exposure), the sham control group and the cage control group using the Evans blue (EB) method (*7), the Horseradish peroxidase (HRP) method (*8) and the albumin immunostaining method (*9).

(*7) Evans blue, an azo dye that identifies areas of increased vascular permeability, was injected into the veins and quickly adhered to the serum albumin. The existence of EB outside the blood vessels in the brain is abnormal because the normal BBB prevents the entry of serum albumin into the brain parenchyma.

(*8) HRP, a glycoprotein (molecular weight: 44,000), cannot pass through the normal BBB. The HRP method is useful for the localization and identification of proteins at the electron microscopic level. The existence of HRP outside the blood vessels in the brain is abnormal.

(*9) An antibody of the rat albumin was injected into the blood vessels and stained to detect albumin in the brain. The existence of albumin outside the blood vessels in the brain is abnormal.

Histopathological study (the morphological effect on nerve cells)

The rat brain tissues were stained with Hematoxylin-Eosin (HE) and the morphological changes of the nerve cells were observed by light microscopy. In particular, the shape of the Purkinje cells and the cell density of the granular layer of the cerebellum were examined; the Purkinje cells are susceptible to hypoxia, alcohol or fatigue, all of which can easily cause structural transformations, and the cell density of the granular layer tends to decrease due to the existence of degenerative diseases.

No morphological changes were observed in the exposed group (for 2 weeks and 4 weeks), the sham control group and the cage control group.

Body weight changes

There were no detectable changes in the body weights among the three groups throughout the entire exposure periods (2 weeks or 4 weeks); therefore, the rats did not experience stress from microwave exposure, which would have caused body weight changes.

(4) Conclusion

There was no evidence in this experiment that exposure of male rats to microwave radiation without thermal effects induced BBB permeability changes or morphological changes of the nerve cells. However, the effects of long-term exposure should be studied, as the duration of short-term exposure experiments might not be sufficient to cause histopathological changes.

Studies in 1998

1. Development of exposure setups for biological studies

(1) Objective

- The exposure setups developed in 1997 were improved in order to realize the following exposure condition.
- Brain SAR (7.5 W/kg), which was reported to affect the blood-brain barrier (BBB) by Fritze et al.
- Whole-body SAR (over 4 W/kg), which was higher than the threshold of thermal effects.

(2) Improvements and modifications of the exposure setups

Four 720-g SD rats were used because more localized exposure could be realized with a smaller number of rats used.

Condition (1): Brain-averaged SAR = 7.4 [W/kg] and whole-body-averaged SAR = 1.4 [W/kg] (non thermal condition).

Condition (2): Brain-averaged SAR = 25 [W/kg] and whole-body-averaged SAR = 4.5 [W/kg] (above the threshold of thermal effects)

(3) Dosimetry

Numerical simulation showed that a more localized brain exposure could be achieved by decreasing the number of rats from 8 to 4.

2. Short-term exposure

(1) Objective

To evaluate the safety margin of microwave exposure on the brain. Thirty-six Sprague Dawley (S.D.) rats were divided into three groups; exposure, sham control and cage control. The rats of each group were exposed to microwaves under the following three conditions.

(2) Exposure conditions

I. Study without thermal effects (exposure for 1 day, 4 hours per day)

Fritze et al. reported that the BBB permeability of the brain increased due to microwave exposure at the brain average SAR of 7.5 W/kg. However, under these conditions, the inner body temperature was likely to increase because the whole body average SAR was 4.2 W/kg, which exceeded the threshold of the thermal effects (4.0 W/kg). Therefore, in order not to raise the body temperature of the rats, the whole body average SAR of our study was lowered to 1.4 W/kg, which is far below the threshold of the thermal effects.

(a) Intensity of microwaves
Antenna radiation power: 6 W
Brain average SAR: 7.4 W/kg
Whole body average SAR: 1.4 W/kg

(b) Duration of exposure
1 day, 4 hours per day (same as Fritze et al.)

II. Study without thermal effects (exposure for 5 days, 1 hour per day)

(a) Intensity of exposure
Same as I.(a)

(b) Duration of exposure 5 days, 1 hour per day (different from Fritze et al.)

III. Study with thermal effects (exposure for 1 day, 1hour per day)

(a) Intensity of microwaves
Antenna radiation power: 20 W
Brain average SAR: 25 W/kg
Whole body average SAR: 4.5 W/kg

(b) Duration of exposure
1 day, 1 hour per day

(3) Results

- Effects on BBB permeability

Under exposure conditions I and II, no effects were observed by the albumin immunostaining method. Under exposure condition III, the permeability of the BBB increased one hour after exposure. Although albumin was detected outside of the blood vessels one hour after exposure, no leakage was detected after 24 hours.

- Histopathological examination (morphological effects on nerve cells)

Under exposure conditions I, II and III, no morphological changes were observed.

- Evaluation of thermal effects of microwave exposure

The local inner body temperatures of the frontal subcutis, laryngeal subcutis, dorsal subcutis and intraperitoneal cavity were measured. An increase of the inner body temperature due to microwave exposure was not observed under condition I (the body temperature was not measured under condition II). However, an apparent increase of the inner body temperature was observed under condition III.

4. Results and Discussion

It was reported that the increase of the permeability of the BBB due to microwave exposure was caused by the thermal effects of microwaves. In this study, an increase of the permeability of the BBB and an elevation of the inner body temperature were observed immediately after microwave exposure, only under condition III (with thermal effects). The brain average SAR of this study was almost the same as that of Fritze et al. However, Fritze et al. used a whole body average SAR of 4.2 W/kg, which exceeded the threshold of the thermal effects, whereas, our whole body average SAR of 1.4 W/kg was far below the threshold of the thermal effects. Thus, our study also directly evaluated the effects of local exposure to microwaves on the brain without thermal effects.

Our study showed that no increase of the BBB permeability was observed under the conditions of non-thermal effects, and that the thermal effects could cause an increase of the BBB permeability. Therefore, the elevation of the inner body temperature due to other body-heating hazards can cause an increase of the BBB permeability.

In conclusion, microwave exposure at much stronger intensities than emitted by cellular phones does not affect the permeability of the BBB when there are no thermal effects.

Studies in 1999

1. Development of exposure setups for biological studies
(1) Objective
The localized exposure setups for 2-year bioassay were developed.

(2) Required exposure conditions and limitations

- In order to expose a large number of animals simultaneously, 10 rats were positioned in each exposure setup.

- The rat (F344/DuCrj) usually grows from 70 to 550 grams in weight during the experimental period (5 to 109 weeks of age). In order to fix the position of the rats and decrease the stress on rats due to immobility, six-size tubes for positioning rats were developed.

(3) Dosimetry
- Numerical simulation
  Three rat models of various weights (126, 263, and 359 g) with heterogeneous tissue structure were developed from MRI data. It was shown that localized exposure of brain tissue, i.e., (brain-averaged SAR/whole-body averaged SAR = 4~7), could be achieved regardless of the size of rats.

- Comparison between experiments and numerical analyses
  The SAR distribution estimated from the measured temperature increase in homogeneous rat phantoms by using a thermographic camera was in agreement with the calculated results.

Consequently, the localized exposure condition within rat brain, where the brain-tissue averaged SAR was 2 W/kg and whole-body averaged SAR was not more than the threshold of thermal effects, could be achieved.

2. T-maze experiment
(1) Objective
To evaluate the effects of microwaves on the retainment and acquisition of “reference” memory in rats using a food-rewarded T-maze. (The memory system is supposedly composed of two components, long-term “reference” memory and short-term “working” memory.)

(2) Methods
<Effect on the retainment of reference memory>
Sprague Dawley (S.D.) rats (over 30 weeks old) were trained for 4 days to memorize the location of food that was placed at the end of one of the arms of a T-maze. Eight days after the training period, the rats were exposed to microwaves (1,439 MHz PDC system) at a whole body average SAR of 1.7 W/kg and a brain average SAR of 7.5 W/kg for 4 hours. After the exposure, the rats performed 16 tasks in the T-maze and the number of correct choices was evaluated. The exposed group and the sham control group (placement in the exposure system, without exposure) consisted of six rats each.

<Effect on the acquisition of reference memory>
Four days after the training period, the food was placed on the reverse side of the training period location and the rats performed 16 tasks per day for four days. Consequently, the rats initially chose the wrong arm, but eventually memorized the new location of the food. (This method has been used in some studies to evaluate the acquisition of reference memory.) Four days after the training period, the rats were exposed to microwaves for 1 hour per day for 4 days at a brain average SAR of 7.5 W/kg and a whole-body average SAR of 1.7 W/kg. Immediately after the 1 hour exposure, the rats performed 16 tasks per day for 4 days and the transition in the number of correct choices was evaluated.

(3) Results
<Effect on the retainment of reference memory>

No remarkable difference was found between the number of correct choices during the training period and after the exposure for the exposed and sham control groups.

<Effect on the acquisition of reference memory>

No remarkable difference was found between the number of correct choices during the training period or after the exposure.

In conclusion, microwave exposure at levels much stronger than emitted by cellular phones does not affect the memory and learning processes of rats.

3. Study of the Local Exposure Effects to Electromagnetic Waves on the Cerebral Microcirculation in Rats

(1) Objectives

The aim of this study evaluates the biological effects of local exposure to electromagnetic waves on the cerebral microcirculation. Hemodynamic parameters (blood vessel diameter, blood flow velocity, blood flow volume), behavior of the blood cells (red blood cells, white blood cells, platelets) and blood-brain function were investigated intravital-microscopically in rats.

For this purpose, we have developed a new cranial window method (repeated continuous observation can be performed *in vivo*) to evaluate local exposure of electromagnetic waves on the cerebral microcirculation with acute (10 min) and chronic(4 weeks) exposures conditions.

(2) Exposure conditions

- Acute Effects (10 min exposure)

We have evaluated three exposure levels of mean brain SAR at 1W/kg that is weaker than the partial-body absorption guideline value (2W/kg) for cellular phone terminal, 4 and 8W/kg which are stronger than this guideline value, respectively. All the exposure levels were within a non-thermal range, i.e., lower than 4W/kg mean whole-body SAR.

- Chronic Effects (4 weeks exposure)

We have evaluated one exposure level of mean brain SAR at 4W/kg with 0.91W/kg mean whole-body SAR that is stronger than the partial-body absorption guideline value (2W/kg) for cellular phone terminal. The exposure duration was 60 minutes. The exposure was intermittently performed 5 days a week for 4 weeks.

(3) Results and conclusion

The results showed that no noticeable changes in any parameters of the cerebral microcirculation including BBB function were observed under the both exposure conditions mentioned above by using our *in vivo* model.

4. Long-term, large scale animal exposure experiment (preliminary experiment)

(1) Object

A preliminary animal experiment was performed in order to check that rat holders, which are used for EMF exposure in the long-term animal study, work well, as well as to eliminate any problem for entire experimental procedures.

(2) Exposure conditions

1439MHz, PDC, Average brain SAR is 2 W/kg

EMF exposure: 2 hours a day, 5 days a week, for 4 weeks

(a) Animals, 5-week-old F344/DuCrj, male and female rats

Exposure group (5 and 5), Sham-exposure group (5 and 5) and Control group (5 and 5 rats)

Body weights of male and female rats were 75-83g and 85-97g, respectively.

(b) Animals, 21-week-old F344/DuCrj, male rats

Exposure group (10 rats)

(3) Results

(a) 5-week-old rats

i) Survival and clinical conditions:

All animals survived until the end of EMF exposures.

No clinical abnormal signs were detected.

ii) Body weight:
Body weights of exposed and sham-exposed groups were not different.
However, those values of both groups were lower than those of control group.
iii) Food consumption and water intake:
Values of food consumption and water intake of both exposed and sham-exposed groups were lowered than those of control group.
iv) Pathological examination:
Gross observation at autopsy:
There was nothing particular change in any organ.
Organ weight:
Adrenal glands' weight in exposed and sham-exposed groups was increased and prostate and seminal gland weights in those group were lowered than that of control group.
Serum hormonal levels:
Serum hormonal levels were not different among groups.

(b) 21-week-old rats
i) Survival and clinical conditions:
All animals survived until the end of EMF exposures.
No clinical abnormal signs were detected.
ii) Body weight:
During the first 2 weeks, body weights decreased, and then from Week 3, those slightly increased.
iii) Pathological examination:
Gross observation at autopsy:
There was nothing particular change in any organ.

(4) Conclusion and discussion

There were some changes observed due to the stress by holding animals in a rat holder, such as body weight retardation, decreased food consumption and water intake, increase of adrenal gland, decrease of prostate and seminal vesicle weights. Therefore, proper size of animal holders, which must be fit to different size of rats, should be used for the long term exposure experiment. Several size of rat holders are necessary.

5. Epidemiological Study (Pilot Study)

(1) Objective

To examine the feasibility of an international epidemiological study coordinated by the International Agency for Research on Cancer (IARC), the World Health Organization (WHO).

(2) Methods and Results

- Information for estimation of individual exposure level

The individual exposure level was estimated from service plan, monthly charges, and answer to the questionnaire.

- Incidence rate of brain tumors in Japan

The incidence rate of brain tumors was estimated from the Nationwide Brain Tumor Registry and 7 population-based cancer registries.

- Questionnaire

The Japanese version questionnaire was developed, based on the original English version questionnaire developed by the IARC.

- Interviewing

Twenty-one healthy volunteers were interviewed to examine the validity of Japanese version questionnaire. The billing records of 11 volunteers were crosschecked with the answers to the questionnaire.

- Report to the IARC

English report was submitted to the IARC on December 27, 1999. The statistical summary of questionnaire answers was reported. The results of crosscheck between questionnaire answers and billing records were also reported. Other relevant statistics, such as incidence and mortality rates of brain tumors in Japan, were also reported.

(3) Discussions and Conclusion

- The main study should be started in 2000.
- Include into the questionnaire the questions regarding the exposures to organic solvents should be requested to the IARC.
- The subcommittee for the epidemiological study should be organized to discuss the details of main study.

Studies in 2000 and future

1. Development of exposure setups

Novel exposure setups for in vivo studies on cerebral microcirculation will be developed. These exposure setups are expected to realize more focal exposure within rats' brain by using small loop antennas than ordinary exposure setups using resonant monopoles.

2. Maze learning experiment

(1) Objective

To evaluate the effect of microwave exposure on the cognitive functions and memory restoration of rats.

(2) Exposure conditions

- Research in 2000.
  1,439 MHz PDC system, brain average SAR of 7.5 W/kg
  Exposure for 4 hours per day for 1 day
  Exposure for 1 hour per day for 4 days
- Research in 2001
  Same strength as the exposure system used in 2000
  Exposure for 1 hour per day for 4 weeks

(3) Subject of assessment

Using the food-rewarded T-maze, the effects of microwaves on the learning and memory processes of three groups of rats (exposed, sham control, and cage control groups; each group will consist of about 15 rats) will be evaluated.

3. Long-term, large-scale animal exposure experiment

(1) Object

The purpose of this experiment is to investigate the effect of EMF exposure to male and female rats, which were exposed by ethylnitrosourea (ENU) intra-uterously, to initiate brain tumorigenesis while they were fetus.

(2) Exposure conditions

1439MHz, PDC, Average brain SARs are 2.0 and 0.67 W/kg
EMF exposure: 2 hours a day, 5 days a week, for 104 weeks
Animals, 5-week-old F344/DuCrj, male and female rats
Groups:
ENU - EMF (2.0W/kg), 50 female and 50 male rats
ENU - EMF (0.67W/kg), 50 female and 50 male rats
ENU - Sham-exposure, 50 female and 50 male rats
ENU - Control, 50 female and 50 male rats
Control, 50 female and 50 male rats

Estimated body weights of male and female rats are 70-350g and 75-550g, respectively.

(3) Items of observation and measurement

- During EMF exposure (2000 - 2002)
  Observation items:
  General conditions, toxic symptoms and survival check in every morning and evening (twice a day)
  Measurements:
  Body weights and food and water consumptions are measured every week during the first 14 weeks and then those are measured bi-weekly until the end of experiment.

- After EMF exposure (2002 -)

Body weight:
The final body weights will be measured after 24 hours fastening before their sacrifice
Serum hormonal levels:
Hormonal levels will be measured from randomly selected 5 female and 5 male rats
Pathological examination:
Measurements of organ weights and histopathological examination will be performed.

(4) Statistical analysis

Statistical analysis will be performed among ENU-EMF(2.0W/kg), ENU-EMF(0.67W/kg), ENU-Sham and Control groups for following items:

survival rates, body and organ weights, tumor incidence and non-neoplastic lesion's incidence.

4. Study of the Local Exposure Effects to Electromagnetic Waves on the Cerebral Microcirculation in Rats

(1) Objectives

The aim of this study evaluates the biological effects of local exposure to electromagnetic waves on the cerebral microcirculation in comparison with the experiment performed by mono-pole antenna emission in 1999, but using new equipment that more localized emits electromagnetic waves with loop antenna emission into the rat's head.

(2) Methods and Materials

Acute exposure effects of electromagnetic waves on cerebral microcirculation including hemodynamic parameters (blood vessel diameter, blood flow velocity, blood flow volume), behavior of the blood cells (red blood cells, white blood cells, platelets) and blood-brain function were investigated intravital-microscopically by use of the cranial window(repeated continuous observation can be performed *in vivo*) in rats, as performed in 1999.

5. Epidemiological Study

(1) Objective

To conduct an epidemiological study in Japan, based on the protocol developed by the IARC.

(2) Protocol of the study

Four interviewers were trained for interviewing, and interviews of brain tumor cases and healthy controls were conducted. The results will be reported to the IARC in 2002.