Non-Ionising Radiation – Health and Environment

Programme Synthesis Report

National Research Programme NRP 57

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What are National Research Programmes (NRP)?

The research carried out by National Research Programmes consists of targeted research that contributes to the solution of contemporary problems of national importance. Under the provisions of Article 6, paragraph 2, of the Federal Act on Research of 7 October 1983 (as of 1 March 2010) the Federal Council selects the topics and foci to be researched in NRPs and mandates full responsibility for implementing the programmes to the Swiss National Science Foundation (SNSF, Division IV).

Article 4 of the Federal Ordinance on the Federal Act on Research of 10 June 1985 (as of 1 January 2009) describes the purposes and contents of NRPs as follows:

„[1] National Research Programmes are a means to direct and support coordinated research projects that have a common goal. Where needed, National Research Programmes should strengthen scientific research capacities.

[2] Topics of research are generally appropriate for National Research Programmes if:

a. scientific research on the problem is of national importance;

b. Swiss research can make a significant contribution to the resolution of the problem;

c. solutions require research contributions from multiple disciplines;

d. the research goals cannot be met exclusively through basic research, through research within a specific section of the administration, or through industrial applications research;

e. research on the problem can be expected to produce research results that have practical applications within a five-year time period.

[3] The following criteria should be taken into consideration in setting forth the topics of National Research Programmes:

a. the programmes can provide the scientific basis for decision-making by government and the administration;

b. the programmes can be conducted with international collaboration and are also of great interest to Switzerland.“

1. Executive Summary

Non-ionising radiation (NIR) or electromagnetic fields (EMF) are produced by mobile phone communication devices as well as by electrical power supplies, electrical devices and a variety of other appliances. The use of mobile phones has witnessed a spectacular growth and reached in 2010 worldwide an estimated number of 5 billion. In Switzerland alone over 9 million mobile phone connections were active in 2010. Concern has been voiced that exposure to radio frequency electromagnetic fields (RF EMF) emitted by these devices may have adverse effects on health. Although presently there is no clear evidence for health risks, the question has not been settled. The uncertainty is also due to controversial reports on low-dose EMF effects on biological systems.

Origin of the National Research Program "Non-ionising Radiation – Health and Environment"

In June 2003, the former Federal Office for Education and Science (FOES), now State Secretariat for Education and Research (SER) requested the Swiss National Science Foundation (SNSF) to evaluate the establishment of a National Research Programme (NRP) addressing potential effects of NIR on human health. In June 2004, the SER requested the SNSF to develop an implementation plan for an inter- and trans-disciplinary, four-year research program with a total budget of CHF 5 million. A steering committee (SC) was established and asked to draft the implementation plan. The main objective of the plan was to address key scientific questions regarding potential adverse health effects of NIR emitted by a range of present and future technologies. The program was to be complementary to international research activities in the field of NIR with a focus on specific issues defined in the electromagnetic field (EMF) research agenda of the World Health Organization (WHO). Specific emphasis was put on implementation, so that the program would directly address the increasing uncertainties in the Swiss population regarding potential health hazards. In March 2005, the Federal Council approved the "NRP 57: Non-Ionising Radiation – Health and Environment" and in November 2005 the Federal Department of Home Affairs approved the implementation plan. The official call for projects was issued in December 2005. A total of 36 proposals were submitted and evaluated by the SC and external reviewers. The SC proposed 11 projects for funding, a recommendation that was approved by the SNF Research Council in November 2006. The research projects started in January 2007.

Aims and topics

Since international efforts primarily focused on the endpoint of cancer, the implementation plan specified that the NRP would address other potentially adverse health effects and aim to clarify the basic mechanisms underlying EMF effects on biological systems. Consequently, the main topics of research were defined as follows:

- Dosimetry and exposure assessment
- Human experimental exposure experiments and epidemiological studies including the topic of electromagnetic hypersensitivity (EHS)
- Cellular biology of NIR effects
- Risk management, risk stratification and risk communication

Outcome of the projects

The present synthesis report (May 2011) is based on the project reports submitted in September 2010. Since the data of some projects were still in the process of analysis, the reader is referred to forthcoming scientific publications for a complete picture of the results.

Dosimetry and exposure assessment

So far, pregnancy had received no particular consideration with respect to exposure limits. Moreover, only limited data existed with respect to foetal exposure in the near field. *Nicolas Chavannes' and Andreas Christ's (IT'IS Zurich)* project dealt with the quantification of electromagnetic fields and their specific absorption in the tissues of the mother and the unborn child in different stages of pregnancy during everyday exposure situations. The absorption was simulated using mathematical

models and numerical techniques. Detailed anatomical computer models of a woman were developed for three gestational stages (month 3, 7 and 9 of pregnancy). The models were subsequently exposed to representative, everyday types of electromagnetic fields. The fields represented exposure from field sources at large distances, such as electronic article surveillance systems operating at different frequency ranges, induction cooker hobs as well as wireless devices operating in the close environment of the abdomen. The results showed that when the incident field is compliant with the reference levels for the general public, the basic restrictions are invariably met. In contrast, when the expectant mother is exposed to the limits of occupational exposures, then the exposure of the foetus can exceed the basic restrictions for the general public.

The project of *Niels Kuster* and *Sven Kühn (IT'IS Zurich)* addressed the exposure of the central nervous system. The aim was to determine the cumulative exposure to RF EMF from the most prominent sources in our society, both in the near- and far-field. The study covered the frequency range from 30 MHz to 6 GHz, thus comprising current as well as foreseeable future devices and sources, including mobile phones, base stations, cordless phones, baby surveillance devices, wireless network devices and hands-free kits. In addition, other factors that affect the exposure, such as communication technology, user behaviour (e.g. effects of the hand holding a phone) and environment (e.g. travelling in a car) were also considered for a realistic assessment of exposure to RF EMF over time. While the incident electric fields from far-field sources were measured in free-space, the induced fields from near-field sources or the Specific Absorption Rate (SAR) were measured in phantoms representing the electrical properties of the human body. Anatomical models were originally derived from magnetic resonance images of healthy volunteers. A variety of human models ranging from children to adults of both genders were included.

The study showed that the strongest source of brain exposure to EMF is the mobile phone. The exposure thereby depends on usage patterns and phone selection, e.g., the design of the phone, usage of hands-free kits (exposure is reduced with hands-free kits by more than 10-fold), choice of phones supporting the UMTS communication system or only GSM (UMTS reduces the average exposure by more than 100-fold). The study also demonstrated large variations with respect to the exposure of different brain regions between different mobile phones by more than 1000-fold. Far-field or quasi-far-field sources generate much lower exposure of the brain. On average, the levels of SAR induced from indoor base stations, e.g., from cordless phone or wireless network access points, are of the same order of magnitude as the levels of SAR from outdoor mobile telephony base stations.

Andreas Christ's and *Myles Capstick's (IT'IS Zurich)* project, a state-of-the-art imaging system was developed that enables the direct monitoring of processes in cell cultures during exposure of extremely low-frequency magnetic fields (ELF MF). This required the integration of the device with a microscope system. The novel ELF exposure system allows flexible signal analysis, intermittent exposure protocols and a variety of micromanipulations during live cell imaging. The system is easy to handle due to automated software control, provides continuous information on field strength and cell temperature, and also supports blinded protocols. The system was used successfully in another project of the NRP 57 program (*Genotoxic effects of non-ionizing radiation*).

Human experimental exposure experiments and epidemiological studies

There is evidence that RF EMF can affect physiological processes in the brain. Effects on electrical brain potentials (electroencephalogram; EEG) and on cerebral blood flow have been reported previously. The project of *Peter Achermann (University of Zurich)* focused on RF EMF-induced EEG changes. A first subproject was designed to investigate the critical signal characteristics. Subjects were exposed for 30 min to RF EMF with pulsed low-frequency components of either 14 Hz or 217 Hz. (the strongest component of the GSM signal). In a follow-up experiment, exposure conditions included 2 Hz pulse-modulated RF EMF and a 2 Hz pulsed magnetic field. This latter condition was designed to see whether the slow modulation component alone is sufficient to elicit a biological effect or whether its combination with RF EMF is required. In all experiments a sham-exposure condition served as the control. After exposure the subjects went to sleep and their sleep EEG was recorded. The 2-Hz and 14-Hz pulse-modulated condition resulted in an increase of spectral power of the sleep EEG in the frequency range of sleep spindles (12-15 Hz). However, a 2-Hz pulsed magnetic field without the RF EMF part did not induce this effect. Sleep quality and the sleep stages were not affected by any manipulation.

A second subproject aimed to determine whether the thalamus, a subcortical brain structure, is critical for mediating the effects of RF EMF on the sleep EEG. Prior to sleep the subjects were exposed either to a GSM handset-like signal with carrier frequencies of 900 MHz or to a signal with carrier frequencies of 2140 MHz. The latter was chosen because it does not penetrate into deep brain areas. However, both exposure conditions induced the typical changes in the sleep EEG over both brain hemispheres. Therefore subcortical structures do not appear to be the primary targets of RF EMF.

The third subproject was designed to investigate the effect of RF EMF on cognitive performance and the waking EEG in early adolescence. Mobile phones are a dominant source of RF EMF exposure for teenagers, and in the WHO EMF research agenda 2006/2010, investigation of EMF-induced effects on cognition and the EEG in children was identified as a high priority research need. To test whether specific components of the wake EEG are affected in a dose dependent manner, adolescents (11-13 years old) were exposed to GSM handset-like signals with a carrier frequency of 900 MHz at two different intensities. The data are still being analysed.

Universal Mobile Telecommunication System (UMTS) is the third generation (3G) of mobile telecommunications technology and the new widespread standard in mobile communication. The effect of intermittent UMTS RF EMF exposure at two different intensities on cerebral circulation was investigated in *Martin Wolf's (University Hospital Zurich)* project. The data were obtained by Near Infrared Imaging (NIRI), which is a sensitive, non-invasive method for imaging blood flow and oxygen concentration in the brain. The NIRI technique was adapted to measure short-term (effects occurring within 80 s) and medium-term (effects occurring within 80 s to 30 min) changes in cerebral blood circulation and oxygenation in response to UMTS RF EMF exposure. Exposure-induced effects on cerebral blood circulation and heart rate were obtained. The short-term effects were smaller than the ones observed during a normal functional activation of the brain and the mid-term effects were in the range of physiological fluctuations. The short-term effects were only present at the lower intensity, which makes it unlikely that thermal effects were involved.

The aim of *Martin Röösli's (University of Basel)* project was to characterize the RF EMF exposure distribution of a population sample, to develop and validate the exposure assessment method and to investigate the association between RF EMF exposure and symptoms of ill health by means of a cohort design. In the first part, personal exposure to typical sources of RF EMF was measured with portable exposimeters during one week. Exposure to fixed site transmitters at the place of residency was modelled with a geospatial computation model, which used accurate parameters from all fixed site transmitters of the study region. These data were used to predict environmental RF EMF exposure in everyday life in the frequency range of 88-2500 MHz in 1375 individuals who took part in a baseline survey. Thereof, 1122 individuals completed a follow-up investigation one year later. In addition, objective data on mobile phone use was collected from the mobile phone operators' traffic records of all incoming and outgoing calls of the last six months. Measurements revealed an average exposure of 0.21 V/m, which is far below the regulatory exposure limits. Environmental far-field RF EMF exposure was mainly due to other people's mobile phones (39%), cordless phone systems (24%, not including one's own phone use) and mobile phone base stations (22%). Exposure to environmental RF EMF exposure at baseline was not associated with health disturbances one year later and similarly, an increase or decrease of the personal RF EMF exposure within a year was not accompanied by a respective change of health disturbances. No association between actimeter recordings during sleep and RF EMF exposure in the sleeping room could be observed. With respect to sources operating close to the body, the use of mobile and cordless phones was not associated with health related quality of life. Also, the study did not provide indications that individuals considering themselves as hypersensitive to EMF (electromagnetic hypersensitivity; EHS) were more susceptible to RF EMF exposure than non-EHS individuals.

Cellular biology of NIR effects

Both *Pierre Goloubinoff (University of Lausanne)* and *Meike Mevissen (University of Berne)* used in their projects the nematode Caenorhabditis elegans (C. elegans) as a model system. This roundworm has a size of about 1 mm in length and a life- span of 2-3 weeks, its genome is completely sequenced and all the 959 somatic cells of its transparent body are visible in a microscope. It is thus simple to detect fluorescent proteins (and aggregates) that accumulate in transgenic animals when the proper reporter genes are expressed. Whereas *Pierre Goloubinoff* detected significant biological effects following small variations of ambient temperature, the exposure to continuous or alternate RF EMF

regimes had no detectable effects. Even after creating a more sensitive C. elegans subtype due to an additional impairment of protein homeostasis, no response to RF EMF was observed. Negative results were obtained also in a transgenic moss plant. Therefore, based on the parameters examined in the experiments, RF EMF does not appear to affect cellular protein homeostasis. Mevissen focused her experiments on the transcription factor DAF-16, a key player in the stress-signalling pathways. When activated, DAF-16 translocates into the cell nucleus and activates the transcription of a large number of effector genes. Her results showed that in a transgenic strain of C. elegans, exposure to RF EMF appeared to affect DAF-16 mediated signalling.

As a second model, *Meike Mevissen* used cell cultures of mammalian (human and rat) cells that could remain in their original state (undifferentiated) or adopt some characteristics of neurons during differentiation when exposed to certain substances. To analyse the stress response, the time course of the changes in heat shock protein regulation was investigated. For monitoring apoptosis (programmed cell death), the regulation of two apoptosis-related proteins was analysed. Nuclear changes were revealed in some cells after 16 hours of RF EMF exposure. Moreover, some changes in the time course of heat shock proteins were observed which may indicate that RF EMF might act as a genuine stressor and may trigger proteins in the apoptosis pathway.

Primo Schär (University of Basel) addressed in his project the question whether EMF exposure affects the integrity of the genetic material and thereby has a potential to cause adverse health effects associated with genetic instability, such as cancer or premature ageing. Controversial experimental results from a number of genotoxicity studies suggested that exposure of certain human cells to high and low frequency EMF causes strand-breaks in the genomic DNA. This led the WHO to rate the problem of genomic instability as a "High Priority Research Need" in its 2006 research agenda for RF EMF. The scientific discussion circled around the question whether or not these effects exist and little effort was devoted towards understanding what they actually mean and how they should be interpreted. The results were based on the Comet assay, which is a sensitive technique for detecting DNA damage at the level of the single cell. The previously reported effects could be reproduced for human primary fibroblasts exposed to ELF MF, and partly also for cells exposed to RF EMF. Specifically, it was found that intermittent, but not continuous exposure of human primary fibroblasts to a 50 Hz sinus MF at 1 mT induces a slight but significant increase of DNA strand breaks when measured in the Comet assay. Novel insights were obtained with respect to the origin and nature of this effect. It was shown that the small effects in the Comet assay resulted from minor disturbances of DNA-synthesis and occasional triggering of cellular apoptosis rather than the generation of DNA damage. Results obtained from biochemical analyses and live cell imaging strongly suggest that the apparent genotoxic effects observed in the Comet assay following intermittent ELF MF exposure of human fibroblasts are most likely accounted for by a secondary cellular response to the field rather than by ELF MF induced direct or indirect generation of DNA-damage.

Risk management, risk stratification and risk communication

The limited knowledge about potential health risks of long-term exposure to the radiation of mobile phones and mobile phone base stations resulted in a widespread increase in public concern. Difficulties in determining effective communication strategies arise from the nature of the hazard: as the true risk of NIR is not yet known, it is a challenge to inform the general public in an appropriate and comprehensive way.

Peter Schulz (University of Lugano) performed in a first subproject a content analysis of a web forum and of the mass media coverage of NIR-related topics in Switzerland. A cluster of a few prolific contributors was observed in the web forum, while the attention of the mass media focused on base stations and neglected the potential risk of appliances. In a second subproject, reactions to a press release concerning the health risk of base stations were examined. It was found that in terms of NIR risk perception, the pre-existing attitude towards possible health effects rather than the source of information and its credibility are the determining factors in forming an opinion. In a third subproject a survey was conducted in two different Swiss language regions to test how the recommendation of a precautionary measure against the effects of NIR contained in an information brochure affects risk perception and whether the wording of the measure can alter the effect. While the different types of precautionary messages (neutral, authoritative or empowering) did not differ in terms of effects, the empowering message was liked best. It was also evident that predisposition affects communication outcomes. Persons highly worried about health effects of NIR tend to misprocess

messages indicating that there is little reason to worry. This effect poses a severe problem for the planning of communication.

Martin Siegrist (ETH Zurich) investigated in his project the role of affect, a factor that might play an important role in the evolution of attitudes and opinions about NIR. Affect is an important determinant of perception and behaviour. Affective responses occur rapidly and automatically. The research project aimed to investigate which factors determine perceived risks and benefits of mobile communication, and also the acceptance of this technology. The Single Category Implicit Association Test (SC-IAT) measures implicit attitudes by assessing the response latencies of automatic evaluations. When the test was applied to various groups of participants, the results indicated that affective evaluations of different risks are carried out very rapidly. In addition, it was found that base stations evoked positive implicit associations in a group of experts on mobile communication, neutral associations in a lay people group, but negative associations in a group of base station opponents. A further result was that anger strongly determined the benefit perception and the acceptance of mobile phone base stations; fear, in contrast, strongly influenced risk perception of base stations. In comparison to other attributes, the location of the base station is of capital importance for citizens. Preferences for base station sites were also related to health beliefs, trust, and demographic variables. Eventually, the project demonstrated that participants who were provided with technical knowledge expressed more favourable base station siting preferences, i.e. those that would cause less exposure for the phoning population. In sum, it was shown that affect is central in the perception of non-ionising risks and differs remarkably between experts, opponents, and laypeople. Taken together these results imply that mere affect serves as fast, frugal, and first evaluation of mobile communication and other risks. This first evaluation tells us whether the stimulus is good or bad for us, or in other words, if it is personally relevant.

Accomplishments and limitations

If exposure to EMF affects health, it must influence biological processes. The aim of 5 projects was to investigate whether such effects can be demonstrated. Once such effects have been clearly and repeatedly demonstrated, the investigation of the mechanism of action must follow. Three previously reported RF EMF effects were confirmed and extended: (1) the enhancement of power in the sleep EEG in a specific frequency range; (2) changes of cerebral circulation; and (3) an increase of DNA fragmentation. Two of the projects provided insights into the mechanism of action.

- ***Effects on the brain:*** One of the most consistent effects of RF EMF is the enhancement of power in the sleep EEG within a specific frequency range (12-15 Hz). This effect has been reported by Achermann and colleagues in four separate previous studies as well as by another research group, and has been confirmed within the present program in three additional studies. By varying the field characteristics to which the subjects were exposed, it was shown that pulse-modulation is a prerequisite. The carrier frequency alone does not cause the typical EEG change in the 12-15 Hz range. Moreover, it was demonstrated that the effect is still present for a field with a higher carrier frequency that has a reduced penetration in the brain. This observation is a step towards identifying the critical target structures in the brain. Also, previously reported effects of RF EMF on cerebral blood circulation were confirmed. Wolf demonstrated such an effect with a novel non-invasive imaging procedure that is more easily applied in experimental studies than positron emission tomography. Moreover, UMTS RF EMF was shown for the first time to be effective. Various aspects render the interpretation of the results and their further investigation difficult. These include the large interindividual variability of the EEG changes and their delayed manifestation. It should be noted that the EMF-induced effects were restricted to the EEG and did not extend to the sleep stages and sleep quality which remained unaffected.
- ***Effects on DNA:*** A previous report that DNA fragmentation in mammalian cells is enhanced after RF EMF exposure raised concern about potential adverse health consequences due to DNA damage. Schär confirmed in human fibroblasts the previous findings. More importantly, he showed that the enhanced DNA fragmentation after ELF MF exposure was however due to minor disturbances of DNA synthesis and the occasional triggering of cellular apoptosis. Neither direct physical damage of DNA nor an indirect impairment due to an increase of reactive oxygen species was observed. Thus, EMF does not induce the irreparable DNA damage that is caused by ionising radiation. Therefore, in addition to confirming the effect itself, the study provides for the first time an insight into the mechanisms.

- ***Model systems:*** Model systems may be useful for documenting effects of EMF. The initial enthusiasm about the positive results in experiments with the roundworm C. elegans was tempered by subsequent negative findings. The studies of Meike Mevissen and Pierre Goloubinoff confirmed that while being exquisitely sensitive to various environmental influences, this model system is not promising for further EMF-related studies. The data of Meike Mevissen on EMF-induced changes in proteins involved in stress response and apoptosis are too preliminary for interpretation.
- ***Epidemiology:*** In the study of Martin Röösli objective traffic data about mobile phone use was used for the first time to investigate potential effects on symptoms, and in particular headache. Novel features were also the cohort design to study the effects of RF EMF exposure over the period of one year and the exposure measurements with a portable device for one week. This allowed the quantification of the exposure level and the specification of the contribution from various sources. The main finding was the absence of an association between health disturbances and environmental RF EMF exposure in daily life. In particular, no association was obtained between sleep behaviour and exposure in the sleeping room. Also, the study did not provide indications that individuals considering themselves as hypersensitive to EMF (electromagnetic hypersensitivity; EHS) were more susceptible to RF EMF exposure than non-EHS individuals. Overall, there was no indication that the current RF EMF exposure situation in Switzerland causes health disturbances. However, the study has also its limitations. For example, the average exposure level of the population was much lower than the currently applied exposure limit in Switzerland and the exposure level had uncertainties. Therefore, no conclusions can be drawn as to effects at higher exposure levels. Potential further limitations include a possible selection bias, the sample size and the limitation of the evaluation to one year. Nevertheless, it should be emphasized that the results did not indicate that the current RF EMF exposure situation causes health disturbances. This supports the majority of findings reported in the literature and increases the evidence for the true absence of an effect.
- ***Dosimetry:*** The merit of Niels Kuster's and Sven Kühn's project lies in the detailed assessment of brain exposure to RF EMF emanating from both near-field and far-field sources. Before the start of the project, many of the parameters and methods to accomplish such dosimetric measurements were lacking. Phantoms representing the electrical properties of the human body and brain, and simulation tools were developed and used to assess the SAR in various brain regions. Large variations were obtained, which were due to differences in usage, device design and signal characteristics. The models are able to predict the SAR induced by various RF EMF sources in brain regions. They will be valuable for dose estimation in epidemiological studies and consumer information on exposure of individuals. To assess the exposure of the foetus, Nicolas Chavannes and Andreas Christ developed computer models of women in different stages of pregnancy in which the electrical tissue characteristics were incorporated. The main findings were that occupational exposure limits are too high for pregnant women and that some product standards (induction cooker hobs) must be revised, since they may lead to excessive SAR levels in the foetus. In the third dosimetric study, Andreas Christ and Myles Capstick opened new avenues to cellular studies by designing and developing a miniature ELF MF exposure real-time imaging system.
- ***Risk communication:*** The study of Martin Siegrist showed that affective reactions are crucial for risk perception. Affect can serve as an important shortcut within decision making. Hence, trust and other affect-related elements must be considered in risk communication. Interestingly, knowledge provision was able to dispel misconceptions as it led to a more realistic evaluation of base-station location, which is more in line with public health considerations. From the Peter Schulz project it appears that persons rating the health risks of EMF as very low were further reassured by a reassuring message, whereas those rating the health risks as high became more worried. An empowering precautionary message appears to be most convincing.

Perspectives

The research topics covered in the program correspond largely to the high priority research fields listed in the WHO agenda 2010 for radiofrequency fields. In view of the results, follow-up studies will be particularly important in regard to the action of EMF on brain functions and on DNA metabolism. These approaches have proved to be most promising for gaining insights into the mechanisms

underlying effects of EMF on biological systems. While physiological and cellular effects could be demonstrated in the respective studies, their relevance for health could not be established and will necessitate further investigation. It is evident that the NRP 57 has strengthened EMF research in Switzerland and enhanced the interactions between the groups on a national level. It has also increased the international visibility of Swiss research. To preserve the expertise and know-how gathered during the programme it will be important to explore avenues allowing the continuation of key projects. EMF research is a long-term endeavour that requires an appropriate organisational and financial framework. The rapidly evolving technologies provide a challenge that can be met only by a further close collaboration of experts in dosimetry, life sciences and epidemiology. The NRP 57 programme has laid the groundwork.

2. Introduction and goals of NRP 57

2.1 Framework

Research carried out by National Research Programs (NRPs) is targeted research that contributes to the solution of contemporary problems of national importance. Under the provisions of Article 6, paragraph 2, of the Law on Research of 7 October 1983, the Federal Council selects the topics and foci to be researched in NRPs and mandates full responsibility for implementing the Programs to the Swiss National Science Foundation (SNSF, Division IV). The purpose and contents of the NRP instrument are defined in article 4 of the Federal Ordinance to the Law on Research of 10 June 1985.

In June 2003, the former Federal Office for Education and Science (FOES) requested the SNSF to evaluate the establishment of a NRP related to potential effects of non-ionising radiation (NIR) on human health. This initiative was based on an extensive report by the Federal Office for the Environment (FOEN) that included a meta-analysis of over 200 scientific publications. The research council division IV evaluated the proposal with respect to its suitability and feasibility, thereby relying on a comprehensive assessment by a group of international experts. The positive outcome of the feasibility study (June 2004) initiated the formal procedure that is set off by a program proposal submitted by the SNSF to the Swiss government. In June 2004, the State Secretariat for Education and Research (SER) requested the SNSF to develop an implementation plan for an inter- and trans-disciplinary, four-year research program with a total budget of CHF 5 million.

A steering committee (SC) was established and asked to draft the implementation plan. The main objective of the plan was to address key scientific questions regarding the potential adverse health effects of NIR emitted by a range of present and future technologies. The program was to be complementary to international research activities in the field of NIR with a focus on specific issues defined in the electromagnetic field (EMF) research agenda of the World Health Organization (WHO). Specific emphasis was put on implementation, so that the program would directly address the ever-increasing uncertainties in the Swiss population regarding potential health hazards by NIR in the environment.

Since international efforts primarily focused on the endpoint of cancer, the implementation plan specified that the NRP would address other potentially adverse health effects and aim to clarify the basic mechanisms underlying potential EMF effects on biological systems. A better understanding of the causal relationship between NIR and neurophysiologic responses as well as responses at the cellular level is expected to facilitate the risk assessment of current and future technologies. Consequently, the main topics of research were defined as follows:

- Dosimetry and exposure assessment
- Human experimental exposure experiments and epidemiological studies including the topic of electromagnetic hypersensitivity (EHS)
- Cellular biology of NIR effects
- Risk management, risk stratification and risk communication.

In March 2005, the Federal Council approved of the "NRP 57: Non-Ionising Radiation – Health and Environment" and in November of the same year, the Federal Department of Home Affairs approved the implementation plan.

The official call for projects was issued in December 2005. A total of 36 proposals were submitted and evaluated by the SC and external reviewers. The SC recommended 11 projects for funding, a proposal that was subsequently approved by the SNF Research Council in November 2006. The approved projects were launched in January 2007 with an overall duration of three years.

2.2 Former state of research and rationale for the program

In the 10-15 years prior to the NRP 57, international (e.g., 5th Framework Program) and national programs (e.g., in Great Britain, Finland, France, Italy, Japan and others) as well as industry

sponsored programs (e.g. MMF, NTTDo-CoMo) focused on those topics of the WHO agenda that were directly related to cancer risk. Only a few studies addressed different endpoints. Also, little attention had been paid to exposures other than those of mobile phone systems and few studies explored a potential interaction mechanism between EMF and biological responses. Numerous comprehensive research reviews from national and international agencies (including the WHO, the U.S. National Institute of Environmental Health Sciences (NIEHS), the National Radiological Protection Board in the U.K, the FOEN in Switzerland and reports from the Netherlands, France, Canada and Sweden) summarised the findings. The reports generally concluded that several questions regarding possible effects of NIR on human health remain to be addressed. Besides the association between increased incidence in childhood leukaemia and extremely low frequency magnetic field (ELF MF) exposure, and acoustic neuroma and radiofrequency (RF) exposure, a variety of subtle effects in animals, humans and cell cultures were described. The data suggested that the effects may depend on intermittency of exposure, frequency content in the power and other signal characteristics, aspects increasing the uncertainties in the evaluation of health risks.

Many international and national public and private research agencies have solicited projects aiming at the assessment of possible health effects of NIR at intensities below the levels recommended by the International Commission on Non-Ionizing Radiation Protection exposure (ICNIRP) guidelines. International research focused on the following subtopics:

- ***Dosimetry***: Significant progress in Dosimetry was achieved during the last decade. Methodologies, instrumentation and procedures for detailed dosimetric analyses have been developed for both experimental and epidemiologic studies and exposure assessments of current technologies. Very few assessments however included novel and future technologies.
- ***Controlled exposure studies in humans:*** Laboratory studies on non-cancer health effects in humans covered a wide array and have investigated the effects of NIR on electrical brain activity (usually measured by electroencephalography (EEG)), sleep physiology, cognitive performance, heart rate variability, mood, hormone levels and immune function. Outcomes provided little evidence for an association between NIR and heart rate variability, mood disturbances, immune function as measured by various immunological variables (blood chemistry, leukocyte or lymphocyte counts and others) or changes in the concentration of hormone levels. However, various effects have been observed in studies on sleep physiology and cognitive performance parameters. They included RF induced EEG alterations in the spindle frequency range of non-rapid eye movement (non-REM) sleep as well as subtle changes in cognitive performance assessed by reaction speed and accuracy of performance. These observations suggested that brain function may be influenced by EMF. Due to difficulties in designing appropriate experiments, only a small number of studies have addressed electromagnetic hypersensitivity.
- ***Epidemiology:*** Considerable resources have been dedicated to multinational large scale studies (e.g., Interphone Study) that focused on the association between EMF exposure emitted by mobile phones and the development of brain or other types of cancer. Exposures by power lines and other ELF sources were classified as possibly carcinogenic (2B) by the International Agency for Research on Cancer (IARC) as well as by the NIEHS. Regarding health effects other than cancer, the Federal Office for the Environment (FOEN) inferred from a number of studies investigating possible EMF effects on wellbeing (considering symptoms such as e.g., headaches, dizziness, fatigue, insomnia or tinnitus) that on the basis of available data no conclusive assessment of the risk to human health could be made. With respect to ELF exposures, NIEHS concluded that there is little, if any evidence for an association between ELF exposure and the incidence of neurodegenerative and neurobehavioral disorders, cardiovascular disease or pregnancy outcome.
- ***In vitro studies***: Studies at the cellular level are essential to determine the mechanisms of potential adverse effects. Some studies examined NIR effects on the cell membrane level, gene expression, and signal transduction pathways. In addition, various studies investigated in vitro cell proliferation and cell cycle regulation, and reported modifications as well as a potential genotoxic and cytotoxic effects. Also, calcium homeostasis and the expression of stress (heat shock) proteins in mammalian cells were monitored under exposure.
- ***Animal studies:*** A number of large-scale animal studies on carcinogenicity have been conducted in an international framework. No causal association of EMF with any particular malignancy

could be established. Small-scale studies concentrated on issues relevant to human endpoints, such as behaviour, effects on the inner ear and cochlea, the permeability of the blood-brain barrier as well as neurodegenerative diseases, but the evidence for an association remained inconclusive. Similarly, no evidence for NIR effects was found with respect to haematological parameters, the immune system and development and reproduction.

- ***Risk management and communication:*** Several research programs included projects on the subject of risk management and communication. The respective studies considered the evaluation of the impact of risk communication strategies, individual risk perception, cognitive maps of persons suffering from self-reported electromagnetic hypersensitivity, and the interpretation and evaluation of the impact of precautionary measures.

2.3 Objectives

Despite numerous studies carried out in a large number of research fields, the picture of potential low-dose NIR effects on human health remained unclear. Due to the persisting uncertainty and given that even small health effects could have considerable implications for public health, federal agencies and other governmental bodies requested further research in this area to close existing knowledge gaps. Of specific interest to the NRP 57 was research investigating the basic mechanisms underlying EMF effects on biological systems, as so far, there were no comprehensive international initiatives on in vitro studies and cellular mechanisms. In view of the importance of such studies and their potential to identify critical characteristics of EMF fields, this approach was selected as a major focus of the NRP 57. Also, since optimized exposure setups and comprehensive dosimetric information are prerequisites for any sound EMF studies, a high priority was assigned to dosimetry. Another focus of NRP 57 was the growing concern among large parts of the Swiss population with respect to NIR and NIR risk management and the question about the parameters influencing public awareness and perception.

Research regarding occupational exposure and exposure from medical treatments and diagnostics was not included in the program. In view of the large cost and the comprehensive international research effort, neither large-scale animal studies nor epidemiological cohort and case control experiments with the endpoint of cancer were part of NRP 57.

The primary goal of the NRP 57 was to establish a coordinated and comprehensive effort to address some of the knowledge gaps regarding the effects of low-dose NIR on human health. The findings were expected to provide data on the question whether and how EMF exposure leads to changes of biological systems and to potential health impairments. Both the health authorities and industry need more data to assess the potential risks of EMF for health and well-being. Assessment and measures based on scientific evidence would increase public trust in the appropriate use of present communication technology. The promotion of international research collaboration was a further aim. Hence, a high scientific standard of the projects was mandatory.

In the longer term, a better understanding of exposure parameters causing biological responses and the respective interaction mechanisms would foster a comprehensive risk assessment including the evaluation of NIR from new technologies. In addition, it was assumed that the research projects of NRP 57 could render Swiss research more competitive, and promote the participation of Swiss teams in large international programs.

2.4 Selected projects and budget

In accordance with customary procedures for NRPs, the SC of the NRP 57 (see Appendix 7.2) agreed on a two-phase submission procedure for research projects. Projects were selected according to the criteria described in the call. Quality assurance throughout the program was conducted as specified in the program manual.

The SC evaluated all projects with the support of international experts according to the following criteria:

- Scientific quality and originality: the project outlines and the research proposals should correspond to international state-of-the-art with respect to scientific originality and methodological standards.

_ Feasibility and compliance with the objectives of NRP 57: the projects should reflect the program's scientific objectives and comply with its overall framework.

_ Applicability: NRPs are explicitly called upon to promote practical applications and implementation; in consequence, priority would be accorded to projects that are implementation-oriented and have a high level of practical relevance.

_ Personnel and infrastructure: Projects should be carried out in an environment providing adequate infrastructure and personnel.

11 projects were selected and grouped into four different modules:

Module 1: Dosimetry and exposure assessment

Determination of the exposure of the foetus to electromagnetic fields in an uncontrolled environment *Dr. Nicolas Chavannes, IT'IS Foundation for Research on Information Technologies in Society, Zurich*	CHF 211'675.–
Cumulative exposure in time and frequency domains of the central nervous system *Prof. Dr. Niels Kuster / Dr. Sven Kühn, IT'IS Foundation for Research on Information Technologies in Society, Zurich*	CHF 296'909.–
Live cell imaging during EMF exposure *Dr. Andreas Christ, IT'IS Foundation for Research on Information Technologies in Society, Zurich*	CHF 241'285.–

Module 2: Laboratory studies and epidemiology

Effects of pulse-modulated radio frequency electromagnetic fields on the human brain: Critical field parameters, site of interaction and sensitivity in early adolescence *Prof. Dr. Peter Achermann, Institute of Pharmacology and Toxicology, University of Zurich*	CHF 563'828.–
Radio frequency electromagnetic field exposure and health related quality of life: Prospective cohort study *Prof. Dr. Martin Röösli, Swiss Tropical and Public Health Institute, University of Basel*	CHF 553'255.–
Effects of UMTS radiation on cerebral blood circulation assessed by near infrared imaging *PD Dr. Martin Peter Wolf, Clinic of Neonatology, University Hospital Zurich*	CHF 303'394.–

Module 3: Cell biology

Characterization of effects of non-ionizing radiation on the nematode Caenorhabditis elegans as a model organism *Prof. Dr. Pierre Goloubinoff, Department of Plant Molecular Biology, University of Lausanne*	CHF 310‘802.–
Effects of electromagnetic fields in vitro and in vivo: Identification and characterization of stress-response pathways *Prof. Dr. Meike Mevissen, Division of Veterinary Pharmacology and Toxicology, Vetsuisse Faculty Bern, University of Bern*	CHF 480‘554.–
Genotoxic effects of non-ionizing radiation *Prof. Dr. Primo Schär, Institute of Biochemistry and Genetics, Department of Clinical and Biological Research, University of Basel*	CHF 695‘850.–

Module 4: Risk perception

Structure and effects of societal communication on non-ionizing radiation *Prof. Dr. Peter J. Schulz, Health Care Communication Laboratory, Facoltà di Scienze della Communicazione, Università della Svizzera Italiana*	CHF 166‘750.–
Affect and perception of non-ionizing radiation: Implications for risk communication *Prof. Dr. Michael Siegrist, Consumer Behavior, Institute for Environmental Decisions (IED), ETH Zurich*	CHF 173‘078.–

Overview distribution of program budget in CHF

Module 1: Dosimetry and exposure assessment	749‘869.–
Module 2: Laboratory studies and epidemiology	1‘420‘477.–
Module 3: Cell biology	1‘487‘206.–
Module 4: Risk perception	339‘828.-
Implementation and Administration	1‘002‘620.–
TOTAL	**5’000’000.–**

2.5 Implementation, communication and publications

Public discussion on risks and benefits of mobile communications and concern with “electrosmog” is controversial. Implementation focused therefore on:

_ Transferring knowledge from research projects to practice

_ Managing issues

_ Communicating the process of research and the results of the projects and the overall program to different stakeholder groups.

The communication aimed to:

_ Inform the different stakeholder groups in a timely and transparent manner on the framework and the workflow of the NRP 57

_ Give a realistic picture of the expected outcome of the research projects

_ Present the research projects in the context of international research efforts

_ Provide support for the research teams in communicating their results to target groups outside the scientific community.

To fulfil these goals implementation of the NRP 57 addressed several target groups:

(1) Politics and government agencies

_ Parliamentarians on a national level

_ National political parties

_ Federal Council

_ Federal agencies (BAFU, BAG, BAKOM, BFE, METAS, ESTI, COMCOM)

_ Cantonal councils

_ Cantonal agencies

_ Local and community councils

(2) Economy and industry

_ Telecom industry in Switzerland

_ Energy industry

_ Industrial organizations

(3) NGOs

_ National consumer organizations

_ National environmental organizations

_ National, regional and local organizations concerned with mobile communication

_ National health related organizations

(4) General public

_ National media

_ Science journalists

To provide general information, a website in German (www.nfp57.ch), French (www.pnr57.ch) and English (www.nrp57.ch) was developed and launched at the beginning of the research phase. In parallel, a general brochure was edited and widely distributed to the target groups mentioned. The launch of the program was accompanied by the nationwide distribution of a press release by the SNSF.

To inform interested audiences and to discuss specific questions, the SNSF organized two meetings addressing politics and government agencies as well as industry, NGOs and media, respectively. During the research program, interested people were also informed regularly on the progress of the program via the website and an electronic newsletter. Selected publications from research projects

were accompanied by media releases. In December 2010 a round table with the stakeholders supporting research on NIR was organized in Bern to discuss future plans and perspectives.

To disseminate the results of the NRP 57, a lay summary of each research project will be presented on the website and a brochure on the findings and the appraisal by the SC will be widely distributed to the target groups. In addition, a national media conference will be organized by the SNSF in which the overall findings as well as some selected projects of the NRP 57 are presented. A public event to discuss the findings with specific target groups will be held in Bern.

3. Synthesis of Findings

This chapter is based on the reports of the project leaders. Many findings have not yet been published in peer-reviewed scientific journals. Chapters 4-6 contain the assessment of the findings and of their implications by the Steering Committee.

3.1 Module 1: Dosimetry and exposure assessment

Assessment of the exposure of the foetus to electromagnetic fields in uncontrolled environments
PI: Dr. Nicolas Chavannes/Dr. Andreas Christ, IT'IS Foundation for Research on Information Technologies in Society, Zurich

The research project dealt with the quantification of electromagnetic fields and their specific absorption in the tissues of the mother and the unborn child in different stages of pregnancy during everyday exposure situations. Such exposure assessments are crucial to assure compliance with exposure limit values, since so far pregnancy received no particular considerations with respect to exposure limits. Moreover, only limited data exist with respect to foetal exposure in the near field.

The absorption was simulated using mathematical models and numerical techniques. For this purpose, highly detailed anatomical computer models of a woman for three different gestational stages (month 3, 7 and 9 of pregnancy) were developed. In view of the currently existing models that have been used in other studies, the models developed within the framework of this project can be considered as the most accurate and detailed ones. Imaging datasets for the development of anatomical models of pregnant women are generally assembled from different sources, as ethical constraints usually prohibit whole body scans. So far, a dozen models of pregnant women have been described in recent dosimetric studies. However, the models developed within the NRP 57 are superior in several respects. For instance, the models consist of approximately 80 different tissue types in the mother and up to 17 different tissues in the foetus (e.g., bone, subcutaneous tissue or skin). The electrical characteristics of these tissues are available in an appropriate database and in the recent scientific literature. This allows a more realistic rendering of the field and current distribution in the simulations.

The models were subsequently exposed to representative, everyday types of electromagnetic fields. The fields represented exposure from field sources at large distances, such as electronic article surveillance systems operating at different frequency ranges, induction cooker hobs as well as wireless devices operating in the close environment of the abdomen. The goal was to characterize the exposure of the mother and the foetus by conducting a large number of numerical simulations in different exposure positions and by evaluating induced currents and the specific absorbed radiation as well as temperature elevations.

At frequencies above 100 kHz, the basic restrictions of the safety standards are defined in terms of the specific absorption rate (SAR). The SAR is a measure of the electromagnetic power absorbed in the tissue of the body and therefore related to tissue heating. Safety limits for the local exposure, the peak spatial SAR (psSAR) and whole body specific absorption rate (wbSAR) are defined for these frequencies. At frequencies below 10 MHz, the currents induced in body tissues can excite nerves, and exposure limits are defined below this threshold in terms of the current density averaged over a small cross section of tissue. Since these quantities cannot be easily measured under real-world exposure conditions, the guidelines on EMF exposure define reference levels or limits which are the incident field values without the presence of an exposed person. These reference levels were derived using simplified mathematical models of the average human body aiming at a conservative assessment, i.e., if the reference levels are met, the basic restrictions should always be met as well. Otherwise, particular measures have to be taken to assert whether the basic restrictions are met. Different limits are defined for the general public and for occupational exposure.

The most important findings of this project were that when the incident fields are compliant with the reference levels for the general public at the location of the foetus, the basic restrictions are met in all cases examined. However, due to the small safety margin, the statement cannot be generalized based on current data and additional research is needed to better characterize the uncertainty boundaries.

In contrast, when the mother is exposed to the limits of occupational exposures, which are higher than the reference levels for the general public, then the exposure of the foetus can be above the basic restrictions for the general public. Thus, pregnant women must be particularly considered by product standards and some product standards must be revised since they may result in exposures that exceed tenfold the safety limits.

A large number of studies assessed the exposure of the mother and the foetus to whole body exposure in the far-field. These publications generally come to the conclusion that the unborn child is sufficiently protected by the mother and therefore the basic restrictions are not violated by the reference level for the general public. In spite of the large differences of the models used in these studies, their results agree with respect to the order of magnitude, and they are in good to satisfactory agreement with the findings of this study. Little work has been published so far with respect to near-field exposure, but generally results are also in good agreement with the findings of this project. A direct comparison, however, is difficult because of the different anatomies considered and because of the closer distances of the target tissue to the devices.

Cumulative exposure in time and frequency domains of the central nervous system

PI: Prof. Dr. Niels Kuster/Dr. Sven Kühn, IT'IS Foundation for Research on Information Technologies in Society, Zurich

Public exposure to electromagnetic fields in the radio-frequency (RF) spectrum has increased dramatically during the last 20 years. This is particularly true for the maximum RF EMF induced in the human brain, which has been classified as a primary organ that is potentially sensitive to such fields and may be adversely affected, especially during development. However, little is known about the actual levels electromagnetic fields induced in the human brain and its functional subregions from RF sources.

The aim of this project was therefore to establish a basis to determine the cumulative exposure of the central nervous system (CNS) to RF EMF from the most prominent sources in our society, both in the near- and far-field. Comprehensive information about the exposure of the CNS is crucial to create a meaningful exposure matrix for epidemiological studies and to improve the exposure planning for future research projects about adverse health effects on the CNS. It is also needed to appropriately weigh the experimental evidence about CNS effects and to provide agencies with the basis for exposure evaluations and also, if necessary, for the development of suitable recommendations for the public for exposure reductions. Moreover, information about the exposure of the CNS may help to detect potential gaps in current product standards for testing compliance with EMF limits.

The study covers the frequency range from 30 MHz to 6 GHz, thus comprising current as well as foreseeable future devices and sources, including mobile phones, base stations, cordless phone, baby surveillance devices, wireless network devices and hands-free kits. In addition, other factors that affect the exposure, such as communication technology, user behaviour and environment, were also considered for a realistic assessment of exposure to RF EMF over time. Since the general public is not uniformly exposed to RF EMF, the study distinguished different user types, for example, non-users and extensive users of mobile phones.

The devices were characterized into two categories: near-field sources directly operated at the human head, e.g., mobile phones, and far-field sources which are operated at larger distances from the body. Since it is not possible to directly measure EMF induced in the human head and body, the incident electric fields from far-field sources were measured in free-space.

From the near-field sources, the induced fields or the Specific Absorption Rate (SAR) were measured in phantoms representing the electrical properties of the human body. The incident E-field and the SAR induced in the homogeneous phantoms were related with the SAR in the various tissues and brain regions of anatomical human models through estimation factors that were obtained using simulation tools. These anatomical models were originally derived from magnetic resonance images of healthy volunteers. A variety of human models ranging from children to adults of both genders were included. The SAR variability was derived from the differences in the human anatomy of the different models. A tool for the determination of the SAR in the functional subregions of the brain, that cannot be discriminated anatomically, was developed.

The RF EMF exposure of the different tissues of the human body and various brain regions were assessed with the developed tools. The model was used to compare the exposure from different sources, especially in the sensitive regions of the brain. This was obtained by developing transformations for various kinds of EMF sources to induced region-specific SAR. These transformations were then used to show how different sources contribute to the total exposure and the influence of factors such as usage/exposure duration and modulation.

Large differences were found between the sources. The strongest source of brain exposure to EMF is the mobile phone. The exposure thereby depends on usage patterns and phone selection, e.g., the design of the phone, usage of hands-free kits (exposure is reduced with hands-free kits by a factor > 10), choice of phones supporting the UMTS communication system or only GSM (UMTS reduces the average exposure by a factor of >100), etc. Differences in exposure between UMTS and GSM derive from a very efficient power control and coding in UMTS that maintains the output power at a minimum level. Compared to a UMTS phone, a cordless phones used inside homes might cause higher exposure of the brain.

The study also demonstrated large variations with respect to the exposure of different brain regions between different mobile phones by more than a factor of 1000. To disseminate this knowledge to the public and health agencies, the research results were implemented in the most widely used SAR measurement system. Every phone can now be characterized with respect to the brain region specific exposure, which is a much better exposure surrogate than the currently published SAR values.

Far-field or quasi-far-field sources generate much lower exposure of the brain. On average, the levels of SAR induced from indoor base stations, e.g., from cordless phone or wireless network access points are of the same order of magnitude as the levels of SAR from outdoor mobile telephony base stations.

Before the start of this NRP57 project, many of the parameters and methods to accomplish such dosimetric measurements were missing. One major achievement of this project was to provide a dosimetric relation between various radio-frequency electromagnetic sources. The conducted work has also advanced the state of science by establishing the foundation for evaluating the changes in exposure from current mobile phones in real networks for rural and urban areas. The evaluation of the power control behaviour in real networks is especially important, as the statistical evaluation of existing mobile phone compliance test data revealed that the communication system is the strongest predictor of the exposure.

Further, a novel method to derive the tissue and brain region-specific SAR from incident fields was developed. This model will be useful to estimate the induced SAR from far-field and quasi-far-field sources, which is of particular importance for dose estimations in epidemiologic studies, as the general public is almost constantly exposed to low-level EMF due to the increasing number of mobile phone networks and wireless devices.

Live cell imaging during ELF MF exposure

PI: Dr. Andreas Christ/Dr. Miles Capstick, IT'IS Foundation for Research on Information Technologies in Society, Zurich

For studying biological effects of the exposure of cell cultures to ELF magnetic fields, well characterized and uniform exposure conditions must be established to assure minimal disturbance to the experiment. The most common approach is to expose cells to particular field conditions for defined time periods. A considerable variety of in-vitro exposure setups have been used in the past. Commonly, the response of the cells is analysed after exposure on the basis of specific cell parameters. Such experiments have shown various biological end points ranging from no effect to increased DNA strand breaks. This approach can be conclusive regarding the overall change induced during MF exposure. However, where effects have been seen, the exact mechanism of interaction has remained unknown, because transient responses of the cells during actual exposure could not be observed. Thus, no specific information could be gathered on cell responses to MF stimuli or on the pathways involved in the changes observed. Moreover, for biological experiments in which the expected outcomes are extremely subtle and the differences between exposed and unexposed cells are small, a system providing only the possibility of exposing cell cultures to MF is inadequate. A

computer control system is required for setting up, monitoring and recording the exposure level and other relevant parameters throughout the experiment.

The aim of the project was to develop an instrument that would enable direct insight into cell responses to MF. Such a system would allow investigating the mechanism involved in effects such as DNA strand breaks. The instrument would constitute a highly effective tool for studying possible non-thermal interaction mechanisms and performing concomitantly various micromanipulations without interference with the microscope system. More specifically, the objective was to develop a miniature ELF exposure system that can be integrated with a microscope system, thus enabling live cell imaging and other state of the art microscopic techniques including confocal scanning and fluorescence microscopy during ELF exposure. In addition to developing the system itself, numerical and experimental tools including near-field scanning and fast thermal probes were needed to closely monitor the exposure conditions during the experiment. These requirements are essential for providing the information for verifying experimental results by other research groups.

The final miniature ELF exposure system enables direct insight into the cell's response to MF, thereby going beyond the classic post-experimental analysis. It allows flexible signal analysis, intermittent exposure protocols and a variety of micromanipulations during live cell imaging. The system is easy to handle due to automated software control, provides continuous information on field strength and cell temperature, and also supports blinded protocols. Coil currents and chamber temperatures are monitored throughout the experiment. Temperature differences between exposed and sham-exposed cells are kept below 0.1°C with temporal variations less than ± 0.1°C up to 3mT rms.

The final experimental system was used successfully in another project of the NRP 57 program (*Genotoxic effects of non-ionizing radiation, by Prof. Primo Schär*). The setup was optimized for uniform magnetic field exposure and minimum non-magnetic field differences between the exposure and sham (no) exposure.

3.2 Module 2: Laboratory studies and epidemiology

Effects of pulse-modulated radio frequency electromagnetic fields on the human brain: Critical field parameters, site of interaction and sensitivity in early adolescence
PI: Prof. Dr. Peter Achermann, Institute of Pharmacology and Toxicology, University of Zurich

There is increasing evidence that RF EMF, such as emitted by mobile phones, can affect physiological processes in the brain. Effects on brain function are usually addressed by investigating RF EMF induced changes in the EEG or alterations in cognitive performance, such as attention or memory. In addition, some imaging studies have been performed to assess possible changes in regional cerebral blood flow (rCBF).

A considerable amount of research has been carried out in recent years concerning short term effects of RF EMF exposure on human brain physiology. To date, the most consistent effects are changes in electrical brain activity in waking and sleep. Spectral power of the EEG in the so-called alpha band (8-12 Hz) and in the frequency range of sleep spindles (12-15 Hz) are the two most consistently affected variables in waking and non-REM sleep, respectively. Furthermore, it seems that the pulse modulation of the field is crucial for inducing an effect. Compared to effects on the EEG, effects on cognitive performance are not consistent. Whereas older studies reported an improvement of performance with decreased reaction times or elevated accuracy scores, more recent studies revealed an impairment of mental abilities or no effect aThe site of action of RF EMF in the brain is still unknown. The fact that unilateral and bilateral head exposure showed EEG changes in both hemispheres indicates that the sensitive sites may be deep in the brain.

To investigate the mechanisms involved in RF EMF effects on brain function, three subprojects were designed. The first subproject aimed to clarify which of the low frequency modulation components of the RF EMF emitted by mobile phones is responsible for the biological effects. It was hypothesized that frequency components in the spindle frequency range may play a major role. Thus, in a first experiment, pulse modulation components of 14 Hz (spindle frequency range), of 217 Hz (strongest component of the Global System for Mobile Communications (GSM) signal) and a sham control condition (no field) were applied. In a follow-up experiment, exposure conditions included 2 Hz pulse-modulated RF EMF, a 2 Hz pulsed magnetic field and a sham control condition. This latter

condition was designed to see whether the slow modulation component alone is sufficient to elicit a biological effect or whether its combination with RF EMF is required.

The second subproject aimed to determine whether the thalamus, a subcortical brain structure involved in sleep regulation, is critical for mediating effects of RF EMF on the sleep EEG. It was hypothesized that relatively intense exposure of the thalamus (as used in many previous studies) would lead to increased EEG spectral power, whereas a superficial exposure of the brain involving mainly the cerebral cortex would reduce or eliminate this effect or lead to predominant changes in one hemisphere. The exposure conditions included a GSM handset-like signal with carrier frequencies of 900 MHz ('subcortical exposure' or 'thalamus exposure') and 2140 MHz ('superficial exposure' or 'thalamus non-exposure') and a sham control condition.

Each of the two subprojects involved 24 to 30 healthy, young males and followed the same study protocol consisting of three sessions of two nights separated by one week. In each session, an experimental night was preceded by an adaptation night. The adaptation night served to familiarize the participants with the EEG procedure and the laboratory environment. On the experimental night, participants were either exposed to a field or sham-exposed (no field, control condition) for 30 min directly before their sleep was recorded during an 8h-nighttime episode. Subjects also performed a series of reaction time and working memory tasks during exposure.

The third subproject was designed to investigate the effect of RF EMF on cognitive performance and the waking EEG in early adolescence. Mobile phones are a dominant source of RF EMF exposure for teenagers. In the WHO EMF research agenda 2006/2010, investigation of EMF-induced effects on cognition and the EEG in children was identified as a high priority research need. Children start to use mobile phones extensively in early adolescence (age 11-13 years), and there is concern that they might be particularly sensitive to RF EMF as brain maturation is not yet completed. A number of previous studies in healthy young adults showed an increase in EEG spectral power in the alpha frequency range either during or following RF EMF exposure; however, very little research exists regarding the presence and/or magnitude of this effect in children. To test whether alpha activity in the wake EEG is affected in a dose dependent manner, 23 adolescents (11-13 years old) were exposed to GSM handset-like signals with a carrier frequency of 900 MHz at 1.4 W/kg and 0.35 W/kg, in addition to a sham control condition (three sessions at weekly intervals, exposure at the same time of day for each individual). During the 30-min exposure, the adolescents performed a series of reaction time and working memory tasks. In addition to a baseline recording prior to exposure, the waking EEG (3 min of eyes closed followed by 3 min of eyes open) was recorded immediately after exposure, and again at 30 min and 60 min after exposure.

The 2-Hz and 14-Hz pulse-modulated exposure to RF EMF resulted in an increase of spectral power of the sleep EEG in the spindle frequency range. However, a 2-Hz pulsed magnetic field without the RF EMF part did not induce this effect. These results, in conjunction with previous findings, show that neither the pulsation alone nor the RF EMF carrier frequency alone causes the typical change in the sleep EEG that has been repeatedly observed with pulse-modulated RF EMF exposures. The results indicate that pulse-modulated components in the physiological frequency range (i.e., 2 Hz and 14 Hz) may be important for inducing the EEG changes. Although the 14 Hz and 2 Hz RF pulse modulation exposures both led to a significant increase in sleep EEG spectral power, there was also a smaller but non-significant increase following the 217 Hz pulse-modulated exposure. This suggests that the specificity of the pulse modulation may not be the most important factor, as several different pulse modulation frequencies resulted in an effect in the spindle frequency range during sleep. With respect to cognitive performance (first study), overall reaction speed tended to be lower during exposure conditions than under sham condition, whereas the accuracy of performance was unaffected.

The results of the second subproject showed that the unilateral exposure to RF EMF fields caused an increase of spindle frequency activity in both hemispheres, despite the limited penetration depth of the radiation. Therefore, it is unlikely that subcortical structures, such as the thalamus, are the primary targets mediating the EEG effect. The RF EMF-induced increase of power in the spindle frequency range may alternatively be caused by an indirect involvement of the thalamus and/or an action on the cerebral cortex. The time-course of these effects on the EEG showed some variability across the studies with the effect either being seen throughout sleep (2-Hz pulse modulation), increasing in the course of sleep (both subcortical and superficial exposure) or only being seen at a specific time-point within the sleep episode (14-Hz pulse modulation). The different exposure

conditions could be an explanation for this variability. Sleep architecture was not affected by any of the exposure manipulations, confirming previous findings that the EEG effects are not paralleled by changes in sleep architecture or sleep quality.

The results of the third subproject are still in the process of analysis.

Effects of UMTS radiation on cerebral blood circulation assessed by near infrared imaging

PI: PD Dr. Martin Peter Wolf, Clinic of Neonatology, University Hospital Zurich

Universal Mobile Telecommunication System (UMTS) is the third generation (3G) of mobile telecommunications technology and the new widespread standard in mobile communication. Yet, whereas most research studies performed so far have used a second generation (2G) GSM signal in their experiments, only very few studies have investigated potential effects of UMTS EMF on human brain physiology.

The uncertainty about the potential effects of UMTS RF EMF combined with its rapidly ongoing implementation leads to public concern in many countries. A number of recent studies using imaging techniques such as Positron Emission Tomography (PET) indicate that an increase in regional cerebral blood flow (rCBF) after GSM RF EMF exposure is likely whereas no change was observed with UMTS EMF. Near Infrared Imaging (NIRI), sometimes also called Near Infrared Spectroscopy (NIRS), Diffuse Optical Imaging (DOI) or Optical Topography (OT), is another sensitive, non-invasive modality for imaging brain function, blood flow and oxygen concentration. The technique uses invisible near infrared light (~ 650 nm – 1000 nm on the electromagnetic spectrum) and consists of a source and a highly sensitive light detector. The light penetrates the biological tissue deeply and is absorbed by oxygenated haemoglobin [O_2Hb] and deoxygenated haemoglobin [HHb]; the amount of brain activation is inferred from the patterns of hemodynamic change, given that neuronal discharge is tightly coupled to cerebral blood flow and blood volume. Other effects that may possibly influence blood circulation are detected as well.

For this project, the NIRI technique was specifically adapted to measure short-term (effects occurring within 80 s) and medium-term (effects occurring within 80 s to 30 min) changes in cerebral blood circulation and oxygenation (i.e., the amount of blood carrying oxygen) in response to intermittent UMTS RF EMF exposure at powers typical for a handheld mobile phone. A standard NIRI instrument was made sufficiently inert to EMF by developing new fibre optic sensors and by shielding. Each participant completed three different exposure conditions (0.18 W/kg, 1.8 W/kg both at a carrier frequency of 1.9 GHz and a sham control condition) on three different days. In addition, on a fourth day, the brain was stimulated by finger tapping to compare potential effects of UMTS RF EMF to this brain activation. A measurement consisted of 16 cycles, the exposure/stimulation segments, (20 s) of UMTS RF EMF exposure (ON) or finger tapping were alternated with 60 s recovery (OFF). A measurement lasted 31 min in total, including baseline measurements before and after the exposure. In addition to oxy-, deoxy- and total haemoglobin concentration, the heart rate, subjective well-being, tiredness and counting performance were recorded.

The data showed a significant short-term increase in oxy- and total haemoglobin concentration during exposure to 0.18 W/kg. A decrease in the medium-term response of deoxy-haemoglobin concentration in the range of physiological fluctuations was detected in response to 0.18 W/kg and 1.8 W/kg exposures. Moreover, the medium term heart rate was significantly higher for 1.8 W/kg than for sham exposure. No other variables were affected.

The study revealed that intermittent exposure to UMTS RF EMF can affect cerebral blood circulation and heart rate. The short-term effects were smaller than the ones observed during a normal functional activation and the mid-term effects were in the range of physiological fluctuations. The short-term effects were only present at the lower intensity which makes it unlikely that thermal effects were involved. The medium-term effects may be due to a decrease in oxygen consumption. Although an effect on heart rate was obtained, the controversial findings in the literature indicate that further confirmatory studies are required.

In conclusion, the present study shows that UMTS RF EMF may also affect cerebral blood circulation and oxygenation. The field intensities applied correspond to those used in handsets, while the modulation corresponds to base stations. In future studies, handset type modulation should be applied to simulate more closely the exposure by mobile phones.

Prospective cohort study on health-related quality of life and radiofrequency electromagnetic field exposure

PI: Prof. Dr. Martin Röösli, Swiss Tropical and Public Health Institute, University of Basel

There has been a substantial increase in environmental exposure to RF EMF over the last few decades leading to concerns regarding the possible health effects of technologies such as mobile and cordless phones, W-LAN or broadcast transmitters. Most concerns are related to impaired health related quality of life due to long term exposure to RF EMF in the everyday environment. Whereas acute effects of RF EMF exposure have been investigated by randomized double blind trials conducted with volunteers in laboratory settings, long term effects need to be investigated by means of observational studies. So far, such epidemiological studies were mostly of cross-sectional design, which means that exposure and health were measured at the same time. This limits the ability for causal interpretation. Moreover, due to the lack of reliable exposure assessment methods several previous measurement studies relied on self-reported exposure data or distances between place of residence and the nearest transmitter. Such an exposure assessment is inaccurate. In the meantime, portable RF EMF exposure meters ('exposimeters') allow more accurate measurements of the personal exposure and several studies have demonstrated the applicability of exposimeter measurements in population samples.

The aim of this project was to characterize the RF EMF exposure distribution of a population sample to develop and validate an exposure assessment method and to investigate the association between RF EMF exposure and symptoms of ill health by means of a cohort design. The question was whether exposure to RF EMF in daily life causes health disturbances such as headache, concentration difficulties or sleep impairments.

In the first part, personal exposure to typical sources of RF EMF was measured by means of portable exposimeters in 166 study participants during one week. Exposure to fixed site transmitters at the place of residency was modelled with a geospatial computation model which used accurate parameters from all fixed site transmitters of the study region. These data were used to predict environmental RF EMF exposure in everyday life in the frequency range of 88-2500 MHz in 1375 individuals who took part in a baseline survey. Thereof, 1122 individuals completed a follow-up investigation one year later. The feasibility and reproducibility of the geospatial propagation model and the predictive exposure assessment model have been previously demonstrated. In addition, objective data on mobile phone use was collected from the mobile phone operators' traffic records of all incoming and outgoing calls of the last six months.

As the latency time for potential health effects was not known and also no biological mechanism has been established so far, various analyses were conducted. In addition to cross-sectional analyses, a longitudinal analysis was performed to investigate whether exposure at baseline was related to a subsequent change in the health status one year later. Additionally, it was evaluated whether a change in the exposure situation between baseline and follow-up was accompanied by a corresponding change in health status.

In a nested sub-study, sleep behaviour was recorded in 120 individuals during two weeks by means of wrist worn actigraphic devices (devices measuring movement during sleep). Sleep behaviour was compared with the RF EMF exposure situation in the bedroom.

Overall, there was no indication that the current RF EMF exposure situation in Switzerland causes health disturbances. Measurements revealed an average exposure of 0.21 V/m which is far below the regulatory exposure limits. In 131 participants representing the general population, environmental far-field RF EMF exposure was mainly due to other people's mobile phones (39%), cordless phone system (24%, not including one's own phone use) and mobile phone base stations (22%). Exposure to environmental RF EMF exposure at baseline was not associated with health disturbances one year later and similarly, an increase or decrease of the personal RF EMF exposure within a year was not accompanied by a respective change of health disturbances. No association between actimeter recordings during sleep and RF EMF exposure in the sleeping room could be observed.

With respect to sources operating close to the body, the use of mobile and cordless phones was not associated with health related quality of life. Also, the study did not provide indications that individuals considering themselves as hypersensitive to EMF (electromagnetic hypersensitivity; EHS) were more susceptible to RF EMF exposure than non-EHS individuals.

By using a prospective cohort design instead of a cross-sectional design, the analyses of the association between RF EMF exposure and non-specific symptoms of ill health in this NRP 57 study allows for more robust conclusions than previous studies on this topic. A comprehensive exposure assessment method was applied by considering potential effects of both, exposure to far-field environmental sources and exposure to sources operating close to the body and by using objective exposure data for both. Nevertheless, some degree of uncertainty is unavoidable for exposure measurements and modelling. The exposure model could explain about 50% of the observed exposure variance. The unexplained variation is expected to be randomly distributed in the study collective. Random exposure misclassification would attenuate any true exposure-response associations.

It should be noted that previous cross-sectional epidemiological studies with crude exposure assessments based on self-reported exposure measures showed health effects whereas studies based on objective exposure measurements mostly did not reveal such effects. Such a pattern was also observed in this NRP 57 project.

Since the exposure levels of the population are far below the regulatory exposure limits, no conclusions regarding health effects at levels close to the exposure limits or health effects after more than one year of exposure can be drawn.

3.3 Module 3: Cell biology

Characterization of effects of non-ionising radiation on the nematode Caenorhabditis elegans as a model organism

PI: Prof. Dr. Pierre Goloubinoff, Dept. of Plant Molecular Biology, University of Lausanne

Man-made technology increasingly exposes organisms to new environmental conditions such as EMF whose biological effects are still poorly understood. The popular use of cell phones and the proliferation of dedicated antennae have generated exposure of living beings to radio-frequency electromagnetic fields (RF EMFs), raising public concern about possible damaging effects on human health and the environment. However, despite intensive research, it is yet unclear what the biological effects of RF EMFs are and whether exposure is significantly harmful, as compared to other natural environmental stresses such as heat, oxidative stress etc.

Organisms have evolved efficient molecular mechanisms to defend themselves against naturally occurring stresses from the environment. In particular, plants, bacteria and animals can accumulate a network of molecular chaperones under heat-stress that can prevent the formation of stress damages in native proteins and membranes. In biology, chaperones are proteins whose function is to assist other proteins in achieving proper folding. Many chaperones are heat shock proteins, that is, proteins expressed in response to elevated temperatures. The reason for this behaviour is that protein folding is severely affected by heat, and therefore chaperones act to counteract the potential damage. Although most proteins can fold in the absence of chaperones, a minority strictly requires them.

Mutant or aging organisms that become deficient in chaperone expression or suffer from a chronic overload of the chaperone network by protein aggregates are particularly sensitive to mild environmental stresses. RF EMFs are suspected to increase the risk for protein misfolding diseases, such as Alzheimer or Parkinson's diseases and accelerate cellular ageing in general. Accordingly, biological effects of RF EMF might be detected in organisms that are artificially defective in protein homeostasis.

The nematode *Caenorhabditis elegans (C. elegans,* a roundworm that is also used as a model system for Parkinson's disease) is the best-known model system for a non-chordate animal, as far as developmental, behavioural and genetic biology are concerned. The animal has a size of about 1 mm in length and a life- span of 2-3 weeks, its genome is completely sequenced and all the 959 somatic cells of its transparent body are visible in a microscope. It is thus simple to detect fluorescent proteins (and aggregates) that accumulate in transgenic animals when the proper reporter genes are expressed. The nematodes are easily handled and maintained in the laboratory and provide a good compromise between complexity and tractability. Moreover, C. elegans completes its life-cycle in a few days, which means that only a relatively short time is needed to apply treatments of interest over many generations.

The project aimed to detect possible biological effects of RF EMFs on a transgenic *C. elegans*, expressing tagged polyglutamine-expansion proteins (polyQ proteins) whose cellular toxicity is associated with the formation of protein aggregates in muscle cells resulting in a progressive temperature- and age-dependent paralysis. Also, a plant was used as a model system using a recombinant moss (*Physcomitrella patens)* reporter line (HSP-GUS) for mild temperature-stress. Generally, with longer polyQ repeats or higher growth temperature, the paralysis sets in earlier and is more severe. Because RF EMFs are suspected to have both thermal and non-thermal effects on organisms, the possible impact of exposure on the PolyQ35-nematode was analysed under strict temperature control. Thermal and possibly non-thermal effects of EMFs were distinguished by applying various fields either in a continuous or in an intermittent manner. After exposures, effects of temperature or RF EMF were measured using motility assays of the nematodes and b-glucuronidase (GUS) assays from moss plant extracts.

PolyQ35-nematodes showed a strong temperature-dependent motility phenotype: between 20°C and 24°C, they precisely and reproducibly developed different phenotypes in response to the growth temperature with a detectable range of 0.5°C. This high sensitivity of the Q35-*C. elegans* to mild variations of growth temperature within the physiological range was optimal for testing potential thermal and non-thermal biological effects of RF EMFs or of low frequency magnetic fields.

Whereas significant biological effects were detected following variations of ambient temperature as little as 0.5°C and increments in growth temperature as little as 0.3°C, it was found that exposure to continuous or alternate (2h-on/ 2h-off or 5-min on/ 10-min off) RF EMF regimes either at 5 or 500 V/m, had no detectable effects on the mobility/ paralysis assay of polyQ35-*C. elegans*. Even after creating an even more sensitive *C. elegans* subtype due to an additional impairment of protein homeostasis and thereby further affecting the worms' motility, no response to RF EMF was observed. Negative results were obtained also in the transgenic moss plant expressing the GUS reporter. Whereas an increment of as little as 0.5°C resulted in a significant increase of GUS expression, various EMF exposure protocols were without effect.

In summary, whereas in both animal and plant systems, minute variations of temperature showed highly significant biological effects, exposure to various RF EMF regimes showed an overall lack of detectable biological effects, both on the mobility/paralysis and ageing assays of the polyQ35-YFP nematodes and on HSP-GUS expression in moss. Therefore, based on the parameters examined in the present experiments, RF EMF does not appear to damage cellular protein homeostasis.

Effects of electromagnetic fields in vitro and in vivo: Identification and characterization of stress-response pathways

PI: Prof. Dr. Meike Mevissen, Division of Veterenary Pharmacology and Toxicology, Vetsuisse Faculty Bern, University of Berne

For the past three decades, there has been concern and controversy about the effects on human health by increased exposure to RF EMF. The precise mechanisms, if any, by which RF EMF may affect biological functions, have proven difficult to define and in many cases, results of various studies were not reproducible. Flaws in the exposure design and lack of accurate dosimetry have rendered the interpretation of data difficult. An additional problem is that exposure to RF EMF may induce a rise of temperature and therefore RF EMF effects must be discriminated from thermal effects.

In this project, state-of-the-art instrumentation was applied under controlled conditions (defined SAR) that limit thermal effects to the strict minimum (less than 0.1°C). Two different models were used to investigate possible effects of RF EMF. One of the models is the roundworm *Caenorhabditis elegans*. Despite its apparent low complexity, it exhibits a large number of functions including stress response pathways that have been evolutionarily conserved (i.e., they also exist in more complex organisms like humans). In addition, in a large number of mutant strains, many of them impaired in important biological functions such as the ability to survive heat or oxidative stresses, reporter genes [e.g. green fluorescent protein (GFP)] allow monitoring the changes of gene expression upon exposure to various stressors.

A variety of transcription factors in the insulin-like-signalling pathway regulate stress, aging and reproduction. In this project, the effects of EMF exposure on stress signalling pathways in genetically homogenous, synchronized worm populations were investigated by focusing on the key player

in all stress-signalling pathways, the DAF-16 (human ortholog FKHRL1) transcription factor. When activated, DAF-16 translocates into the cell nucleus and activates the transcription of a large number of effector genes. Therefore, worm strains with a GFP transgene were chosen that could be directly used as a reporter of DAF-16 activation upon exposure to RF EMF. The aim of the next step was the identification of key players in the EMF activation pathway.

Examination of whole worms by fluorescent microscopy was performed after exposure of a synchronized population of animals to RF EMF. No nuclear translocation was observed in animals with the wild-type (wt) genetic background. In order to enhance the potential DAF-16-mediated signal evoked by RF EMF, additional reporter strains were tested. Using the same exposure regime, an increase of GFP fluorescence was observed in another reporter strain (sod3:GFP) having the DAF-2 null mutant genetic background; the effect was not present in strains with the wt genetic background. In an attempt to identify a strain in which the effects of RF EMF would be readily observed, a transgenic strain (CF1580) was identified which appeared to show an increased fluorescence after exposure. This indicates that RF EMF may have biological effects. The strain responding to RF EMF could be used as a tool to identify key-players in the RF EMF stress response pathway.

As a second model of the research project, cell cultures of mammalian (human and rat) cells were used that could remain in their original state (undifferentiated) or adopt some characteristics of neurons during differentiation when exposed to substances such as retinoic acid or nerve growth factor. Stimulus-induced changes in alternative splicing of the enzyme acetylcholinesterase (AChE) have previously emerged as a mechanism of neuronal adaptation to a variety of stimuli including heat stress and oxidative stress. Two catalytically active AChE isoforms with distinct functions in development and repair exist in the brain. The rare, read-through isoform AChE-R is preferentially induced by injury and appears to promote repair and protect against neurodegeneration. Here, the effects of RF EMF exposure on alternatively spliced AChE isoforms using PC12 cells *in vitro* were explored. PC12 cells derived from pheochromocytoma of rat adrenal medulla are a useful model system for cell differentiation. Furthermore, PC 12 cells served to investigate effects of RF EMF on the stress response while the human neuroblastoma cell line SH-SY5Y was used to study effects on apoptosis, which is the process of programmed cell death. To analyse the stress response, the time course of the changes in heat shock protein 25/27 (HSP25/27) regulation was investigated. For monitoring apoptosis, the regulation of two apoptosis-related proteins (BAX and BcL-2) was analysed. These proteins appear to have opposing functions with regard to their effects on the apoptotic sensitivity of a cell. In the experimental conditions used, exposure to RF EMF did not alter the expression level or the intracellular localization of the stress-associated AChE-R isoform in undifferentiated and differentiated PC12 cells. No alteration of the expression of the 'synaptic' AChE-S isoform was observed under similar conditions. However, an increased number of the SC35 splicing factor nuclear speckles were revealed in undifferentiated PC12 cells after 16 hours of RF EMF exposure. This effect was temperature independent as the temperature difference between the exposed and sham chambers never exceeded 0.03°C.

During RF EMF exposure of PC12 cells, the time course of changes in the steady state level of HSP25 and P-HSP25 differed in untreated and NGF-treated cells. After basic exposure to GSM, a decreased level of HSP25 at the earlier time points (1h and 4h in differentiated cells; 1h-12h in undifferentiated cells) was observed. In parallel, a decrease in P-HSP25 levels was noticed at different time points (1h-8h in differentiated cells; 4h-48h in undifferentiated cells). In contrast, after 12h and 24h EMF exposures, the P-HSP25 increased again only in differentiated cells.

The project leader concludes from the results that (1) RF EMF may be a genuine stressor as it is able to modify the quantities of some proteins that are known to play a role in stress responses; and (2) that RF EMF also appears to trigger proteins in the apoptosis pathway, a cellular pathway that is known to be involved in anti-cancer defences.

Genotoxic effects of non-ionizing radiation

PI: Prof. Dr. Primo Schär, Institute of Biochemistry and Genetics, Department of Clinical and Biological Research, University of Basel

A question of particular interest and importance is whether EMF exposure affects the integrity of the genetic material and thereby has a potential to cause adverse health effects associated with genetic instability, such as cancer or premature ageing.

DNA is a nucleic acid that contains the genetic instructions used in the development and functioning of all known living organisms. Despite considerable research efforts in the past, solid and undisputed evidence for the existence of EMF induced DNA toxicity (genotoxicity) has not been presented. A major difficulty of the research in this area has been the borderline nature of the EMF dependent DNA-directed effects, the measurement of which demands a high standard of experimental design, i.e. the use of well-defined experimental systems that allow an unambiguous readout of the EMF effect and a clear separation of the effect from the noise background.

Controversial experimental results from a number of genotoxicity studies, some of which were carried out in the context of the European REFLEX program, suggested that exposure of certain human cells to high and low frequency EMF causes strand-breaks in the genomic DNA. This led the WHO to rate the problem of genomic instability as a "High Priority Research Need" in its 2006 research agenda for RF EMF. Positive effects were mainly observed in the Comet assay but much of the scientific discussion then circled around the question whether or not these effects exist and little effort was devoted towards understanding what they actually mean and how they should be interpreted. The Comet assay is a sensitive technique for the detection of DNA damage at the level of the single cell. When DNA in a cell is damaged, its structural organization within the nucleus is disrupted in a way that its migration properties in electrophoretic separation are changed. The Comet assay measures these changes, allowing a quantitative assessment of the amount of DNA damage in the cell.

The project aimed to replicate previous key experiments which indicated the existence of genotoxic effects of EMF exposure in the Comet assay and to investigate underlying molecular causes and biological consequences. The specific aims were: a) the molecular characterization of the DNA-related effects of EMF exposure, b) the characterization of the cellular response to EMF-induced DNA-directed effects and c) an assessment of biological consequences of EMF-induced genotoxic effects.

An important initial effort was the confirmation of the DNA-directed effects in the Comet assay as observed previously in human cells exposed to ELF MF and RF EMF. The effects could be reproduced in the Comet assay for human primary fibroblasts exposed to ELF MF, and partly also for cells exposed to RF EMF. Specifically, it was found that intermittent, but not continuous exposure of human primary fibroblasts to a 50 Hz sinus MF at 1 mT induces a slight but significant increase of DNA strand breaks when measured in the Comet assay. Novel insights were obtained with respect to the origin and nature of this effect. It was shown that the small effects in the Comet assay resulted from minor disturbances of DNA-synthesis and occasional triggering of cellular apoptosis rather than the generation of DNA damage. In contrast to a previous publication regarding RF EMF, no genotoxic effect with ES-1 human fibroblasts was observed but HR-1d fibroblasts showed a small and significant tail factor increase on the Comet assay following exposure to a talk-modulated field at a SAR value of 1 W/kg RF EMF (1950 MHz, 1-2 W/kg SAR).

Another important part of the project dealt with the development of tools allowing a direct assessment of potential impacts of ELF MF on the DNA itself, on DNA-protein/enzyme interactions, or on DNA-relevant aspects of cell physiology. This involved the establishment of biochemical assays as well as procedures for live-imaging of cells under ELF MF exposure, both of which was successful in yielding a novel and powerful technology for EMF research. These methods were used to clarify whether ELF MFs have the potential to induce physical DNA damage or to alter formation or levels of reactive oxygen species (ROS) production in cells. The biochemical experiments with purified DNA in solution showed that ELF MF exposure does not generate DNA damage above a threshold detectable by the Comet assay, as validated by ionizing radiation controls at doses yielding Comet effects comparable to those of intermittent ELF EMF exposure. Similarly, highly sensitive live-cell methods for ROS measurement revealed that ELF EMF exposure does not affect intracellular ROS levels to an extent that could damage DNA sufficiently to cause effects in the Comet assay. In this case, the sensitivity of the assay was validated with H_2O_2 treatment controls.

Together, these results strongly suggest that the apparent genotoxic effects observed in the Comets assay following intermittent ELF MF exposure of human fibroblasts are most likely accounted for by a secondary cellular response to the field rather than by ELF MF induced direct or ROS-mediated generation of DNA-damage.

ELF MF exposure of human cells can consistently and reproducibly generate Comet tailfactor / tail-moment changes in certain cell types (primary human fibroblasts) under specific culture conditions

(proliferating cells). These are minor and most likely reflect cellular responses associated with a small accumulation of naturally occurring DNA strand breaks (cell cycle, DNA replication, apoptosis). It must be noted that a critical discussion of the broader implications of the results obtained on the basis of existing publications is difficult due to the heterogeneity of experimental setups, biological models and study designs used. However, the emerging concept that cellular responses rather than an induction of DNA damage explain the effects of MF exposure in the Comet assay is consistent with the atypical genotoxic properties observed across all studies; i.e. the dependency of the effect on intermittent exposure and cell-type, the complex dose - effect relationship observed, and latent and transient occurrence of the effect.

3.4 Module 4: Risk perception

Structure and effects of societal communication on non-ionising radiation
PI: Prof. Dr. Peter J. Schulz, Health Care Communication Laboratory, Facoltà di Scienze della Communicazione, Università della Svizzera Italiana, Lugano

Central to the idea of a health literate consumer is the ability to understand health information and to use that information effectively in making judgments and choices about health behaviour. Concerning NIR, difficulties in determining effective communication strategies arise from the nature of the hazard: as the true risk of NIR is not yet known, it is a challenge to inform the general public in an appropriate and comprehensive way. Consequences of NIR for human health and well-being are an issue that medical science and biology have to answer. Reviewing the present state of research, NIR does not appear to pose a high and immediate risk of damage to people's health, though detrimental effects on people's health and well-being cannot be ruled out completely. Accordingly, informing the public about potential risks is necessary.

In the last two decades, societal concern about the possibly detrimental effects of NIR has increased, resulting in a growing and sometimes alarmist attention that various communication media pay to the subject. This means that any attempt at communicating the risk of NIR to the general population now occurs in a rather complex situation.

The overall research project aimed to understand the underlying perceptual and motivational forces that give rise to this problem and to develop strategies for healthcare professionals and other information providers enabling them to deliver information on NIR more effectively. In this context, the focus was on the perception of risk associated with NIR emitted by cell phones, cell phone towers and similar sources among German-speaking and Italian-speaking Swiss residents.

The first subproject investigated the structure and development of communicative behaviour with regard to NIR. For this purpose, a content analysis of an activists' web forum and a content analysis of the mass media coverage in Switzerland were conducted with the aim to provide a first basis for effective communication strategies to inform the population of different language regions about NIR. Content analysis is a method that defines and then counts content elements of interest in large bodies of texts.

The second subproject examined people's reactions to a press release which denies the likelihood of health effects of radiation from mobile phone masts. Specifically, risk perception of NIR and the evaluation of the text were assessed for four different kinds of information sources. This was achieved by presenting to 240 customers/ visitors of supermarkets in Ticino an identical message in form of a news report but indicating different sources of different credibility.

In the third subproject a survey was conducted simultaneously in Lugano (TI) and Winterthur (ZH) to determine whether the language region has an influence on risk perception, behaviour and knowledge in the field of NIR. Along with the questionnaire, an experiment was conducted to test how the recommendation of a precautionary measure against the effects of NIR contained in an information brochure affects risk perception and whether the wording of the measure can alter the effect. 640 customers/ visitors of supermarkets in Ticino and the German-speaking part of the country participated in the sub-study. This was repeated with 400 persons in sub-project 4, testing only the neutral precautionary message but including the full measurement of psychological constructs related with risk perception (these constructs were only rudimentarily contained in subproject 3).

The structure of internet forums allows for a great variety of contributors. However, levels of information and civic engagement are not distributed equally among the population, and they are not equally distributed among people concerned about effects of radiation, either. Data analysis confirmed a cluster of a few very prolific contributors in the web forum, while the majority of users contributed far less intensely. Data on mass media revealed that newspaper articles were generally written on the occasion of typical events such as construction of cell phone towers, closely followed by political initiatives. The structure of newspaper coverage amounted to a misappropriation of media attention to cell phone towers and other facilities and a relative neglect of the risks of appliances such as the phones themselves, widely considered to be the more important source. Interestingly, the trend of increasing newspaper attention to the issue of NIR was entirely limited to German-language newspapers, while for three Italian-language newspapers analysed attention was rather decreasing, albeit from a high level.

Further results indicated that in terms of NIR risk perception, the pre-existing attitude towards possible NIR health effects rather than the source of information and its credibility are the determining factors in forming an opinion. Interestingly, respondents who associated NIR with a high risk before the experiment became more worried after reading the risk-assuaging message. This effect was independent of the source of information. Whereas in general Swiss-Italians were clearly more concerned about the risks posed by NIR, precautionary messages did not lead to more concern among the German- or Italian-speaking study sample.

The comparison of three different precautionary messages, a neutral one, an authoritative one and an empowering one, showed that while they did not differ in terms of effects, the empowering message was liked best. Results on the role of the psychological constructs in risk perception are forthcoming and will help to provide insights into cultural worldviews (measured with 12 items), desire for control (measured with 20 items), health locus of control (measured with 18 items), and intolerance of uncertainty (measured with 22 items).

Previous studies indicated that predisposition affects communication outcomes. The finding that persons who perceive a high risk from NIR understand a message intended to assuage fears as increasing their worries still further, irrespective of the information source of the message, relates to this but adds a new perspective. This perspective implies that worried individuals may not only not be reached by messages intended to reduce their worries, but may in fact turn these messages into their opposite. It suggests that persons highly worried about health effects of NIR misunderstand or misprocess messages that intend to tell them there is little reason to worry. This effect was independent of source and might pose a severe problem for the planning of communication.

Affect and perception of non-ionizing radiation: Implications for risk communication

PI: Prof. Dr. Michael Siegrist, Consumer Behavior, Institute for Environmental Decisions (IED), Swiss Federal Institute of Technology (ETH) Zurich

Little is known about the effects of long-term exposure to the radiation of mobile phones and mobile phone base stations and whether such exposure may induce adverse health effects. As a result and due to the overall rapid growth of this technology, this leads to a widespread increase in public concern.

A vast amount of research suggests that experts and lay people differ in their risk perception. Whereas experts' risk estimates are often correlated with statistical data, qualitative aspects determine perceived risks for lay people. The psychometric paradigm is probably the most popular research approach used to identify factors that influence the perception of various hazards. In this approach, participants use a variety of rating scales to evaluate a set of hazards. For example, participants may evaluate each hazard for severity of consequences (how likely is it that the consequences will be fatal). Most of these studies present a very heterogeneous set of hazards, ranging from alcoholic beverages to nuclear power. This research approach can be used to answer the question of why various hazards are perceived differently. However, the psychometric paradigm neglected differences in lay people's risk perception, thus leading to a variety of criticisms. An explanation why different people perceive the same technology differently is an important question which has not been satisfactorily answered yet. Recently it has been suggested that affect may be an important factor in risk perception. In most studies the role of affect has been neglected. However, affect might play an important

role in the evolution of attitudes and opinions about NIR and more knowledge is needed about how different risk communication strategies may influence the affect associated with NIR.

Affect is an important determinant of perception and behaviour. Affect has been described as "the specific quality of ‚goodness' or ‚badness' (1) experienced as a feeling state (with or without consciousness) (2) demarcating a positive or negative quality of a stimulus. Affective responses occur rapidly and automatically." (Slovic et al. 2002).

The implicit association test (IAT) can be used to assess affect evoked by a technology. It measures implicit attitudes by assessing the response latencies of automatic evaluations and thus overcomes the problems associated with directly asking people about their attitudes toward an object. It must be noted that the IAT is the most utilized, but not the only technique for measuring implicit attitudes. For example, affect has also been measured by means of imagery techniques in which for example respondents are asked to rate each association on a scale ranging from bad to good. Mean values of these ratings can be viewed as affect evoked by a certain hazard which is correlated with perceived risks. The advantage of the association task, however, is that it provides more specific information than a numerical value indicating positive or negative affect. Associations can be classified in categories, and this procedure provides information about which images are most often associated with a certain hazard.

The research project aimed to investigate which factors determine perceived risks and benefits of mobile communication, and also the acceptance of this technology. Specifically, it focused on the role of affect in risk perception since it is accepted that affect can serve as an important shortcut within decision making. In a first step a valid and reliable Single Category Implicit Association Test (SC-IAT) instrument was developed. Data analysis was based on altogether 61 participants consisting of EMF-experts, mobile phone base stations opponents and people from the general population. The groups were matched according to age, gender, and education.

In the second subproject, affect was measured using a free association technique, which indicated what kind of images come to people's mind when they think of mobile phone base station. A survey was carried out in 503 people in the urban area of Zurich, followed by a face-to-face interview at the participant's home.

In the third subproject it was investigated how fear and anger determine risk and benefit perceptions and the acceptance of a technology. The same sample of 503 participants, drawn from the face-to-face interview in their homes, was asked to fill in a paper-and-pencil questionnaire which contained a wide range of items on the issue of mobile communication. Twenty-eight variables were used for measuring control, fairness, anger, fear, acceptance and risk and benefit perception.

The fourth subproject concentrated on public preferences for different base station sites focusing on the four key attributes that previously turned out to be crucial for base station siting decisions (i.e. location, appearance, building, decision process) and the impact of specific information provision on base station siting preferences.

The fifth subproject explored the effects of specific knowledge in the field of mobile communication and in regard to base station siting decisions. Public education or specific knowledge enhancement are considered as possibilities to enforce laypeople's ability making informed decisions. Accordingly, it was hypothesized that specific knowledge enhancement would decrease the negative perception of base stations and increase the critical perception of mobile phones and lead to better base station siting choices that account for less radiation for the phoning population.

Overall, results of a SC-IAT indicate that affective evaluations of different risks are carried out very rapidly. In addition, it was found that base stations evoked positive implicit associations in a group of experts on mobile communication, neutral associations in a lay people group, but negative associations in a group of base station opponents. This indicates that experts, lay people, and base station opponents show different affective responses in perceiving the risks associated with mobile communication.

Respondents from a large-scale Swiss sample mentioned predominantly negative images connected to mobile phone base-stations. Noteworthy, respondents who attached high risks to base stations expressed different images than respondents who ascribed only low risk to base stations. Also, it was

found that anger strongly determined the benefit perception and the acceptance of mobile phone base stations; fear, in contrast, strongly influenced risk perception of base stations. In comparison to other attributes, the location of the base station is of capital importance for citizens. Preferences for base station sites were also related to health beliefs, trust, and demographic variables. Eventually, the project demonstrated that participants who were provided with technical knowledge expressed more favourable base station siting preferences, i.e. those that would cause less exposure for the phoning population.

In sum, implications for research and practice can be derived from the results obtained within this line of research. It was shown that affect is central in the perception of non-ionising risks and differs remarkably between experts, opponents, and laypeople. Moreover, it was found that risk perception differs due to important demographic variables and that knowledge influences base station siting decisions. Also, evidence was provided that citizens prefer distant and covered base station sites.

Taken together these results imply that mere affect serves as fast, frugal, and first evaluation of mobile communication and other risks. This first evaluation tells us whether the stimulus is good or bad for us, or in other words, if it is personally relevant. It has been previously suggested that affect may play an important role in risk perception. Specifically, it was argued that people make use of the "affect heuristic" when assessing risks because it is easier and more efficient to rely on spontaneous affective reactions than to analyse all available information. The theoretical framework of the 'affect heuristic' distinguishes two modes of thinking, the experiential system and the analytical system. Whereas the analytical system relies on probabilities, logical reasoning and evidence, the experiential system relies on images, metaphors and narratives. It seems plausible that lay people may use the experiential system and not the analytic system when they are asked to evaluate a set of hazards.

Results obtained indicated that age and gender are important demographic variables that influence perception of mobile communication. Younger respondents attributed fewer risks to mobile phone base stations than older respondents. Presumably, younger participants are also more familiar with mobile communication and familiarity has been previously identified as an important factor that diminishes people's worries about risk. Moreover, participants that preferred a base station location in the middle of the village (i.e., a more advantageous site in regard to precautionary health protection) were predominantly male. These participants also perceived less risks and higher benefits from mobile communication. Interestingly, this was also characterized by more knowledge concerning the interaction patterns of mobile phones and base stations.

4. Scientific implications and future needs

4.1 Module 1: Dosimetry and exposure assessment

Exposure of the foetus

The goal of this project was to characterize the exposure of the foetus with respect to the field conditions for different types of electromagnetic exposure, in particular of the ratio of the values of the basic restrictions of the female versus the foetus. For this purpose, three highly detailed anatomical computer models of a woman in the 3rd, the 7th and the 9th gestational month were developed. Such high-resolution anatomical model for the foetus did not exist previously.

The creation of the foetus models is an important achievement in the field of dosimetry. For the first time it is possible to evaluate induced currents and the SAR in the mother and the foetus in everyday exposure situations in uncontrolled environments. These results are important for health risk evaluations and epidemiologic research. The results also give valuable input for setting guidelines and exposure limits, as it is now possible to predict the exposure in different tissue types. When the former ICNIRP guidelines were produced in the 1990-ies the relation between the external fields (reference values) and the induced currents and SAR-values (basic restrictions) could only be calculated for simple geometric homogenous models (prolate spheroids). A prediction of exposure of different organs in humans was not possible at that time.

This changed when the first Visible Human Male data set was released in November 1994 (U.S. National Library of Medicine). Later, further data sets for different body types have been developed. The IT'IS Foundation has played an important role in developing human models (virtual family and virtual class room) and making them available for research. Input data to the models is generally obtained from Magnetic Resonance Imaging (MRI) images. As pregnancy is a contraindication for MRI, however, there is a lack of MRI data for foetuses. Accordingly, different sets of medical images had to be combined to develop anatomical models of the foetuses.

Future research on the exposure of the foetus will focus on a) a generic approach to identify the main parameters that determine the exposure and b) on the enhancement of the flexibility of the developed anatomical models in order to strengthen the interpretation of the results with respect to their applicability to the general population of pregnant women. Moreover, the development of enhanced numerical methods will be considered in order to overcome the restrictions of the current techniques with respect to anisotropy and the representation of the relevant electrical characteristics of the peripheral nerves. Additional experimental research should focus on the improved evaluation of the dielectric tissue properties in the low frequency range. Large uncertainties still exist, in particular with respect to a complete characterization of the anisotropy, and little work has so far been done regarding the age dependence of the tissue conductivity for low frequencies.

Cumulative exposure in time and frequency domains of the central nervous system

The focus of this project was to accumulate a comprehensive amount of knowledge about exposure from all existing wireless communication systems and relate this to brain internal structures. Several operational conditions, like travelling in a car, and types of phones, mobile and cordless, were considered for a frequency range from 30 MHz to 6 GHz. The resulting exposures in SAR values in specific regions of the brain for various types of persons (the virtual family) also included variations due to the hand and the way of holding a mobile phone. Similar results have been partly reported in the scientific literature, however, not in such a comprehensive and detailed form.

Some of the results are of direct relevance for other scientific communities, like for example the epidemiological community, where exposure in normal living and working indoor conditions, including multiple incidences of the fields, are of particular importance. Another useful scientific implication refers to provocation studies on brain physiology, such as human sleep studies, where they are of help in generating hypotheses about the mechanism of action.

Although a dose concept is not yet available for NIR, it is customary to find the cumulative effect of many different exposures by integration. The tools and results developed in this project make it possible to calculate such integrated doses over time of usage and over types of exposure. The future

needs will be to keep the information updated when new exposure types come into common usage. The future 4th generation of mobile communication systems, Long Term Evolution (LTE) is already operational in various countries and it has a different signal structure and access techniques compared to previous generations. It is also worthwhile mentioning that usage of modern smart phones and other similar devices will have a different position near the body, removed from the brain.

The present studies were limited to frequencies below 6 GHz. It can be foreseen that in the future, much higher frequencies like millimetre wave frequencies such as 60 GHz will be used in order to accommodate high data rates.

Live cell imaging during MF exposure

The scientific literature shows that a considerable variety of exposure setups have been used in the past to investigate the biological effects of the exposure of cell cultures to ELF magnetic fields. Common to most of these systems is that the cells are exposed to particular field conditions, for defined time periods and the analysis is performed post exposure. These experiments have shown various biological end points ranging from no effect to increased DNA strand breaks.

However, the exact mechanism of interaction where effects have been seen is unknown. This project was in particular triggered by the need to further investigate the mechanism behind the observed increase in DNA strand breaks. Therefore, a miniature ELF exposure system that is integrated with a microscope system, thus enabling live cell imaging and other state of the art microscopic techniques including confocal scanning and fluorescence microscopy during the ELF exposure, was developed. The project was of high impact as the system has been successfully applied in the NRP 57 project of Prof. Dr. Primo Schär in Basel at the Department of Biomedicine.

With the development of more and more sophisticated exposure systems allowing state of the art real-time imaging of cells during exposure, the opportunity for significant breakthroughs in the understanding of the interaction mechanisms of electromagnetic fields with cells has been considerably enhanced. The ELF magnetic field exposure system has opened the way for the development of further sophisticated exposure systems designed for investigation of electric fields and the interaction of modulated and continuous wave RF EMF with cell cultures. Overall, it is expected that the developed exposure system will play a role in any future studies investigating the mechanism of EMF exposure.

4.2 Module 2: Laboratory studies and epidemiology

EMF effects on the brain: Changes of the sleep EEG

This project confirms and extends previous research which had shown that pulse-modulated RF EMF emitted by mobile phones affects the human EEG. In particular, following the 14 Hz modulated exposure, the authors observed a significant average increase of power in the spindle frequency range during sleep, which was most prominent in stage 2 sleep of the second sleep cycle. However, the effect varied greatly from subject to subject. Sleep architecture remained unaffected. The observations that pulse-modulated, but not continuous-wave RF EMF affect the waking and sleep EEG rules out a thermal action. The observed increase in the spindle frequency range indicates that the modulation with frequency components in the physiological range may be sufficient to generate an effect. Given the higher absorption of energy in the heads of children and adolescents compared to adults, the preliminary data indicating an absence of age group related differences with respect to RF EMF effects on the waking EEG were unexpected.

With regard to the mechanisms involved, it is interesting that the effect was present in both hemispheres despite exposure of one hemisphere only; this finding corroborates the authors' hypothesis that a central brain structure such as the thalamus may be critically involved in mediating the effect. On the other hand, the effect did not depend on the penetration depth of the radiation (restriction to cortex *versus* inclusion of subcortical structures) indicating that direct exposure of the basal ganglia / thalamus may not be the crucial factor.

Analysis of cognition showed that overall reaction speed tended to be lower during exposure than during sham condition, and slowest reaction speeds were found in the 217 Hz pulse-modulated condition. However, accuracy of performance in the cognitive tasks seemed largely unaffected.

Importantly, the fact that the participants were unable to identify the exposure conditions shows that the field could not be perceived.

In summary, the results of this project are scientifically relevant and need to be continued by follow-up experiments. Obviously, the mechanisms of the observed effects must be investigated in more detail. In view of the variability of the effect, the question of reproducibility over time within individuals should be addressed as a next step. Furthermore, the question of long term effects of human exposure seems important. As most of the research has focused on healthy young subjects or children, elderly or other potentially sensitive participants and possibly even patients with neurological or psychiatric disorders should be studied. As a future perspective, novel applications of RF EMF, for example for investigations on brain mechanisms or diagnostic or even therapeutic purposes are conceivable.

EMF effects on the brain: Changes in cerebral blood circulation

Near infra-red imaging (NIRI) was used to measure local cerebral blood circulation and oxygenation. This optical method using infrared light is not directly influenced by electromagnetic fields. A limitation of NIRI is that measurements are restricted to superficial cortical regions and deeper structures such as basal ganglia or brainstem are beyond reach.

Using intermittent UMTS EMF at exposure levels typical for a handheld mobile phone but with base station type modulation, small but statistically significant effects on blood circulation and oxygenation were detected: 1st A medium-term (from 80 s to 30 min) decrease of deoxy-haemoglobin concentration in response to 0.18 W/kg and 1.8 W/kg exposures in the range of physiological fluctuations of the brain was found; 2nd a short term (< 80 s) change that was six times smaller than the medium-term effect was detected which consisted in an increase in oxy- and total haemoglobin concentration during exposure to 0.18 W/kg. Also, the medium term heart rate was slightly higher following the high dose exposure as compared to the sham exposure, while other parameters (subjective well-being, tiredness, counting performance) remained unaffected.

It is important to realize that under real-life conditions, the exposure to base station like modulation of UMTS is much inferior to the one applied in the present study. From a scientific point of view it is important to investigate whether the present results can be confirmed and whether other study populations (e.g. elderly subjects, younger subjects, females, and persons with self-reported EMF sensitivity) show similar effects. Furthermore, not only intermittent exposure but also continuous exposure to UMTS, and exposure to EMF with different carrier frequencies, such as used in WIFI, Bluetooth, or DECT, should be examined. The aim of all studies should be to gain insight into the underlying mechanisms.

Prospective Cohort Study on Health-Related Quality of Life and RF EMF

Short term health effects of exposure to RF fields have been studied previously in adequately designed randomized trials, or provocation studies, and have generally been unable to show any association between RF exposure and ill health. Such designs cannot easily be applied to the study of long-term effects, which instead have been addressed in cross-sectional studies measuring exposure and outcome at the same point in time. However, this approach has severe implicit limitations. The present study utilized a much superior prospective design in which exposure to RF was measured at base line and outcome was measured as change in health status between base line and health status one year later. This study also took advantage of the development of an exposimeter that could be worn by study subjects. The exposimeter was used to validate a model for assessment of RF exposure from base stations that also was developed as part of this project.

Analysis of the follow up data did not display any association between exposure to RF EMF and ill health, with ill health being measured with scales including headache, sleep disturbances, and other quality of life variables. Thus, the results are consistent with the ones for short-term exposure obtained in provocation studies. However, the current results are at odds with some results from cross-sectional studies, but the cross-sectional design is prone to recall bias that may generate positive associations. The results from the prospective design are therefore important on theoretical grounds, though they also may be prone to bias, particularly selection bias.

The exposimeter data also facilitated a long needed systematic survey of the relative importance of different sources to RF exposure. In the current study exposure to far fields was dominated by three sources, namely others phones, base stations, and cordless (DECT) phone systems (not including one's own phone use). . The average exposure levels are very low compared to the current exposure standards.

In summary, this study used an important novel approach to study the health related quality of life and RF exposure. No association between estimated RF exposure and health symptoms was found. Yet, one must keep in mind that the exposure levels were those experienced by the general population, which are orders of magnitude below current exposure limits, and that the results therefore say little about possible health effects at higher levels of RF exposure. The information about sources of RF exposure in the general population is most welcome, but needs of course a follow up on more populations and in bigger samples.

4.3 Module 3: Cell biology

The most important function of in vitro laboratory studies is to provide information about possible biophysical and biochemical mechanisms that might be responsible for the effects observed in epidemiological and human volunteer studies. In vitro results may offer a mechanism based framework for assessing the human studies.

When planning the scope of the NRP 57 research program it has been decided to address some selected issues concerning exposure to ELF MF and RF EMF. In selecting the most relevant study topics the recommendations included in the WHO Research Agenda for ELF EMF (2007) and the WHO Research Agenda for RF EMF (2006) were considered. The projects focused on the effects of ELF MF (emitted by electric power transmission lines, household electric wiring, and household electric appliances) on the integrity of cellular DNA (genotoxic effects), and of RF EMF (radiation emitted by mobile phones and mobile phone base stations) on cellular stress responses, cellular signalling pathways and programmed cell death.

ELF MF effects on DNA

Based solely on epidemiological evidence, ELF MF has been classified by IARC as a possible human carcinogen (category 2B carcinogen). However, animal studies and in vitro laboratory studies did not provide supportive evidence for such a classification. Especially, the biophysical and biochemical mechanisms that could be responsible for the effects observed in epidemiological studies are unknown One of the most controversial issues is whether exposure to low-energy EMF (ELF MF and RF EMF) is genotoxic (i.e. damages the DNA). The findings of Schär and co-workers suggest that ELF MF does not damage DNA directly or indirectly, but that it has an inhibitory effect on the DNA repair pathway This, in turn, could cause an accumulation of unrepaired DNA that may appear as an increase of the amount of damaged DNA. The apparently damaged DNA can occur in cells either spontaneously (as a part of normal physiological processes) or as a consequence of DNA damaging agents (chemical or physical). Schär and co-workers speculate that the accumulation of spontaneously occurring DNA damage in cells may not be very risky for cells as such damage is likely to be easily repaired, even though the repair may be delayed by ELF MF exposure. However, a similar ELF EMF induced delay of damage repair may have more serious consequences if the damage is caused by chemical or physical agents.

The findings need to be confirmed by other groups. It will be also necessary to determine the impact of the accumulation of damaged DNA on cellular processes and on the transformation of a cell into a tumour cell.

RF EMF effects on C. elegans

C. elegans has been introduced by de Pomerai's research group (Daniells et al. 1998) as a biological model to study effects of RF EMF. Initially, the results indicated that RF EMF exerts non-thermal effects on the stress response pathway. However, further studies by the same group showed that the results were probably caused by imprecise dosimetry of the exposure chamber (Dawe et al. 2006). The paper by de Pomerai et al. (2000) published in Nature was subsequently retracted (Retraction in: Nature. 2006, 440, 437). Finally, further studies exhibiting a lack of response to exposure strengthened the view that C. elegans model is not responsive to RF EMF (Dawe et al. 2008; 2009).

The groups of Goloubinoff and Mevissen used two different mutant strains of C. elegans to explore their responsiveness to RF EMF. No clear effect to exposure to non-thermal RF EMF was revealed (the increase in GFP fluorescence in one transgenic strain is too preliminary to be regarded as a clear positive effect). Thus, their results are in accordance with the previous studies mentioned. Taken together, C. elegans does not show any EMF-induced changes.

The observation by Mevissen that RF EMF may modify some proteins in cultured cells is interesting but still too preliminary for interpretation. Further data are needed.

4.4 Module 4: Risk perception

General considerations

Providing appropriate information about the risks and benefits of mobile communication to the public is not trivial. The aim of proper information brokering is to convey the current state of knowledge in an objective and educational manner. It is equally important that laypersons should be informed in such a way that they understand and trust the information. In general, risks are rated higher by laypersons than by experts if the following points pertain: a) the hazards are unknown; b) the technologies are not familiar; c) there is a lack of influence or control over exposure; d) the risks are not offset by benefits, and those who are exposed are not those who benefit (unfairness); and e) potential serious consequences cannot be excluded (e.g. long-term effects, health impairment of future generations). All these points apply to mobile communication and therefore pose a real challenge to risk communication. To inform the public in a comprehensive way, peoples' concerns and attitudes must be taken into account as behaviour depends not only on facts or reality, but also on what people believe to be reality. In a recent project focusing on the development of optimal strategies for health care professionals and other information providers it was concluded that "At its best, risk communication is not a top-down form of communication from experts to the lay public, but rather a constructive dialogue between all those involved in a particular debate" (Lofstedt, 2010).

It is important to realize how differently risks of NIR are perceived. Opponents of mobile communication technologies argue that in the case of smoking or asbestos, hazards which eventually emerged as serious threats to health have been neglected for too long by experts. In their view, also the risks of NIR are underestimated and they sometimes claim that government and industry suppress information indicating health risks. In contrast, advocates of mobile communication emphasize its huge benefits to society and argue that testing the technologies before they reach the market would counteract technological progress. Moreover, they point out that so far there is no hard evidence for serious health risks within the SAR range accepted by the authorities.

In a study of Siegrist and coworkers (2005) concern about EMF was associated with the opinion that most chemical substances cause cancer. It appears that for some persons technology is per se associated with harm. The authors argue that for some people a scientific explanation is not a valid discourse, and does not influence their risk perception. People's belief in inexplicable phenomena therefore poses a particular challenge for risk communication.

Mass media are key players in communicating information on risks. The way of reporting may lead to the amplification or attenuation of risk perception. One way to assess the situation in Switzerland is through content analysis of the media. A similar approach has been recently taken in Germany (Elvers et al., 2009). The present study by Schulz showed that in an activist web forum and in newspapers major attention is devoted to base stations and that the establishment of a new base station is a common occasion for newspaper articles. Mobile appliances received six times less coverage than base stations. This contrasts with a questionnaire study in Denmark where the concern about mobile phone radiation, base station radiation and pollution was assessed (Kristiansen et al. 2009). While the highest number of respondents was concerned about pollution (82%), concern about mobile phone radiation (28%) exceeded that about base station radiation (15%). In other studies concern about base station is higher than concern about mobile phones (see Cousin and Siegrist, 2010). Overall, it appears that media coverage is not a reliable indicator of the concerns within a population.

The analysis of newspaper articles allows assessing the perception of health issues. A major finding by Schulz was that mild negative health consequences such as headache or sleep disturbance are often depicted as an established fact whereas this is less the case for serious ailments such as cancer.

The general negative evaluation of health effects showed no differences between source groups (e.g. business interest, politics, science, regular citizens). Also, the German newspapers related the topic "mobile phones and health" to risk and danger, but did not specify the relationship (Elvers et al., 2009).

There is evidence for micro-cultural differences between German-Swiss and Italian-Swiss. However, the results are inconsistent and further research is needed.

Affect is central to assessment of EMF risk

One of the main thrusts in module 4 was the investigation of the role of affect in risk assessment as this aspect has been neglected in most previous studies. The information provided by authorities is mainly based on the cognitive abilities of the recipients, with the implicit assumption that attitude will change with the accumulation of knowledge. However, attitudes include also affective and behavioural components, and affective judgments may be independent of behavioural judgments (Siegrist et al., 2005). Two systems can be discriminated in risk assessment: the 'experiential system' relying on images, metaphors and narratives, and the 'analytical system' relying on probabilities, logical reasoning and evidence. In the evaluation of hazards, laypersons tend to use the experiential system. It serves as a fast, first evaluation for deciding whether a stimulus is good or bad. According to Siegrist, images in people's mind are tagged with affect; an individual's "affect pool" contains the positive and negative markers associated consciously or unconsciously with the images. In the case of mobile communication, the hazard is highly stigmatized due to the fact that radiation is referred to as "electrosmog". Therefore, the negative attribute of air pollution is attributed to radiation without any evidence that it constitutes a genuine health hazard.

The importance of trust in risk communication

The present study by Siegrist clearly demonstrated that the affective relations to mobile communication are strongly related to trust. In the SC-IAT (single category – implicit association test) a high correlation of the response to base stations and trust was found. Trust is particularly important when people lack the knowledge about a hazard. Clearly more research is needed to analyse the exact relationship between trust and affect.

The importance of trust in effective risk communication was also impressively demonstrated in a recent Danish study (Nielsen et al., 2010). The study showed that risk communication can be only effective if people believe the person who is imparting the information. Trust between the informant and the recipient of information is a premise for effective communication. Moreover, not only the messenger but also the message must be trustworthy.

The present study by Siegrist confirmed that trust differed among different actors: research institutions and government authorities were considered more trustworthy and competent than activists and industry. The analysis also revealed that risk perception prior to the experiment has a pervasive effect as people with different levels of worry differed in the trust they put in different actors. Research institutions were trusted by the worried and unworried, while industry was trusted by neither of the two. The worried placed high trust in activists and a message intending to decrease worries had the opposite effect in the worried group. Thus, self-reported change in worries was highly dependent on pre-experimental worries. This finding needs to be confirmed by further studies as it was an unexpected finding. That a list of precautionary actions may change the attitude towards base stations in both directions was one of the salient results in a recent study (Nielsen et al., 2010). Other authors had reported that precautionary information increases concern (Wiedemann and Schütz, 2005).

Attitude towards base stations

Base stations contain elements of typical risk scenarios: a) the exposure to radiation is involuntary and without a sense of personal control; b) the health consequences of exposure are unknown but experts have different opinions on this point; c) laypersons know little about technological aspects of radiation emanating from base stations.

Based on the SC-IAT it was shown that the affective responses to perceived risks differed between the groups of respondents. Base stations elicited positive implicit associations in experts on mobile communication, neutral associations in lay persons, and negative associations in base station

opponents. A detailed analysis revealed that fear strongly influenced risk perception, whereas anger was a major component determining the perception of benefits.

Among the demographic variables influencing risk perception age was important. Younger responders attributed fewer risks to base stations than older respondents; this could be due to the fact that younger persons have more knowledge about mobile communication (Cousin and Siegrist, in press). Familiarity is known to reduce people's worries about risks.

Knowledge provision had a positive effect on a realistic base station decision. Providing information diminished concerns and enhanced positive explicit affect. Moreover, providing information shifts health concern away from base stations and towards cell phones, the latter being the more problematic source of radiation (Cousin and Siegrist, in press).

The siting of base stations

One of the hot topics in Switzerland is the location of base stations. Experts agree that a base station located in the centre of a village minimizes radiation exposure to the population in general. Cell phones radiate more when the base station is far away. However, the survey showed that distant base stations are preferred. Moreover, the respondents opted for covering the base station sites, an opinion that is probably adopted also for aesthetic reasons.

A major finding was that knowledge provision had an influence on a realistic base station decision. Participants who were provided with knowledge preferred locations in the centre of the village. They showed also more positive implicit affect as compared to the control group. A conjoint analysis – a fairly new approach in environmental evaluation – conducted in a large sample showed that it is considered important that residents can participate in the decision process for the base station site.

5. Implications for health and environment

5.1 Module 1: Dosimetry and exposure assessment

Exposure of the foetus

Most importantly, the project revealed that if the incident fields are compliant with the reference levels for the general public at the location of the foetus, the basic restrictions are met in all investigated cases. However, due to the small safety margin, the statement cannot be generalized based on current data, i.e., additional research is needed to better characterize the uncertainty boundaries.

The simulations on induction cooker hobs showed problems, and the researchers state: "Devices that are compliant with the reference levels, as measured in [CENELEC, 2002] will significantly exceed the exposure limits at closer distances and in consequence violate basic restrictions on the exposure of both the mother and the foetus. Considering the high gradients of the magnetic field in the immediate environment of the source, this is likely to be true for other household appliances producing strong magnetic fields". Future revisions of the product standards should take into account the characteristics of the magnetic fields appropriately, considering all possible realistic exposure scenarios and positions of the user, and pay sufficient attention to the particular anatomical conditions of pregnant women.

A major concern, however, applies to occupational exposure. For nearly all exposure scenarios, the basic restrictions for the general public can be violated for the foetus if the mother is exposed at occupational exposure levels. Regarding precautionary principles, particularly concerning the unborn child, regulators should consider additional protective measures to prevent pregnant women from being exposed to higher field strengths, such as enforcing basic restrictions for the general population for the exposure of the mother at work places.

The authors state that "In summary, the findings of this study should be regarded as an initiative to standardization organizations to review the current product standards on the assessment of ELF fields emitted by household appliances and revise them where necessary. Manufacturers of induction cooking equipment or other household devices can proactively seek improved solutions with reduced exposure."

Cumulative exposure in time and frequency domains of the central nervous system

Discussions have been going on in various countries about the effect of hands-free kits. It has been claimed that the ear piece of a hands-free kit could increase the local radiation in the ear. The results of the present project could clearly demonstrate that this is not the case.

The results of comparing exposure in a real environment, driving a car, has highlighted the very low power levels from phones operating in the UMTS system, which are by a factor of 100 lower than in the GSM system. The exposure situation is gradually changing to wireless illumination from Wireless Local Area Networks, WLAN, at work places and homes, i.e. indoor situations different from the usual base station illumination outdoors. One of the results of this study is that the exposure is similar for these two situations, except that the illumination may now come from several different sides at the same time. The actual exposure is in both cases very weak.

Live cell imaging during MF exposure

This research is motivated by the growing interest as to whether EMF cause non-thermal biological effects on a cellular level and also addresses the WHO research agenda 2006. The project resulted in a unique tool, which is well characterized, integrated into an optical microscope, and suited for the study of ELF EMF exposure effects on live cells. Live cell imaging will enable testing several molecular and cell specific pathways, which are relevant to cancer or the central nervous system. The outcome of these studies should allow the discrimination of relevant mechanism and the extraction of the relevant exposure parameters. It might contribute to the area of risk assessment and also to new approaches of medical treatments.

5.2 Module 2: Laboratory studies and epidemiology

EMF effects on the brain: Changes of the sleep EEG

The results provide further evidence that exposure to pulse-modulated RF EMF, such as emitted by mobile phones, affects human brain physiology by a non-thermal mechanism. In particular, pulse-modulation frequency components within a physiological range induce short term effects in the EEG of healthy young volunteers. The specific effect of increased power in the spindle frequency range during non-REM sleep is unlikely to be a cause for concern, since sleep spindles are considered to be a feature of "good sleep". It would be a more serious matter if sleep spindles would have been suppressed. It is also reassuring that objective and subjective sleep quality were not affected. Contrary to some claims in public opinion, the participants did not sense whether or not they were exposed to the RF EMF. Furthermore, there is currently no evidence that children and adolescents show a higher sensitivity to RF EMF exposure. A minor impact on cognition may have occurred as the 217 Hz pulse-modulated signal reduced reaction speed, leaving accuracy of performance unaffected. This observation requires confirmation by further studies. All results represent responses to short-term exposure and they cannot be used to predict potential effects of long term exposure. While the mechanism of action remains unclear, some results indicated that the thalamus may be involved.

In summary, the present results do not represent evidence that acute EMF exposure has adverse effects on the human brain. However, the fact that EMFs affect brain physiology is a reason to maintain the existing regulations limiting EMF exposure. Subjects who are concerned about potential health hazards of cell phones should be encouraged to use headsets which reduce dramatically brain exposure. Clearly, more research is needed to further elucidate the mechanism of action and to specify more precisely the crucial EMF parameters which are responsible for the observed effects.

EMF effects on the brain: Changes in cerebral blood circulation

The results indicate for the first time that there may be small effects of intermittent UMTS-EMF exposure on cerebral blood circulation. Since the measured amplitudes of the EMF induced changes in cortical circulation do not exceed those of physiological variations during normal brain activity, and since they are small as compared to changes elicited by physical activity or by stress, the findings should not give rise to health concerns. Also, no negative impact on the wellbeing or cognitive performance of the subjects could be detected. Hence, at this state of research, the results give no indication that exposure limits need be adjusted. However, further studies are required to confirm the results and to extend the study population beyond healthy young men. Furthermore, EMF modalities other than the one tested should be included. As with the EMF effect on the sleep EEG, the fact that EMF might influences cerebral blood circulation is a sufficient reason for continuing the scientific efforts.

Prospective Cohort Study on Health-Related Quality of Life and RF EMF

The results are reassuring in that no association was found between RF exposure and ill health in a prospective design that is superior to cross-sectional designs that previously have been utilized to address this topic. This finding is consistent with the results of provocation studies on short term effects that also do not find health effects from RF exposure. It would, however, be premature to rule out the possibility that RF exposure could cause ill health under some other circumstances, e.g., exposure levels much higher than the ones typically experienced by the general population or in some sensitive part of the population and further studies based on larger sample sizes are needed to validate these results.

5.3 Module 3: Cell biology

Although in vitro laboratory studies are an important part of the efforts to determine whether EMF affects human health, the outcomes can provide only supportive evidence. They must be viewed in combination with the observations from epidemiological studies and human volunteer studies.

5.4 Module 4: Risk perception

In considering the risks of mobile communication, it is important not to lose sight of its benefits. Mobile phones and other mobile communications are highly popular and of vast importance; their

world-wide use is estimated to involve 4 billion persons (Olsen, 2010) with an upward trend. So far, the balance of evidence speaks against health impairment due to NIR exposure at levels below current exposure standards, and it has not been shown that exposure leads to disruption of essential biological processes. However, it would be premature to rule out risks simply because hazards have not been detected and a disease mechanism has not been identified by the research conducted to date. Remaining gaps of knowledge should give rise to more high-quality research that could lead either to the discovery of novel mechanisms of action of EMF and the identification of hidden risks, or to further reassurance that the technology is basically safe. In view of the uncertainties, the authorities advocate the precautionary principle. However, without hard evidence people are unlikely to change their behaviour concerning the use of mobile phones.

Several conclusions can be drawn from the outcome of the projects in this program. The studies confirmed that providing adequate information to the public is of major importance. This includes facts about radiation such as the rapid decrease of its strength with the distance from the base station. Knowledge provision enhances realistic risk assessment of base stations. In addition to factual information, precautionary recommendations for using mobile phones and other wireless devices should be issued. In a recent study in Denmark, information containing precautionary advice was seen as more useful, comprehensible and trustworthy than factual and technical information (Nielsen et al., 2010). People seem to prefer information where the risk assessment is already done and is translated into advice on how to manage the risk. However, it should be also noted that a discrepancy was observed between concern and action taken.

Recommending empowering precautionary measures appears to be more convincing and comprehensible than issuing authoritarian guidelines alone. The advice should be carefully designed and stress people's ability to make sound decisions to protect themselves in their preferred way.

Empowerment is also a central issue with regard to the siting of base stations. An increased participation in decision making and control by the public is expected to reduce the negative affect toward base stations. Citizens should be able to express their needs and be involved in the decisions concerning the siting.

Several measures have been proposed to augment the trust in mobile communication authorities. These include the dissemination of information concerning the location and operation characteristics of base stations. Also, exposimeters could be made available to interested persons so that the multiple sources of radiation can be recognized and precautionary measures taken.

Statements from the mobile phone industry are unlikely to have an impact, since they have been considered as little trustworthy in the present study as well as in previous ones (Kristiansen et al., 2009). It is all the more important how the authorities communicate the state of knowledge including the acknowledgment of uncertainty. A careful use of terminology is essential. Accordingly, the term "electrosmog" implying deleterious effects of radiation comparable to air pollution should be avoided.

6. Accomplishment of the programme

A principal aim of the NRP 57 was to provide the basis for an improved assessment of potential health risks of EMF exposure and considered to be part of the international efforts to clarify these issues. The aim was not to cover comprehensively all issues related to EMF and health, but to focus on specific problem areas where expertise in Switzerland was available and in which research projects could be realised within a 3-year period and with the available funds. Accordingly, the scope of the results is limited. However, the findings corroborate the necessity to further investigate potential effects of EMF and their underlying mechanisms in more diverse model systems. The results of two projects showed that exposure to RF EMF affects the brain. The recognition that signal modulation is a prerequisite for the EEG effects represents an important step in the endeavour to elucidate the mechanism of action. The delayed appearance of the changes induced by RF EMF indicate that exposure possibly triggers a cascade of events.

Confirming EMF-induced DNA fragmentation and showing that the effect is not caused by direct DNA damage is a major contribution to the field. Moreover, the fact that only intermittent exposure is effective indicates that complex cellular processes are involved. The steady-state of DNA strand breaks may be affected by a perturbance of cell-cycle progression, alteration of metabolic activity and the induction of apoptotic cell death.

In summary, the studies of brain physiology and cell biology not only documented EMF effects but took first steps for elucidating the mechanism of action. It is reasonable to expect that insights into the mechanisms will provide the basis for assessing the implications for health. At present such assessments are not yet possible. Nevertheless, in view of the physiological and cellular effects that have been shown to occur, a precautionary policy with respect to EMF exposure is justified.

The epidemiological study did not reveal an association between exposure and health complaints. This is reassuring, particularly since state-of-the-art procedures were used for recording and modelling exposure, though uncertainties remain in particular in estimates of individual exposures. However, the study does not preclude that different results could be obtained with higher exposure levels, over longer exposure periods, and by investigating different endpoints (e.g., chronic diseases).

A particularly valuable feature of the programme is the novel information concerning exposure and dosimetry assessment of the general population for different communication technologies. The introduction of new technologies warrants further monitoring. The data obtained for pregnant women and the foetus have revealed risks that need to be addressed by the health authorities.

Risk communication remains a sensitive issue. The studies showed that dispelling misconceptions is a challenge and that empowering approaches to communication are promising.

6.1 Physiology and cell metabolism

A major objective of EMF research is to provide information about potential effects on health. Documenting effects of EMF on physiological and biological processes is a first, important step. Once such effects have been clearly and repeatedly demonstrated, the investigation of the mechanism of action must follow an approach that has been adopted in some of the projects of the present programme.

EMF research is plagued by the inconsistency of its findings. Findings obtained by one group cannot be replicated by another group, thereby shedding doubt on the validity of EMF effects. The replicability of results is therefore an important prerequisite for unambiguously demonstrating that an effect is indeed present. Within the NRP57 program, three previously reported RF EMF effects were confirmed and extended: (1) the enhancement of power in the sleep EEG in a specific frequency range; (2) effects on cerebral circulation; and (3) an increase of DNA fragmentation.

One of the most consistent findings has been the effect on the sleep EEG. Exposure to RF EMF has invariably caused an increase of power in the spindle frequency range (12-15 Hz) in non-REM sleep. These changes have been observed by Achermann and colleagues in four separate previous studies and were confirmed in three additional studies within the present program. A similar effect has been reported also by another group (Loughran et al. 2005). In an effort to identify the critical signal parameters, Achermann and his team varied the modulation characteristics (handset-like vs.

base station-like modulation), the signal strength (range 0.2 - 5 W/kg), the duty cycle of various components, and the carrier frequency (900 vs. 2140 MHz). It turned out that pulse-modulation is critical for the effect on the sleep EEG, since neither the non-modulated carrier nor low-frequency magnetic pulses without a carrier were effective. Moreover, the studies indicate that the effect is generated by an action on the cerebral cortex, since radiation not penetrating into deeper brain structures was also effective.

Previous studies reporting RF EMF effects on brain circulation have been confirmed by Wolf and co-workers using near infrared spectroscopy. Although an UMTS base station-like signal was applied, the intensity corresponded to handset exposure. The absence of a dose-effect relationship is puzzling and requires further investigation.

A previous report that DNA fragmentation in mammalian cells is enhanced after RF EMF exposure had a considerable impact due to the potential health consequences of DNA damage. Replication of the previous results as well as further studies was warranted. Schär and colleagues confirmed the effect in human fibroblasts. They focused their further efforts on ELF MF exposure, a procedure for which a live cell imaging setup was designed as part of the research programme. Intermittent exposure to 50 Hz MF was shown to increase DNA fragmentation in human primary fibroblasts. Schär and his team showed that this effect was not due to physical DNA damage or to an increase of reactive oxygen species that could impair DNA. The cause of enhanced DNA fragmentation was due to minor disturbances of DNA synthesis and occasional triggering of cellular apoptosis. In contrast to ionizing radiation that may induce irreparable DNA damage, EMF does not seem to exert such an effect. The specification of such an indirect mode of action of EMF on cellular processes is a major contribution to the field.

In the search for cellular effects of EMF, model systems may be useful. Various changes of proteins involved in the cellular stress response and apoptosis were observed by Mevissen and colleagues. These observations, being too preliminary to allow firm conclusions, need to be confirmed and extended in further studies.

A frequently used model organism is the worm C. elegans. The teams of both Mevissen and Goloubinoff investigated potential RF EMF effects on signalling pathways, protein homeostasis and motility. In addition, a transgenic moss plant that is highly sensitive to abiotic stresses and pollutants was studied. None of the variables investigated were clearly affected by EMF exposure. Although these model organisms have been shown to respond to minute environmental changes (e.g. temperature), they do not appear to be influenced by EMF.

In summary, the studies of physiological and cellular effects of EMF yielded two major advances: (1) The evidence for an effect of RF EMF on human brain function as reflected by the EEG has been consolidated and extended, and the field parameters have been further specified. (2) The action of ELF EMF on DNA has been confirmed and at the same time, the indirect mechanism giving rise to this effect has been characterized.

6.2 EMF exposure and health effects

In the study of Röösli and co-workers objective traffic data about mobile phone use was used for the first time to investigate potential effects on symptoms, and in particular headache. Novel features were also the cohort design to study the effects of RF EMF exposure over the period of one year and the exposure measurements with a portable device for one week. This allowed the quantification of the exposure level and the specification of the contribution from various sources. The main finding was the absence of an association between health disturbances and environmental RF EMF exposure in daily life. In particular, no association was obtained between sleep behaviour and exposure in the sleeping room.

The study has also its limitations. For example, the average exposure level of the population was much lower than the currently applied exposure limit in Switzerland. Therefore no conclusions can be drawn as to effects at higher exposure levels. Potential further limitations include a possible selection bias, the sample size and the limitation of the evaluation to one year. Nevertheless, it should be emphasized that the results did not indicate that the current RF EMF exposure situation causes health disturbances. This supports the majority of findings reported in the literature and increases the evidence for the true absence of an effect.

6.3 Dosimetry and exposure assessment

Kühn and collaborators assessed the exposure of the brain to RF EMF. Both near-field and far-field sources were analysed. Phantoms representing the electrical properties of the human body and brain, and simulation tools were developed and used to assess the SAR in various brain regions. Large variations were obtained which were due to differences in usage, device design and signal characteristics. The models are able to predict the SAR induced by various sources in brain regions. They will be valuable for dose estimation in epidemiological studies and consumer information on exposure of individuals.

Christ and colleagues characterized the exposure of the foetus to different types of EMF sources. Detailed anatomical computer models of women in different stages of pregnancy incorporated the electrical tissue characteristics. The main findings were that occupational exposure limits are too high for pregnant women and that some product standards (induction cooker hobs) may lead to excessive SAR levels in the foetus.

Capstick and his team designed and developed a miniature ELF MF exposure system that can be integrated in a microscope system. Live imaging of cells can be combined with exposure to magnetic fields. A computer control system sets, monitors and records the exposure level throughout the experiment which must be conducted under blinded conditions. The system has been successfully used in the project of Schär discussed above.

6.4 Risk perception

Presently there is no evidence that RF EMF affects health. However, potential health risks cannot be excluded. The public expects a ubiquitous use of mobile phones and at the same time is apprehensive of "electrosmog" emanating from base stations in the vicinity. Moreover, 5% of the Swiss population consider themselves to be hypersensitive to electromagnetic fields and to suffer from health problems due to EMF exposure. Under these conditions it is difficult to convey objective information about EMF to the public.

The group of Siegrist investigated which factors determine perceived risks or benefits of mobile communication. Affective reactions were shown to be crucial for risk perception. Hence, trust and other affect-related elements must be considered in risk communication. Interestingly, knowledge provision was able to dispel misconceptions as it led to a more realistic evaluation of base-station location which is more in line with public health considerations.

Schulz and his team reported that source credibility was not an important factor in communicating the message that untoward health effects of mobile phone radiation is unlikely. In contrast, preconceived risk assessment of different groups was shown to be a major factor: Persons who rated the health risks of EMF as very low were further reassured by the message, whereas those rating the health risks as high became more worried. Precautionary measures did not enhance worries. An empowering precautionary message appears to be most convincing. There is preliminary evidence for differences of risk perception between Swiss Germans and Swiss Italians.

6.5 Perspectives

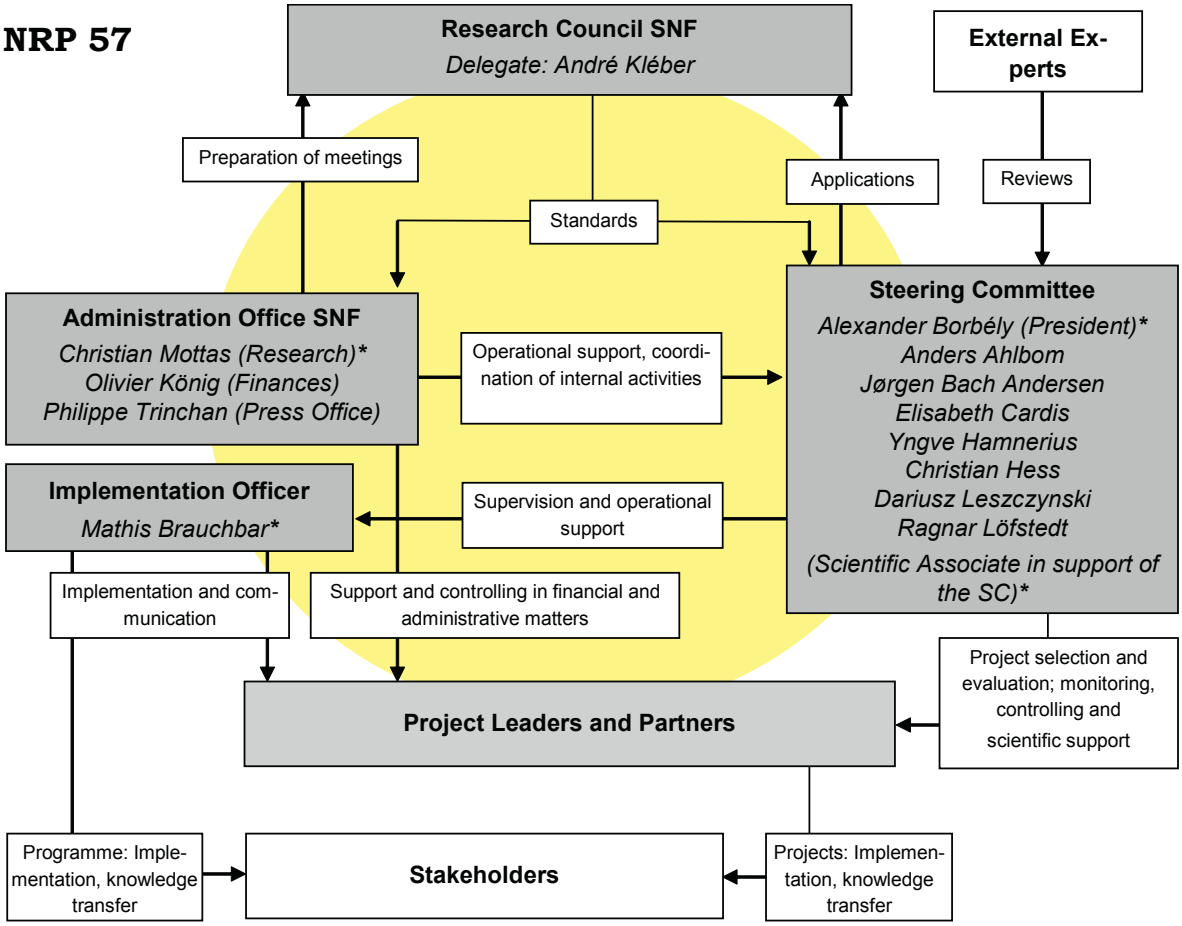
It is evident that the NRP 57 has strengthened EMF research in Switzerland and enhanced the interactions between the groups on a national level. It has also increased the international visibility of Swiss research. The research topics covered in the program correspond largely to the high priority research fields listed in the WHO agenda 2010 for radiofrequency fields. In view of the results, follow-up studies will be particularly important in regard to the action of EMF on brain functions and on DNA metabolism. These approaches have proved to be promising for gaining insights into the mechanisms underlying effects of EMF on biological systems. To preserve the expertise and know-how gathered during the 3-year period it will be important to explore avenues allowing the continuation of key projects. EMF research is a long-term endeavour that requires an appropriate organizational and financial framework. The rapidly evolving technologies provide a challenge that can be met only by a further close collaboration of experts in dosimetry and the life sciences. The NRP 57 programme has laid the groundwork.

7. Appendix

7.1 Course of action time table

	2005	2006	2007	2008	2009	2010	2011
Federal Council approves NRP 57	March						
Launch			Jan				
Ongoing research						End: June	
Implementation and coordination							
Monitoring and controlling							
Progress reports and meetings				March	June	Sep-tember	
Workshops				3			
Satellite symposium EBEA/ BEMS 2009					June		
Program synthesis and end of programme							May

7.2 Organisation and management



* Protagonists forming the office of the NRP 57

Division IV (Section NRP/NCCR) of the Research Council

Division IV of the Research Council has the overall responsibility for conducting NRPs and consists of 20 members representing a wide range of scientific disciplines. Decisions taken by Division IV on accepting or rejecting research projects are submitted to the National Research Council Presidial Board for ratification. Based on the recommendations of the Delegate, the Board selects the SC, appoints the Implementation Officer and defines the standards for project evaluation. In addition, it assesses the intermediate and final reports of the Delegate and the SC and if necessary, supports them in the execution of the programme.

Delegate of the Research Council

Prof. Dr. André G. Kléber
Institute of Physiology, University of Berne, Switzerland

The Delegate of the Research Council represents Division IV of the Research Council in the SC and assures the transfer of information and experiences, thereby safeguarding that the SC conforms to the regulations and standards. He submits the recommendations for the selection of the SC as well as the SC's decisions on acceptance or rejection of research proposals to the Research Council for approval. Moreover, he informs the Research Council about the developments in NRP 57 on a regular basis.

Steering Committee (SC)

The SC consisted of eight members who took on primarily strategic responsibilities for the entire

duration of the NRP 57. It constituted the formative body giving the program its profile, and guaranteeing the necessary continuity and coherence in any decision. Committee members were responsible for assessing the scientific quality and implementation of the NRP 57 by:

- Elaborating the implementation plan
- Evaluating and selecting the full proposals on the basis of external reviews for approval by the Research Council
- Rejecting pre-proposals at its own option
- Supervising the financial planning in collaboration with the program coordinator and yearly financial report for approval by the Research Council
- Organising and supervising the scientific coordination
- Monitoring the progress of the projects and reviewing the intermediate and final reports
- Supporting the president of the SC in the international coordination activities
- Supervising the implementation activities
- Reviewing the implementation documents and their adherence to the quality standards of the SNF for approval by the Research Council
- Recommending the implementation concept (describing future implementation activities; to be issued) for approval by the Research Council
- Monitoring and supporting the implementation activities of the projects and the program as a whole
- Supporting the implementation officer in updating the stakeholder database and in writing editorials for the program newsletter
- Compiling a scientific synthesis and final program report at the end of the programme.

For the review of project outlines and research proposals the SC consulted external experts who anonymously reviewed the scientific quality of the pre-proposals and full proposals according to the criteria defined in the implementation plan.

Members of the Steering Committee

Prof. em. Dr. Alexander Borbély (President)
Institute of Pharmacology and Toxicology, University of Zurich, Switzerland

Prof. Dr. Anders Ahlbom
Epidemiology, Karolinska Institute, Stockholm, Sweden

Prof. Dr. Jørgen Bach Andersen
Institute of Electronic Systems, University of Aalborg, Denmark

Prof. Dr. Elisabeth Cardis
Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain

Prof. Dr. Yngve Hamnerius
Bioelectromagnetics Group, Chalmers University of Technology, Goteborg, Sweden

Prof. Dr. Christian Hess
Department of Neurology, Inselspital (University Hospital), Berne, Switzerland

Prof. Dr. Dariusz Leszczynski
Radiation Biology Unit, Radiation and Nuclear Safety Authority (STUK), Helsinki, Finland

Prof. Dr. Ragnar Löfstedt
IPI King's Centre for Risk Management, King's College London, London, United Kingdom

President of the Steering Committee
Prof. em. Dr. Alexander Borbély
Institute of Pharmacology and Toxicology, University of Zurich, Switzerland

The president of the SC represented the NRP 57 internally and towards the outside. He coordinated contacts between stakeholders and the SC, in particular the federal and cantonal authorities, as well as other social, environmental or economic organisations. In collaboration with the program coordinator, the president was responsible for the scientific coordination of the approved research projects and monitored and supported the implementation officer with his scientific expertise.

Scientific Associates in Support of the President of the SC
Dr. Sonja Negovetic,
Dr. Sabine Regel
Institute of Pharmacology and Toxicology, University of Zurich, Switzerland

The president of the SC was assisted by two part-time scientific associates who supported him as regards the ongoing technical communication with the research groups and the communication with comparable programmes within or outside Switzerland. The associates were responsible for developing the content for outreach activities (NRP 57 Program Website; information events, publications in the media) and for the organisation of the annual meetings and topical workshops for the advancement of an open and interdisciplinary dialogue between the researchers. They further supported the president of the SC in drafting the final synthesis report.

Implementation Officer
Mathis Brauchbar
Advocacy AG, Communication and Consulting, Zurich, Switzerland

In consultation with the SNSF Press and Information Office, the SC nominates an Implementation Officer who is then appointed by the Research Council. The Implementation Officer works closely with the Administrative Offices of the SNSF. The Implementation Officer of the NRP 57 had a clearly defined mandate of responsibility for assuring that the implementation of the program fulfilled the demands of the research topics, the realisation of implementation measures met professional standards, and for assuring quality in the public relations sector. The implementation officer planned, managed and coordinated the implementation activities and advised the SC and the project leaders as regards communication and implementation. He also coordinated the interactions with the media and was responsible for issues management.

Administration Office

Program Coordinator
Dr. Christian Mottas
Division IV, Swiss National Science Foundation (SNSF), Berne, Switzerland

The Secretariat of Division IV of the SNSF is responsible for operations management and implementation of decisions taken by the Research Council and the SC. The Secretariat coordinates administrative and financial support functions and, in collaboration with the president of the SC, is in charge of project supervision, coordination and controlling. The program coordinator advised the project leaders and the SC in these matters, in particular in case of deviations of time plan and budget and supported all protagonists in their task assignments. He assured the information transfer between the president of the SC, the SC and the Delegate of the Research Council. In addition, he archived all documents relevant to the execution and management of the NRP 57.

Accounting
The accounts office is responsible for assisting the researchers and their affiliations in financial matters, reviewing and controlling the financial status of the research projects and administering changes and corrections where needed. In addition, it controls and approves the financial intermediate and final reports and is responsible for the financial administration of the whole NRP 57.

Press and Information Office (PRI)

The Press and Information Office set the quality standards in communication and are responsible for public relations guidelines and their implementation in the programme. It reviews the implementation concept and supports the implementation officer for the duration of the program as regards communication and publicity work. In collaboration with the implementation officer, it organizes and finances all national media contacts (interviews, press conferences and releases).

Office of the NRP 57

An operational office consisting of the president of the SC and his scientific associates, the implementation officer and the program coordinator met regularly to prepare the operational and strategic dealings of the NRP 57 and implement the decisions of the SC. The office represents the NRP 57 towards the outside.

Federal Representatives

Dr. Mirjana Moser
Radiological Protection Division, Federal Office of Public Health (FOPH), Berne, Switzerland

Dr. Jürg Baumann
Air Pollution Control and NIR Division, Federal Office for the Environment (FOEN), Berne, Switzerland

Some ministries deal closely with the topics of NIR and have a strong and direct interest in the proceedings of the NRP 57. Accordingly, the government was one of the main addressees of the programme. To enhance the exchange of experiences, information, knowledge and collaborations and to optimally implement the findings, two observers (no vote) from the Federal Office of Public Health and the Federal Office for the Environment, respectively were included as SC members().

Researchers

Overall, the principle investigators (PIs) were responsible for the efficient scientific and administrative execution of their project and requested to directly and actively partake in implementation activities. They had to deliver all necessary and required paperwork such as intermediate reports, final reports, abstracts or workshop material within an agreed time frame to guarantee the smooth proceeding of the NRP 57. and were the contact persons for all parties involved. The project leaders represented their project at official events of the NRP 57, including topical workshops, thereby complying with the regulations of the Press and Information Office of the NRP 57 as regards publicity work.

As a general rule, the researchers were allowed to inform the media about their own research in the framework of the programme; yet, all media requests regarding the program need to be forwarded to the implementation officer.

7.3 NRP 57 program workshops

_ "Dosimetry meets Epidemiology" (January 2008)

_ "Towards a Mechanism-Based Framework in EMF Research" (May 2008)

_ "Electromagnetic Fields and the Brain" (October 2008)

_ "NRP 57 Satellite Symposium at the EBEA 2009" (June 2009)

To view the meeting agendas or read about the conclusions of the respective workshop please visit www.nrp57.ch.

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7.5 Acronyms

2G	2nd generation of mobile communication systems (see also GSM)
3G	3rd generation of mobile communication systems (see also UMTS)
4G	4th generation of mobile communication systems (see also LTE)
AChE	Acetylcholinesterase
DOI	Diffuse Optical Imaging
EEG	Electroencephalogram
ELF	Extremely low frequency
EMF	Electromagnetic fields
GFP	Green fluorescent protein
GSM	Global System for Mobile Communications
IARC	International Agency for Research on Cancer
ICNIRP	International Commission on Non-Ionizing Radiation Protection
LTE	Long Term Evolution
MF	Magnetic Field
MRI	Magnetic Resonance Imaging
NIEHS	(U.S.) National Institute of Environmental Health Sciences
NIR	Non-ionizing radiation
NIRI	Near infrared imaging
NIRS	Near Infrared Spectroscopy
non-REM sleep	Non rapid eye movement sleep
NRP	National Research Program
OT	Optical Topography
PET	Positron Emission Tomography
PI	Principal Investigator
psSAR	peak spatial specific absorption rate
RF	Radiofrequency
ROS	Reactive oxygen species
SAEFL	Swiss Agency for the Environment, Forests and Landscape
SAR	Specific Absorption Rate
SC	Steering Committee
SER	State Secretariat for Education and Research
SNSF	Swiss National Science Foundation
UMTS	Universal Mobile Telecommunication System
wbSAR	whole body specific absorption rate
WT	Wild type
WHO	World Health Organization