RISK ASSESSMENT TO EMF EXPOSURE BY MOBILE PHONES: OPTIMIZATION OF RF EXPOSURE SETUPS

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Summary

The 1990's have seen the introduction of digital cellular phones and an enormous increase in the use of mobile communications equipment. Several hundred million people were already using this technology at the beginning of the new decade, and growth is still breath-taking. Digital cellular phones operating close to the head expose the user to amplitude-modulated electromagnetic fields at a considerable amplitude. Therefore, it is reasonable that the public and the health authorities demand a careful risk assessment of this new and widespread technology.

Chapter 1 of this thesis tries to categorize the various activities with respect to risk assessment of mobile phones according to a common risk assessment paradigm. Chapter 2 lists the objectives of this thesis and sets them in a wider context by categorizing them according to the discussed risk assessment paradigm. A sound risk assessment is only possible if the bio-experiments performed fulfill numerous requirements. Chapter 3 lists the relevant parameters and proposes a procedure for the design, optimization and realization of exposure setups. Following these instructions will minimize the probability that studies performed with great biological care are useless for risk assessment due to shortcomings in the exposure setup.

Part II deals with the absorption in the head of mobile phone users. The focus of Chapters 4 and 5 is on the question of whether there are differences in energy absorption between the heads of adults and children. This question is of importance since the use of mobile phones is already widespread in all age groups and the phantoms used for compliance tests are based on the heads of adults. Considerable differences between the absorption in a numerical head phantom scaled to different sizes were reported in a study by Gandhi et al. published in 1996. In clear contrast to that, this thesis comes to the conclusion that the absorption in the heads of children is not increased compared to the heads of adults. The study is based on numerical head phantoms derived from MRI scans of a 3-year old child, a 7-year old child and several adults. The study concludes that a phantom representing a reasonable cross section of adult users is also suitable for compliance testing with respect to the user group children.

Chapter 6 in Part III investigates the absorption mechanisms in 60mm Petri dishes and T-75 flasks, both widely used for in vitro studies. The dependence of the absorption on different experimental parameters was studied numerically. Different designs of exposure setups based on TEM cell, RF-chamber, radial transmission line, waveguide, and wire patch cell are compared, and parameters which can be optimized during the realization of the setups are identified. Chapter 7 describes the design, optimization and realization of a waveguide setup for the exposure of embryonic stem cells at 1.71GHz. A detailed numerical and experimental dosimetry and an analysis of the thermal properties are presented. All waveguides including those for the sham exposed group fit into a single incubator. The setup enables the car-
rying out of experiments using various modulation schemes and long term exposure protocols as well as simultaneous logging of exposure parameters.

The carousel setup has been widely used for studies on the effect of electromagnetic fields on the CNS of small mammals. Chapter 8 presents a careful dosimetric analysis of this setup with special emphasis on the IRIDIUM frequency at 1.62 GHz. The influence of neighboring rats, the plastic of the setup, the position and size of the rats and other parameters are investigated. The uncertainties of the dosimetric analysis are carefully investigated, and reasons for the differences between experimental and numerical dosimetry are discussed.
Zusammenfassung


Kapitel 6 in Teil III untersucht die Absorptionsmechanismen in 60 mm Petrischalen und in T-75 Kulturgefäßen, die beide häufig für Untersuchungen in vitro verwendet werden. Die Abhängigkeit der Absorption von verschiedenen experimentellen Parametern wird numerisch untersucht. Verschiedene Arten von Expositionsanlagen, basierend auf einer TEM-Zelle, einer Hochfrequenzkammer, radialem und rechtwin-

Der sogenannte Karussellaufbau wurde bereits mehrfach für Studien über die Effekte elektromagnetischer Felder auf das ZNS von kleinen Säugetieren verwendet. Kapitel 8 präsentiert eine sorgfältige dosimetrische Analyse des Aufbaus mit Schwerpunkt auf der Trägerfrequenz des IRIDIUM-Systems von 1,62 GHz. Der Einfluss benachbarter Ratten, der Größe der Ratten und anderer Parameter wird untersucht. Die Unsicherheiten und Gründe für Differenzen zwischen experimenteller und numerischer Dosimetrie werden diskutiert.
Acknowledgments

After some confusion about the question to which group I would belong, I joined the BIOEM/EMC group, then part of Laboratory for Electromagnetic Fields and Microwave Electronics, in June 1996. This confusion cost Niels Kuster some bottles of champagne. That investment (which I hope he does not regret) is not the only reason why I want to thank him. In numerous discussions he gave me the possibility to profit from his enormous experience in the complex area of Bioelectromagnetics. At the very beginning I had the opportunity to work on the interesting question of whether there are differences in energy absorption between the heads of adults and children. Many thanks are due to Michael Burkhardt who introduced me patiently to MAFIA within this project. This was the basis for three and a half years of excessive use of this tool. At this point I should thank Andreas Christ and Nik Chavannes who not only have done much for the entertainment in room G97 but also have been working hard on the development of the fabulous “Tolles Tool” which will make life so much easier for simulators like me. I thank Katja Poković very much for spending numerous hours in the laboratory with me and my rat cadavers and for carefully reading many chapters of this thesis. Thomas Schmid and Hansruedi Benedikter helped me with their technical advice in all situations in which a physicist was confronted with technical reality. Jeroen de Keijzer helped me very much with the construction and modification of exposure setups. Special thanks to Michelle Stubb, who had the dubious pleasure of reading almost everything I have written during the last 3 1/2 years, including these acknowledgments. I wish all new group members good luck with their work which will partly consist of struggling with similar topics as I did. Thomas Schwitter and Jonathan Gubler guided me in the marvelous world of Macintosh computers and were sometimes able to prevent me from using physical force against these strange boxes. I thank Magnus Sundberg, Theodoros Samaras and all the guests of our group who stayed for a longer period and populated G97. Ray Ballisti always lent immediate support if problems with the UNIX system occurred.

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Many people, but especially Beatrice Miller, introduced me to the field of communicating with the broad public about "electrosmog" and therefore prepared me for my next position.

Finally I want to thank my companion through life, my ancestors, my descendants and my big toe.
List of Publications

Papers Included in this Thesis


3. N. Kuster and F. Schönborn, “Recommended minimal requirements and development guidelines for exposure setups of bio-experiments addressing the health risk concern of wireless communication”, *Bioelectromagnetics*, in press.


Other Publications


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<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>AM</td>
<td>Amplitude Modulation</td>
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<tr>
<td>CENELEC</td>
<td>European Committee for Electrotechnical Standardization</td>
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<td>CNS</td>
<td>Central Nervous System</td>
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<td>CSF</td>
<td>Cerebrospinal Fluid</td>
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<td>DASY</td>
<td>Dosimetric Assessment System</td>
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<td>DCS</td>
<td>Digital Communications System</td>
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<td>DTX</td>
<td>Discontinuous Transmission Mode</td>
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<td>ELF</td>
<td>Extremely Low Frequency</td>
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<td>EMC</td>
<td>Electromagnetic Compatibility</td>
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<td>EMI</td>
<td>Electromagnetic Interference</td>
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<td>EMF</td>
<td>Electromagnetic Fields</td>
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<td>ETH</td>
<td>Eidgenössische Technische Hochschule</td>
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<td>FDTD</td>
<td>Finite Difference Time Domain</td>
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<td>FIT</td>
<td>Finite Integration Technique</td>
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<td>GSM</td>
<td>Global System for Mobile Communications</td>
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<td>HF</td>
<td>High Frequency</td>
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<td>ICNIRP</td>
<td>International Commission for Non-Ionizing Radiation Protection</td>
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<tr>
<td>ITIS</td>
<td>Foundation for Research on Information Technologies in Society</td>
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<td>MPI</td>
<td>Max-Planck-Institut</td>
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<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<tr>
<td>MTE</td>
<td>Mobile Telecommunications Equipment</td>
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<tr>
<td>NAS</td>
<td>National Academy of Science (USA)</td>
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<td>NRC</td>
<td>National Research Council (USA)</td>
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<tr>
<td>PVC</td>
<td>Polyvinyl Chloride</td>
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<td>RF</td>
<td>Radio Frequency</td>
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<td>rms</td>
<td>root mean square</td>
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<tr>
<td>RTL</td>
<td>Radial Transmission Line</td>
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<tr>
<td>SAR</td>
<td>Specific Absorption Rate</td>
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<tr>
<td>SEMCAD</td>
<td>Simulator for Electromagnetic Compatibility, Antennas and Dosimetry</td>
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<td>SPEAG</td>
<td>Schmid &amp; Partner Engineering AG</td>
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<td>TEM</td>
<td>Transversal Electromagnetic</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>ZNS</td>
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Part I

Background and Motivation
Chapter 1

Risk Assessment

The public concern over possible adverse health effects caused by exposure to electromagnetic fields (EMF) emitted by mobile phones has led to a wide range of activities, e.g., research on the effects of electromagnetic fields on in vitro systems and animals, numerical and experimental studies on the absorption of fields in humans, and the definition of exposure limits by regulatory bodies. All of these activities can be classified according to widely used risk assessment and risk management paradigms. A very short overview of two similar paradigms for risk assessment and risk management will be given. The last part of the chapter will discuss contributions to risk assessment with respect to exposure to electromagnetic fields as emitted by cellular phones within the context of the Covello-Merkhofer model of risk assessment.

1.1 Risk, Risk Assessment and Risk Management

According to [1], each definition of risk must involve at least 1) the possibility of an adverse outcome and 2) the uncertainty over the occurrence, timing or magnitude of the outcome. A widely used definition calculates risk as the product of the probability of an adverse outcome and the magnitude of this outcome, e.g., the number of fatalities [1]. This definition has the advantage that risk can be quantified as a number but has been criticized as being too narrow [1][2]. Covello and Merkhofer [1] give a more general definition of risk as a characteristic of a situation or action wherein two or more outcomes are possible, the particular outcome that will occur is unknown, and at least one of the possibilities is undesirable.

Both paradigms described below distinguish between risk assessment and risk management. [3] defines risk assessment as the use of the factual base to define the health effects from the exposure of individuals or populations to hazardous materials and situations. Risk management is defined as the process of weighting policy alternatives and selecting the most appropriate regulatory action, integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision. Very similar to that [1] defines risk assessment as a systematic process for describing and quantifying the risks associated with hazardous substances, processes, actions, or events. Risk management is defined as identifying, selecting, and implementing appropriate actions to control the risk.
1.2 The NAS-NRC Model of Risk Assessment

In 1983 the National Research Council published an influential report called “Risk assessment in the federal government: Managing the process” [3]. The committee authoring this report was formed in 1981 to conduct a study on the institutional means of risk assessment. Though the study was primarily directed toward the issue of increased risk of cancer resulting from exposure to chemicals in the environment, the conclusions and recommendations are applicable across the broad field of environmental health. In the first part of the report, the model of risk assessment and risk management shown in Fig. 1.1 was established. The model divides risk assessment into four major steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization. The first step, hazard identification, is the process of determining whether exposure to an agent can cause an increase in the incidence of a health condition (e.g., cancer, birth defect). Although the question of whether an agent causes an adverse health effect is theoretically a yes-no question, there are few agents on which human data are definitive. Therefore, the question is often restated in terms of effects in laboratory animals or other systems, e.g., “Does the agent cause cancer in test animals?”. The dose-response assessment is the process of characterizing the relation between the dose of an agent and the incidence of the adverse health effect in the exposed population and estimating the incidence of the effect as a function of the human exposure to the agent. Usually, this requires extrapolation from high to low doses and extrapolation from animals to humans. Exposure assessment is the process of measuring and estimating the intensity, frequency, and duration of human exposures to an agent. In its most complete form, it describes the magnitude, duration, schedule and route of exposure; the size, nature, and classes of human populations exposed, as well as the uncertainty in all estimates. Risk characterization is the process of estimating the incidence of a health effect under the various conditions of human exposure described in exposure assessment. It is performed by combining the exposure and dose-response assessments [3].
Figure 1.2: Risk paradigm according to Covello and Merkhofer [1]. In contrast to the NAS-NRC paradigm, hazard identification is a separate process that is necessarily conducted prior to risk assessment. Another obvious difference is the inclusion of release assessment as the first step of risk assessment.

1.3 The Covello-Merkhofer Model of Risk Assessment

Covello and Merkhofer [1] established a modified model shown in Fig.1.2. In contrast to the NAS-NRC paradigm, hazard identification is a separate process that is necessarily conducted prior to risk assessment. In this model hazard identification is a more qualitative process of identifying an agent as potentially hazardous. In contrast to that, risk assessment itself is a quantitative process delivering the basis for the risk evaluation. Risk evaluation means that the significance of risks are compared and judged. These three steps (hazard identification, risk assessment and risk evaluation) together are called risk analysis. Covello and Merkhofer distinguish four steps within risk assessment which are explained in Fig.1.2. A difference to the NRC paradigm is the inclusion of release assessment as a first step. The consequence assessment of the Covello and Merkhofer model is almost equivalent to the dose-response assessment in the NRC paradigm. In both models risk assessment ends with a step of integration. The term risk estimation of the Covello and Merkhofer model pronounces that risk assessment generally cannot give a full risk characterization.
1.4 Risk Analysis to Exposure to EMF by Mobile Phones

This section tries to categorize some of the numerous activities with respect to possible adverse health effects caused by exposure to EMF from mobile phones through the paradigm of Covello and Merkerhofer presented in the last section. It is far beyond the focus of the chapter to review the present state of knowledge regarding effects caused by EMF of mobile phones. This has been done in detailed reviews (e.g., [1] and [5]).

1.4.1 Risk

Based on the definition of [1], exposure to the fields emitted by mobile communications equipment is a risk. Obviously, the undesirable outcome is an adverse health effect caused by the electromagnetic fields. The substantial literature on thermal effects and the numerous but controversial literature on nonthermal effects demonstrates that several outcomes are possible and that there is considerable uncertainty on the outcome that will occur.

1.4.2 Hazard Identification

For a discussion on hazard identification, it is useful to distinguish between thermal and nonthermal effects of electromagnetic fields. According to [6], thermal effects are effects caused by a change in temperature or from heat added to the system. Nonthermal effects occur at exposure levels which neither challenge thermoregulation nor produce any significant change in organism temperature.

The studies discussed in [5] clearly show that excessive absorption of electromagnetic energy in the mobile communications frequency range can lead to hazards caused by thermal effects. Other identified hazards are indirect health effects caused by interference problems of mobile phones with technical systems (e.g., pace makers [4]). With respect to nonthermal health effects the ongoing studies are still mainly dedicated to hazard identification.

1.4.3 Risk Assessment

Release Assessment: While this is a critical point during the risk analysis of classical risk agents released unwillingly or by accidents, electromagnetic fields of mobile phones are released intentionally. The power level of a GSM mobile phone is dynamically adapted according to the quality of the connection [7] and can be monitored easily. The maximum peak power level depends on the system and is 2 W peak for GSM 900 and 1 W peak for GSM 1800. The complexity of the generic GSM signal (pulses of 0.577 μs length with a repetition rate of 217 Hz) is increased by speech modulation, DTX, additional data transfer between base station and cellular phone, etc. The result is a complexly modulated signal with many ELF components in the frequency spectrum.

Exposure Assessment: Determination of the SAR distribution caused by exposure to electromagnetic fields emitted by mobile phones has proven to be rather difficult. Only the combination of the most advanced experimental and numerical methods allows a reliable assessment of the actual level of exposure in the head of a mobile phone user. A detailed review on this matter is given in [8]. The exposure of a mobile phone user to electromagnetic fields emitted by his/her device depends
on a large number of parameters which are difficult to control. Major external parameters influencing the exposure are the type of the phone and position of the phone with respect to the user. The absorption inside the user is determined by the distribution and the electric parameters of tissues. The exposure assessment must allow the determination of the field distribution inside a user for a given external situation (type, operating modus and position of phone), including the expected variation between different individuals and a sound estimation of the uncertainty of the assessment [9][10].

Consequence Assessment: Epidemiology is a powerful method with the primary objective of establishing a statistically significant association between adverse human health effects and exposure to risk agents. However, not many studies of direct relevance to MTE users have been finished [5]. Many experiments on possible adverse health effects of EMF are performed with animals or in vitro systems. Careful design, construction, dosimetry and operation of the exposure setups are indispensable prerequisites for scientifically sound experiments. All technical and biological requirements must be listed carefully, and a close cooperation between engineering and biological groups should be established. A full characterization of the applied electromagnetic fields is necessary to allow the extrapolation from in vivo and in vitro experiments to humans. Most studies with chemicals use high doses during in vivo experiments to assess possible effects and use extrapolation models to extrapolate to the usually much lower doses to which humans are exposed. This possibility is largely barred to researchers on the area of possible health effects of low level RF electromagnetic fields since high doses will result in thermal effects. A careful assessment of the thermal properties of an exposure setup and the expected temperature increase during the exposure is very essential in experiments on possible health effects of RF electromagnetic fields.

Risk Estimation: Integrating the knowledge collected during the preceding steps of risk assessment leads to risk evaluation. With respect to thermal effects the risk evaluation of ICNIRP led to the conclusion that whole body averaged SAR values of 4 W/kg and local values of 100 W/kg pose a considerable risk [5]. However, most of these data are based on experiments with animals. Therefore, the extrapolation to humans requires a factor sufficiently large to exclude the possibility of thermal effects in humans using mobile phones. ICNIRP proposes a factor of 10 for occupationally exposed people and a factor of 50 for the general public. The exposure assessment gives detailed information on the SAR expected in the heads of the users of mobile phones and shows that SAR levels of 2 W/kg (averaged over 10g of tissues) can be reached during mobile phone use. With respect to nonthermal effects the data base was judged by ICNIRP to be insufficient to give a quantitative risk estimation [5].

1.4.4 Risk Evaluation

Well established studies on thermal effects show that no thermal effect is expected in humans if the local absorption is less than 2 W/kg and if the whole body averaged absorption is less than 0.08 W/kg. The knowledge on the range of absorption shows that a local absorption rate of more than 2 W/kg is possible with mobile phones of the GSM standard [9]. A violation of the exposure limit for the whole body averaged SAR is possible within a short distances from a base station antenna. Therefore, the risk cannot be judged as a priori insignificant and risk management is necessary. This is also true with respect to electromagnetic compatibility, since many technical
systems have proven to be sensitive to interference problems. The risk evaluation
of non-thermal effects is very controversial. ICNIRP came to the conclusion that
"overall, the literature on athermal effects of AM electromagnetic fields is so complex,
the validity of the reported effects so poorly established, and the relevance of the
effects to human health is so uncertain, that it is impossible to use this body of
information as a basis for setting limits on human exposure to these fields" [5]. For
comparing and judging the significance of the risk, it is important to note that the
impact on public health and economy could be enormous even for a small adverse
health effect, due to the large and fast growing number of users.

1.4.5 Risk Management

Based on the recommendations of ICNIRP, most European countries adopted or will
adopt the basic limit of 2 W/kg averaged over a tissue mass of 10 g and a time of 6 min
[11]. In the USA a slightly different exposure limit of 1.6 W/kg averaged over a tissue
mass of 1 g and a time of 30 min was defined [12]. However, it is difficult to verify
whether a certain phone is in compliance with the basic limits set by the regulatory
agencies. Therefore, standardized procedures must be defined to guarantee reliable
and reproducible compliance testing [9].

Specific restrictions of the use of mobile phones have been implemented to reduce
the risk of malfunction of sensitive technical devices due to interference problems
(e.g., on board airplanes and in hospitals). Since the effects of low level exposure is
controversial, risk management should also rely on the principle of prudent avoidance.
A reduction of the ICNIRP limits for local exposure may not be justified on the
basis of current knowledge. However, according to prudent avoidance, it may be
recommended that the publication of the results from compliance tests becomes
mandatory. Concerned consumers would then have the possibility to choose a mobile
phone which causes low absorption in the head of the user.

References


[5] ICNIRP, “Guidelines for limiting exposure to time-varying electric, magnetic,
and electromagnetic fields (up to 300 GHz)”, Health Physics, vol. 74, pp. 494-


Chapter 2

Objectives

As described in Chapter 1, a thorough risk assessment must be performed to evaluate possible health risks of exposure to EMF emitted by mobile phones. The objective of the studies performed in the course of this PhD thesis was to add significant contributions to the risk assessment in this area. The main focus has been on the improvement of the design, the experimental and numerical analysis and the realization of setups for in vivo and in vitro experiments in the mobile communications frequency range. The results of such studies are the basis for hazard identification and consequence assessment. In retrospect, many experiments conducted during the last years with great biological care have turned out to be of limited value due to severe shortcomings in the exposure setup. This insight was the starting-point of this thesis. Additionally, the thesis also tries to make a contribution in the area of exposure assessment. A study published by Gandhi et al. in 1996 reported largely increased absorption in the heads of children. With respect to a risk assessment to the effects of EMF of mobile phones, this is a very important issue, since 1) the use of mobile phones by children is already very common and will increase further, 2) head phantoms used for compliance test of mobile phones are based on the heads of adults and 3) children are the group within society which should be protected most carefully against adverse health effects of any agent.

The objectives of this thesis are summarized in the following list:

- Setups have to fulfill a number of technical and biological requirements. A comprehensive list of these requirements is given and a procedure for the realization of exposure setups is proposed.

- Before in vivo and in vitro experiments for risk assessment can be performed, it is essential to know the actual exposure of mobile phone users. A short overview of the knowledge on the absorption in the heads of mobile phone users with special emphasis on children is given. Since the results with respect to the exposure of children were contradictory, the differences in the absorption between the heads of adults and children are analyzed.

- The absorption mechanisms in flasks exposed to electromagnetic fields in the mobile communications frequency range are investigated. Based on that knowledge, the performance of different designs of exposure setups is compared to each others.

- The implementation of a setup optimized for the exposure of embryonic stem
cells under a special biological protocol is described. A careful dosimetric analysis of the setup is performed.

• For in vivo studies about effects of EMF on the central nervous system, the so-called carousel setup has been used for several studies at 835 MHz and 900 MHz. The latest available numerical and experimental methods are used to perform a dosimetric analysis with special emphasis on the frequency of the Iridium system at 1.62 GHz. The influence of size and position of the animal and of the number of rats in the setup on the absorption is evaluated experimentally and numerically. A careful comparison of experimental and numerical dosimetry including an evaluation of uncertainties is performed.
Chapter 3

Recommended Minimal Requirements and Development Guidelines for Exposure Setups of Bio-Experiments Addressing the Health Risk Concern of Wireless Communications

Abstract - The evidence currently available on the potential health effects from electromagnetic field (EMF) exposure has been largely judged as being too tentative and inadequate to meet criteria for assessing health risks. Some of the main reasons for these shortcomings lie in the incomplete description of the exposure and poorly characterized dosimetry. Well defined exposure conditions, however, are essential to obtain reproducible and scientifically valuable results. To facilitate the development of optimized setups for specific bioexperiments, this paper lists basic requirements and provides development guidelines for evaluation, optimization, construction and verification of exposure. In addition, definitions of minimum performance requirements for setups addressing the health risk concern of wireless communications are suggested.

3.1 Introduction

Although well defined exposure conditions for biological experiments are an obvious and indispensable prerequisite for interpretation and repeatability of results, the difficulties involved in obtaining such conditions have been severely underestimated by most groups conducting RF experiments. Consequently, design and characterization of exposure setups have become top priority within most research programs addressing the health effects of radiofrequency (RF) exposures (e.g., WHO [1], WTR [2], COST244 [3]). Indeed, the design and realization of exposure setups is a considerable engineering and scientific challenge requiring profound knowledge of numerical simulation methods and especially their application, near-field measurement techniques,
open and closed transmission systems, anatomy, physiology of tissue thermoregulation, dosimetry, material science and more.

Various reviews on exposure setups and their experimental and numerical dosimetry have been published, e.g., [4], [5], [6], [7], [8], [9]. Several authors have also listed requirements for exposure setups e.g., [10], [11], [12], [13]. Table 3.1 summarizes and extends these requirements in a list subdivided into Biological Requirements, Electromagnetic Requirements and Other Requirements. This list can serve as a checklist for all parameters that should be considered in the evaluation of a particular setup. However, such a list is of a rather general and qualitative nature and thus of limited practical usage.

The objective of this paper is to suggest guidelines and a procedure for design, optimization, construction and verification of exposure setups in order to facilitate the development and utilization of exposure setups which meet all the strict requirements for sound biological experiments. In addition, an attempt is made to define reasonable and achievable minimum quantitative requirements for bio-experiments addressing the health concern of wireless communications. It can be expected that this topic will be the main focus of studies in bioelectromagnetics in the near future. In particular, these minimum requirements might not only be of benefit as a yardstick for setup designers but also for reviewers and evaluation bodies of programs and studies.

### 3.2 Basic Considerations

The justification for lack of engagement in health risk evaluations is often the argument that proving the absence of any health effect of a chemical or physical agent is an impossibility. Although this might be true in the strict sense of proof, it is false with respect to the generation of a strong body of evidence for the absence of any effect. However, a body of evidence can only be considered to be strong if it is coherent and comprehensive with respect to the raised health concern and not an accumulation of more or less randomly collected negative findings. For example, even a large number of negative experiments can be absolutely meaningless if the investigated effects are irrelevant for public health or if the sensitivity of the single experiments is considerably poorer than the socially accepted risk tolerance for the particular agent.

The collection of a strong body of evidence is a considerable effort requiring the involvement of the best available science, sufficient funds and time. It must be based on a comprehensive program, the single studies of which must be driven by a hypothesis of the following kind: the electromagnetic fields X simulating the exposure characteristics of the mobile communications system A cause the response Y in the biological system Z. The relevance of the three variables X, Y, Z for the overall health risk assessment must be carefully examined. The exposure parameters X must be appropriate with respect to current and future exposure of users and the public, the response Y must be significant for public health and the system Z must be sensitive enough to detect even slightly increased risk factors.

Two major difficulties inherent in the risk assessment of low-level RF exposure considerably impair the resolution of this task: 1) the lack of established interaction mechanisms and 2) the impossibility to apply dose levels which are significantly greater than the strongest fields to which the public is exposed. The latter would
allow to extrapolate the results to reflect the relevant exposures after the dose/effect relationship has been established. This common toxicological approach cannot be applied since any dose significantly greater than the strongest daily exposure results in significant tissue heating, which in turn would mask any possible non-thermal effects.

The consequence is that the required body of evidence can only be compiled if 1) a broad range of the most severe health risk factors is investigated and 2) only the most sensitive experiments available are selected. However, the most sensitive biological experiments often require advanced equipment/procedures and adherence to strict standard protocols. Such protocols usually evolve over a long period of time from studies and experience studying the particular response Y of the biological system Z. Any deviations from this protocol entail the danger of introducing additional artifacts and changes in sensitivity. Therefore, any deviations from the standard biological protocol should be minimal. On the other hand, all the electromagnetic requirements must be met, and this often means that very elaborate systems are necessary to create the required fields at the location of the biological system. For example, highly uniform whole-body exposures are preferable for toxicological studies but are very difficult to achieve for RF exposures. This illustrates that fundamental conflicts may exist between the exposure setup and the requirements imposed by the biological experiment. A feasible compromise must therefore be found for each design. Although there are some basic designs for exposure setups, the setup has to be adapted and optimized to comply as well as possible with the particular biological protocol and the selected exposure conditions, i.e., the design and use of standard exposure setups may not be feasible and would only impair the relevance of the experiment.

The path from a hypothesis to the realization of an exposure setup suitable for the particular study design can be quite tedious. A procedure proven to be suitable is discussed in the following. However, even following such a step-by-step approach does not mean that the realization of an EMF exposure setup for a biological experiment is a straightforward procedure. Compromise and agreement are key aspects of the cooperation between biological and engineering groups needed to resolve any conflicting requirements. This means that a great deal of interdisciplinary consultation is required to realize a setup that is optimized with respect to the overall objectives.

3.3 Procedure and Tools for Evaluation, Optimization, Construction and Validation of Exposure Setups

The step-by-step approach presented in this section has evolved from the authors own experience and from others, e.g., [14] in developing exposure setups for biological experiments in the RF frequency ranges. The basic requirements listed in Table 3.1 should be kept in mind throughout all stages of the realization of an exposure setup. However, some requirements become more central during certain stages and are therefore listed explicitly. Fig. 3.1 illustrates the concept that is described in the following.
3.3.1 Working Hypothesis

The working hypothesis of the study should first be precisely formulated. The rationale upon which the hypothesis is based should be carefully examined, and its significance with respect to the overall objective (e.g., health risk, therapeutic applications, etc.) evaluated. This includes implications for the exposure (e.g., minimum number of samples required to achieve the needed statistical significance, induced field strengths, duration, modulation, etc.).

3.3.2 Biological Protocol and Requirements on Exposure Parameters

It is important to describe the basic design of the study in detail before any decision on the exposure setup is made. The following points are of special importance for the design of the exposure setup.

Further points depend on the particular study. In a first step the derived requirements should be ranked according to their priority, since the optimization procedure will most likely reveal that some of the requirements stand in conflict to others.

*Biological Design:*
The most limiting requirements and constraints on the exposure setup are usually those imposed by the minimum requirements of the biological experiment itself. Requirements may dictate the equipment needed (e.g., visual access by microscope, restrictions to certain flasks, etc.), procedures (e.g., handling, fast access during the experiment, animal needs, certain cell distributions within the experiments, etc.), and the environment (e.g., temperature, pressure, atmospheric control, etc.).

- The overall duration of the experiment influences the choice of design and materials for the setup.

- The anticipated extent of the effect and the variation of the biological response are important criteria to determine the required homogeneity of the EMF exposure.

- Number of samples or animals necessary for statistical significance

- Single or double blind study design

*Exposure Parameters:*

- Frequency

- Precise definition of the modulation schemes (e.g., GSM, speech modulation, sub-frames, DTX, rise time of pulses, etc.). The modulation must be relevant with regard to the overall objective of the study.

- Polarization of the induced electromagnetic field with respect to the biological system, e.g., orthogonal or parallel to the cell layer.

- *In vivo* experiments: The target tissue must be defined, and it must be stated whether whole body, partial body or local exposure is required.

- The required SAR levels and field amplitudes at the location of the cell culture or inside the animal tissue must be defined. The SAR levels and field amplitudes must be relevant with regard to the overall objective.

- Definition of the envisaged field distribution at the site of interest, e.g., the maximum tolerable deviation from homogeneous field distribution or the degree of correspondence with the actual exposure in human subjects.

- On and off times of exposure

*Other Requirements:*

- Budget

- Largest acceptable size of the setup
3.3.3 Decision on Basic Design of Exposure Setup

A considerable body of knowledge on the advantages and disadvantages of various setups has been built up in the recent past. For example, various setups have been proposed and used for in vitro experiments: waveguides [13], [15], radial transmission lines [16], Crawford TEM cells [17], [9] and RF chambers [18]. An advanced level of expertise in electromagnetic fields and the performance and characteristics of various exposure setups is necessary to evaluate the different designs. If a new exposure setup design should be used, it is advisable to perform a preliminary feasibility study.

The designs under consideration must be evaluated with respect to the criteria listed in Section 3.2. In most cases the most important criterion is the minimum departure from the biological standard protocol. The initial preference for a particular design might need revision if the detailed adaptation and optimization of the setup described in the next stage reveals shortcomings in the first design.

3.3.4 Adaptation and Optimization of Exposure Setup and Study Design

The adaptation and optimization of the exposure setup with respect to the parameters ranked according to their priorities (see Section 3.3.2) requires an efficient and powerful analysis tool. In most cases, a high-end simulation software package based on the finite-difference time-domain (FDTD) technique is the most suitable tool. For some special cases, packages based on other simulation techniques might also be applicable. Close cooperation between the biological and medical experts who conduct the study and the engineering experts designing the setup must be established in order to achieve a feasible compromise in the midst of many conflicting requirements.

3.3.5 Performance of the Setup and Numerical Dosimetry

After the details of the setup have been fixed, a detailed study must be performed to characterize the electrodynamic performance of the setup. This should include dosimetry. A detailed numerical representation of the setup which also simulates the metallic and plastic material of the setup as well as of the closest vicinity, neighboring samples or animals, etc. must be generated. Special attention must be paid to the modeling of the animals in in vivo studies. The results of the numerical dosimetry must include a detailed description of induced E- and H-fields and the SAR distribution. A thorough uncertainty analysis of the evaluation is of great importance.

In addition, the evaluation must also include a sensitivity analysis on any parameters that might vary during the experiments, e.g., size, posture and movements of animals or amount of medium, location variations of the cells within the flasks and the flasks within the setup.

Based on the results of the performance of the setup, some changes in the details of the design involving a return to the adaptation and optimization stage of the setup might be necessary. Several such cycles may be necessary until the final design of the setup has been fixed.
3.3.6 Construction of the Setup

- Signal Source: Evaluation of the RF equipment (generator, amplifier, couplers, etc.) which meets the requirements (e.g., frequency, modulation scheme, power, noise level, etc.) at reasonable cost. Basic information should already be available during the optimization process.

- Monitoring and Controlling: Implementation of the hardware/software that enables monitoring of all relevant technical and biological parameters during the course of the experiment.

- Sham Exposure: The construction must guarantee that the presence or absence of the specified electromagnetic fields constitutes the only difference between exposed and sham exposed samples/animals. Special attention must be paid to the temperature rise, vibrations and other interferences.

- Manageable by Non-Engineering Personnel: The setup should have a minimal likelihood of failure when handled by non-engineering personnel. This requires a user-friendly interface for the control software.

- Materials: The materials used must be non toxic and withstand the prevailing environmental conditions (e.g., high humidity, periodical sterilization) for the duration of the experiment.

- Costs: The cost of the setup should be reasonable. Commercially available parts (off-the-shelf) should be used if available.

3.3.7 Testing of Setup and Experimental Dosimetry and Validation

None of the setups should be used before the numerical results have been subject to thorough experimental validation. This includes verification of the incident as well as induced fields at specific locations. Tools suitable for such experimental evaluations have been described in the literature (e.g., [7], [19]). The locations chosen for validation should be relevant for the performance of the particular setup. The correspondence should be well within the assessed uncertainty of the combined numerical and experimental assessments. Examples for such evaluations are given in [20], [16], [8], [13].

Other checks and evaluations to be performed are:

- Long-term reliability test;
- Check of controlling and monitoring components for interference under worst-case considerations;
- Check of the environmental requirements under worst-case conditions (e.g., temperature rise inside the samples/animals);
- Assessment of the exposure of the samples to ELF;
- Assessment of the RF leakage.

In addition, one of the first biological experiments should be devoted to confirmation that there are no differences between the exposed group and control group apart
from the electromagnetic exposure, e.g., by a sham-sham experiment. Furthermore, the performance of some standard tests should allow determination of whether the setup introduces any artifacts.

3.4 Minimum RF Performance Requirements

In order to provide some guidelines for experimenters and reviewers, minimum performance requirements are suggested in the following. They are an indispensable prerequisite for obtaining results that can be appropriately interpreted and replicated. Deviations from these minimum requirements might be justified for some experiments, but the implications of any such deviations should be carefully examined and documented in the report.

3.4.1 Signal Characteristics

Since the amplitude modulation of RF signals can be relevant for possible low-level biological effects, the signal should properly reflect the spectrum of amplitude modulation to which an actual user of the investigated wireless system is exposed. For example, an experiment conducted with a simulated GSM exposure only containing the 217 Hz component is, in general, not sufficient. The advantages/disadvantages of also considering other components of ELF amplitude-modulation must be carefully weighted (e.g., those components elicited by the subframes, by the speech signal, utilization of several channels, DTX modes, etc.). In order to provide adequate information for the handset as well as for the base station within the same experiment, use of signals has been proposed which contain the maximum spectral power of all modulation components generated by the handsets as well as by the base stations.

3.4.2 Maximum Possible Exposure

The setup should enable an exposure of the tissue or cell culture to induced field strengths that are considerably larger (factor of 3 or more) but at least equal to the maximum values locally induced in the user's tissue. Although this value largely depends on several parameters (device, tissue, etc.) for the handset, the maximum local exposure (averaged over a small volume, e.g., a few thousand cells) can be considerably larger than the values for the spatial peak SAR (< 6 mW/g) for most wireless cellular systems in use today.

3.4.3 Ambient RF fields and Noise Level

The noise level and exposure to the ambient field should be at least 30 dB below the lowest exposure being tested. The same requirements apply for the sham exposure.

3.4.4 Duration of Exposure

The duration of exposure should reasonably reflect the maximum daily exposure. A growing proportion of previous wire phone traffic is now taking place on cellular systems. This trend will continue with improvements in battery life and lowering of service costs. Accumulated usage of several hours daily shall become the norm for a small but substantial minority of people. On the other hand, long-term exposure in the vicinity of base stations is also an issue of concern raised by the public.
The exposure due to base stations, however, is generally considerably weaker than exposure from handsets.

3.4.5 Field Distribution

The induced field distribution of *in vitro* experiments should be as homogeneous as possible. Although the geometry of the cell culture may be simple (e.g., monolayer of cells in a Petri-dish), excellent homogeneity is quite difficult to achieve. Our experience shows that an overall standard deviation from homogeneity of less than 30% is reasonable and should be aimed at. Reasonably homogeneous field distributions are often not achievable for *in vivo* experiments. However, the setup should enable an accurate description of the distribution and magnitude of the induced fields inside the different tissues and organs.

Since the distributions of the induced field strengths often considerably deviate from Gaussian distributions, distribution charts should be provided as well as an adequate description of the polarization of the induced fields.

3.4.6 Assessment Uncertainty of the Induced Field Strengths

The uncertainty of the absolute assessment of the induced field strength and distribution in particular organs and cell cultures can be quite large, i.e., well exceeding 6 dB. It is therefore important that the uncertainty is carefully evaluated and documented, e.g., by following the NIST guidelines [21]. The value to be aimed at is <1.5 dB (confidence level 95%).

3.4.7 Experimental Variations of the Exposure

The uncertainty evaluation should only include the uncertainty of the dosimetric evaluation for the specific situation. In addition, the dependence of the induced field strength and distribution can significantly depend on the location (i.e., movements), posture and size of the animal, amount and shape of medium liquid, etc. The variation should be small and not exceed 1-2 dB (standard deviation) for *in vivo* studies. This variation can be kept smaller in the case of *in vitro* experiments, i.e., < 0.5 dB. This is a very important parameter, since the variation should be considerably smaller than the separation of the incident power in multi-level exposure experiments, in order to allow interpretations with respect to the dose-effect relation.

3.5 Conclusions

The wide variety of biological protocols and the strict requirements for an EMF exposure setup make it impossible to develop standardized exposure setups. Close cooperation between biological and medical scientists and engineers is necessary to establish setups which are both well adapted to the biological protocol and also meet all requirements for a well characterized EMF exposure. The step-by-step approach and adherence to the minimum requirements with regard to RF performance as presented in this paper provide a guideline for setup development and a basis for reviewers and agencies whose duty it is to evaluate the significance of proposed or published studies. Undoubtedly, an immense effort in time and expense is required to generate the necessary body of evidence. On the other hand, the direct and
indirect costs of continuous concern and uncertainty of the public, consumers and governmental officials regarding possible health implications would certainly exceed this expense by a multiple of magnitudes.

References


Table 3.1: Checklist of basic requirements for setups to be used in RF studies.

<table>
<thead>
<tr>
<th>Biological Requirements</th>
<th>(\text{The setup should only require minimal deviation from the standard biological protocol.})</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Biological Protocol</td>
<td>All environmental requirements for the specific experiment must be strictly adhered to. These usually include sterility, stabilized temperature, low stress levels, atmospheric control, accessibility, etc.</td>
</tr>
<tr>
<td>- Environment</td>
<td>The setup must allow for exposure of a sufficient number of samples or animals in order to achieve the required statistical significance within a reasonable time.</td>
</tr>
<tr>
<td>- Statistical Power</td>
<td>The signal source must be precisely defined. This includes frequency, modulation scheme, power stability, noise level, etc.</td>
</tr>
<tr>
<td></td>
<td>The electric and magnetic field strengths and polarization must be well defined at the site of the cell culture \textit{in vitro} or in specific tissues of the animals \textit{in vivo}, respectively.</td>
</tr>
<tr>
<td></td>
<td>The field distribution should be homogenous, i.e., the deviation from homogeneity should be as small as possible and not greater than the variations of the biological response.</td>
</tr>
<tr>
<td></td>
<td>Although a homogeneous whole-body exposure cannot be achieved in most cases, the exposure should be well characterized for all tissues and, in general, should provide the least possible deviation from homogeneity. If the responses of specific organs/tissues are being investigated, partial body exposures can provide much more homogeneous exposures of the target organ/tissue. Another suitable approach is to generate exposures which provide similar field distributions in the tissues as in human exposures.</td>
</tr>
<tr>
<td></td>
<td>The sensitivity of experimental variation on the induced field strength and distribution (e.g., animal size, posture, location, etc.) should be minimal.</td>
</tr>
<tr>
<td></td>
<td>All controlling and monitoring devices should be rigorously checked for electromagnetic interference (EMI) under worst-case considerations. Otherwise interference may cause failures or malfunctions of system components (e.g., of the temperature controlling circuit).</td>
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<tr>
<td></td>
<td>The fields radiated by the system beyond the confines of the laboratory should be electromagnetically compatible with commercial wireless services.</td>
</tr>
<tr>
<td></td>
<td>The exposure setup should not subject personnel to exposures exceeding the safety standards.</td>
</tr>
<tr>
<td>Electromagnetic Requirements</td>
<td></td>
</tr>
<tr>
<td>- Signal Source</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>- Induced E-/H-Field Amplitude/Polarization</td>
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<tr>
<td>- Field Distribution (\textit{in vitro})</td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>- Field Distribution (\textit{in vivo})</td>
<td></td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>- Experimental Variations</td>
<td></td>
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<tr>
<td>- EMI</td>
<td></td>
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<tr>
<td>- EMC</td>
<td></td>
</tr>
<tr>
<td>- Human Safety</td>
<td></td>
</tr>
<tr>
<td>Other Requirements</td>
<td></td>
</tr>
<tr>
<td>- ELF Fields</td>
<td>RF exposure setups may also produce ELF fields. These unwanted fields must be characterized and kept as small as possible.</td>
</tr>
<tr>
<td>- Monitoring</td>
<td>The setup should enable monitoring of all relevant technical and biological parameters during the course of the experiment.</td>
</tr>
<tr>
<td>- Handling of Setup</td>
<td>The setup should be sufficiently failure tolerant to be handled by non-engineering personnel.</td>
</tr>
<tr>
<td>- Blind Study Design</td>
<td>The design should allow for blind or double blind studies.</td>
</tr>
<tr>
<td>- Cost</td>
<td>The cost of the setup should be reasonable.</td>
</tr>
</tbody>
</table>
Part II

Exposure of Mobile Phone Users
Chapter 4

Short Overview of the Knowledge on the Absorption in the Heads of Mobile Phone Users with Special Emphasis on Children

4.1 Introduction

The assessment of the electromagnetic fields inside the head of mobile phone users is a difficult task. A lately published review [1] gives a comprehensive overview over the experimental and numerical methods and discusses the results of the large number of studies on this topic. This chapter is mainly focused on the absorption in the head of children.

The use of mobile phones is already very widespread in all age groups including children. Since children can be expected to use phones for a considerable period from the age they are starting to speak, studies on the absorption in children’s heads should include children as small as 2 to 3 years. Therefore, it is obvious that it must be ensured that mobile phones are in compliance with the safety limits also for this user group, which is widely considered to be especially sensitive to environmental agents.

4.2 Absorption in the Heads of Adults

Since all established methods of measuring local RF electromagnetic fields are invasive (e.g. [1], [2]), the field inside the head of a mobile phone user cannot be measured directly. Numerical methods, especially FDTD, have been widely used to determine the absorption inside anatomical models of the human head (e.g. [3], [4], [5], [6], [7]). All these studies are based on numerical phantoms derived from MRI scans of adults. Older studies like [3] were restricted to voxels with dimensions of about 2 mm in each direction, which is rather crude compared to the fine anatomical details in a human head. Latest studies use resolutions as fine as 0.5 x 0.5 x 0.5 mm³ [7]. Although these voxel dimensions allow a detailed modeling of the tissue distribution in the head,
they are very crude compared to the small internal structures of a mobile phone.

The distribution of the electromagnetic field in the head of a mobile phone user is mainly determined by the incident H-field [8][9]. Therefore, the exposure caused by an actual phone depends on the current distribution inside the device. Since it is not possible to simulate this current distribution with sufficient precision, the most reliable method available to test the compliance of mobile phones with the safety limits is to evaluate the electromagnetic field caused by the actual phones inside an experimental head phantom [10]. Head phantoms for compliance testing must fulfill several requirements, the most important of which is to ensure that the assessed SAR values do not underestimate the exposure of a reasonable cross section of the MTU user group including children [10]. Therefore, it is essential to have quantitative data on differences in absorption between different individuals. The studies [5] and [6] were mainly focused on this topic and came to the conclusion that the variability of the tissue structures could be best covered by replacing the non-homogeneous structure by a homogeneous phantom of appropriate shape and dielectric material. That the head phantoms used for compliance testing are based on heads of adults (e.g. [10]) underlines the necessity to investigate carefully if there may be differences in absorption between the heads of adults and children.

4.3 Studies on the Absorption in the Heads of Children

In 1991 Dimbylow and Mann [3] published a numerical study on the absorption in an anatomical head phantom exposed at 900 MHz and at 1800 MHz. The field was either generated by a λ/2 antenna or by a λ/4 dipole mounted on the center or the corner of a metal box (15 cm tall, 6 cm wide and 2.4 cm deep). These numerical models of mobile phones were placed in different positions with respect to the head model and in distances between 1.5 cm and 3 cm from the head phantom. The head phantom with 10 different tissues and a resolution of 2 x 2 x 2 mm³ was derived from MRI scans of a male adult. The main focus of the paper was on the dependence of the absorption in the head on positions, distances and modeling of the mobile phone antenna. It also very briefly addressed the question whether the absorption is different in the head of children. The authors downscaled the head phantom linearly with a factor of 0.7 to create a phantom representing a one year old child. For a fixed distance of the box from the head phantom of 2 cm, the authors found that "the SAR values, averaged over 10 g, for the infant are comparable or in most cases lower than the values in the adult phantom".

In 1996 Gandhi et al. [4] published a study on the absorption in the human head and neck exposed at 835 MHz and 1900 MHz. The field was either generated by a λ/2 antenna or by a λ/4 or 3λ/8 dipole mounted on top of a metal box (15.5 cm tall, 5.73 cm wide and 2.96 cm deep) covered by a one voxel layer of dielectric material representing the plastic coating. Unfortunately, the paper does not precisely describe the positioning of the model of the phone relative to the head.

The numerical phantom was derived from MRI scans of a male adult with a height of 176.4 cm and a mass of 61 kg. The distance between the slices was 3 mm and the resolution of the images was 1.875 mm. Based on this data a full body model with voxel dimensions of 3 x 1.875 x 1.875 mm³ was developed which discriminated 15 different tissues in the head. Based on this model the authors created numerical phantoms for 10-year old children (average height 138 cm and average mass 32.5 kg
Table 4.1: Results of [4] for adult, "10-year old" and "5-year old children".

<table>
<thead>
<tr>
<th>MHz</th>
<th>adult</th>
<th>&quot;10-year old&quot;</th>
<th>&quot;5-year old&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>835</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak 1-voxel SAR [W/kg]</td>
<td>10.86</td>
<td>16.82</td>
<td>31.73</td>
</tr>
<tr>
<td>Peak 1-g SAR [W/kg]</td>
<td>2.93</td>
<td>3.21</td>
<td>4.49</td>
</tr>
<tr>
<td>Peak 1-voxel SAR for brain [W/kg]</td>
<td>1.62</td>
<td>3.02</td>
<td>4.62</td>
</tr>
<tr>
<td>Peak 1-g SAR for brain [W/kg]</td>
<td>1.13</td>
<td>1.42</td>
<td>1.56</td>
</tr>
<tr>
<td>Brain average [mW/g]</td>
<td>72.7</td>
<td>187.2</td>
<td>283.2</td>
</tr>
<tr>
<td>in-depth penetration</td>
<td>“increased for smaller heads”</td>
<td>“increased for smaller heads”</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>1900 MHz</th>
<th></th>
<th>&quot;10-year old&quot;</th>
<th>&quot;5-year old&quot;</th>
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<tbody>
<tr>
<td>Peak 1-voxel SAR [W/kg]</td>
<td>3.90</td>
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<td>6.20</td>
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<td>Peak 1-g SAR [W/kg]</td>
<td>1.11</td>
<td>0.90</td>
<td>0.97</td>
</tr>
<tr>
<td>Peak 1-voxel SAR for brain [W/kg]</td>
<td>0.29</td>
<td>0.42</td>
<td>0.61</td>
</tr>
<tr>
<td>Peak 1-g SAR for brain [W/kg]</td>
<td>0.20</td>
<td>0.25</td>
<td>0.31</td>
</tr>
<tr>
<td>Brain average [mW/g]</td>
<td>7.6</td>
<td>19.6</td>
<td>32.9</td>
</tr>
<tr>
<td>in-depth penetration</td>
<td>“increased for smaller heads”</td>
<td>“increased for smaller heads”</td>
<td></td>
</tr>
</tbody>
</table>

1scaled adult head phantom
2results are normalized to a power of 600 mW at 835 MHz
3results are normalized to a power of 125 mW at 1900 MHz

according to [11]) respectively five year old children (average height 112 cm and average mass 19.5 kg according to [11]). The ratio of the average height of children of the required age and the height of the male volunteer was used as scaling factors in vertical direction. This resulted in factors of 0.782 respectively 0.635 for the 10-respectively 5-year old children. The scaling factors in horizontal direction were calculated so that the mass of the resulting scaled numerical phantom were identical with the average mass of children of the required age. This calculation resulted in scaling factors of 0.805 for the 10-year old children respectively 0.693 for the 5-year old children.

The results of [4] are summarized in Table 4.1. The authors state that:

- even though the peak 1-g SAR's are fairly similar for the three models at 1900 MHz, the 1-g SAR’s are considerably higher for the smaller head sizes at 835 MHz;

- the peak 1-voxel SAR’s are higher and a larger in-depth penetration of absorbed energy or higher SAR’s are obtained for the smaller head models both at 835 MHz and 1900 MHz;

- increased SAR’s are obtained for smaller head models at 835 MHz because of the larger depth of penetration;

- the higher 1-voxel SAR’s for the smaller models are likely due to the thinner ears, which results in the antennas being somewhat closer to the region of highest SAR’s.

In conclusion, the results of [3] and [4] are in clear contradiction to each other. While [3] found that the SAR values, averaged over 10 g, for the infant are comparable
or in most cases lower than the values in the adult phantom, [4] reported a drastic increase of the 1-g averaged SAR's in smaller head phantoms at 835 MHz.

Both studies are insufficient, since they make predictions on the absorption in the head of children by using scaled down models of adult heads. Especially the scaling method used in [4] is completely inappropriate for scaling human head phantoms. The proportion of head and body changes drastically between birth and adulthood. Obviously, it is not realistic that the horizontal scaling factors depend on the body weight of the adult volunteer. This clearly shows that additional studies are necessary to investigate in detail if there may be differences in absorption of electromagnetic fields emitted by MTE between the heads of adults and children.

References


Chapter 5

Differences in Energy Absorption between Heads of Adults and Children in the Near Field of Sources

Abstract - This paper was motivated by a recent article [1] in which the levels of electromagnetic energy absorbed in the heads of mobile phone users were compared for children and adults at the frequencies of 835 MHz and 1900 MHz. Significant differences were found, in particular substantially greater absorption in children's heads at 835 MHz. These findings contradict other studies in which no significant changes had been postulated. The clarification of this issue is crucial to the mobile communications industry, since current SAR evaluations as required by the FCC are only performed with phantoms based on the heads of adults. In order to investigate the differences in absorption between adults and children due to their differing anatomies, simulations have been performed using head phantoms based on MRI scans of an adult (voxel size 2 x 2 x 1 mm³) and two children (voxel size 2 x 2 x 1.1 mm³) of the ages of 3 and 7 years. Ten different tissue types were distinguished. The differences in absorption were investigated for the frequencies of 900 MHz and 1800 MHz using 0.45λ dipoles instead of actual mobile phones. These well defined sources simplified the investigation and facilitated the comparison of previously published data obtained from several numerical and experimental studies on phantoms based on adults. All simulations were performed using a commercial code based on the Finite Integration Technique. The results revealed no significant differences in the absorption of electromagnetic radiation in the near field of sources between adults and children. The same conclusion holds when children are approximated as scaled adults in a similar way as in [1].
5.1 Introduction

Mobile phones have become an object of daily use for an ever increasing part of the population in a wide range of countries. Today mobile phone use encompasses everyone from small children to the elderly. Several regulatory bodies world-wide have recently issued safety recommendations or requirements regarding the maximum permissible electromagnetic exposure from handheld mobile communications equipment (MTE), e.g., [2], [3], [4]. Common sense demands that the general practice be such that these requirements are satisfied not only for a certain majority group but for all potential users, including in particular children and the elderly. These last two groups are generally more vulnerable to the hazards of exposure to physical or chemical agents.

At present the industry tests mobile communications devices for compliance with the basic limits for electromagnetic exposure using head phantoms that are based exclusively on data from adults [5], [6]. This approach was called into question in a study recently published by a research group at the University of Utah [1]. The authors of this study reported a deeper penetration and significantly greater spatial peak specific absorption rates (SAR) in children.

However, these results do not correspond with those of [7], [8] and [9], the conclusions of which can be summarized as follows: 1) the spatial peak SAR is scarcely affected by the size and the shape of the human head for electromagnetic sources at a defined distance from the skin. 2) Compared to other factors, such as the distance of the source from the head and design of the device, these studies reported that the effects caused by differences in complex anatomy were minimal, especially when volume-averaged values were considered.

The immediate clarification of this contradiction has become crucial for industry and the public since the US Federal Communication Commission has stipulated routine SAR evaluation of equipment prior to authorization or use. The objective of this study was a detailed investigation of the possible differences in SAR distribution and averaged SAR values for anatomically realistic children's phantoms and the comparison of these findings with data from phantoms derived from adults. In addition, simulations with scaled-down phantoms of the adult head were performed. This allowed a direct comparison with the findings of [1], which are exclusively based on simulations with scaled-down head phantoms.

The following investigations were performed for the major frequency bands utilized for mobile communications in Europe, i.e., 900MHz and 1.8GHz. The frequencies used in [1] differ only slightly, thus allowing the direct comparison of the results.

5.2 Numerical Techniques and Head Phantoms

5.2.1 Simulation Technique

All simulations were performed with the commercially available code MAFIA [10], which is based on the Finite Integration Technique (FIT) [11]. This code has proven to be robust and highly suitable for absorption studies in bioelectromagnetics (e.g., [8], [12], [13], etc.). Although it constitutes a slightly different conceptual approach to that of the Finite Difference Time Domain (FDTD) technique, both approaches lead to the same basic numerical scheme. The open domain was bounded by first-
order Mur absorbing boundary conditions. Simulations with different distances of the boundaries to the EM source showed that a distance of 25 cm was sufficient. Excitation was done by a smoothly-increasing harmonic function and the computation was terminated after steady state was reached (usually after 10 periods). Computational time for circa 5 Million voxels was typically 10 hours on a Sun Sparc Ultra 2 computer. Validated results for similar configurations were available [8], [9], so that experimental verifications could be dispensed with.

5.2.2 Anatomically Realistic Phantoms

Detailed phantoms of heterogeneous human heads can be developed using magnetic resonance imaging (MRI) scans. For this study MRI scans of an adult and two children of the ages of 7 and 3 were chosen. None of these MRI data sets showed any obvious pathological changes. The work of distinguishing ten different tissue types was supported by medical students, whereby no distinction was made between white and grey brain tissue. The discretized heads are shown in Fig. 5.1. The voxel sizes chosen for the simulations were 2 x 2 x 1 mm³ for the adult M_adult and 2 x 2 x 1.1 mm³ for the children M_7y and M_3y, resulting in a total number of cells for the simulation of between 3.8 million and 5.5 million (Table 5.1). Since the EM source was located near the ear, the discretization was made finer along the ear-to-to ear axis, in order to guarantee a suitable representation of the thin tissue layers in this region. The z-axis of the chosen coordinate system is parallel to the ear-to-to ear axis, while the x-axis is parallel to the vertical axis of the body. The origin of the coordinate system is on the external surface of the head phantom directly above the anterior edge and about 5 mm above the upper edge of the pinna.

The values of the relative permittivity εᵣ and conductivity σ assigned to the different tissue types (Table 5.2) were obtained from a dielectric database [14]. The brain was simulated by averaged values between white and grey brain tissue. Comparing the data in different publications reveals a wide spread in the values for the electric parameters of different types of tissues. This uncertainty is not of great importance for this study, since not absolute values but differences were of interest. However,
Table 5.1: Three different head models and three scaled-down head models.

<table>
<thead>
<tr>
<th>model</th>
<th>voxel size (mm$^3$)</th>
<th>total number of voxels</th>
<th>circumference of the head</th>
</tr>
</thead>
<tbody>
<tr>
<td>$M_{\text{adult}}$</td>
<td>2x2x1</td>
<td>5.52x10$^6$</td>
<td>57 cm</td>
</tr>
<tr>
<td>$M_{1.7}$</td>
<td>2x2x1.1</td>
<td>4.05x10$^6$</td>
<td>51 cm</td>
</tr>
<tr>
<td>$M_{3.4}$</td>
<td>2x2x1.1</td>
<td>3.79x10$^6$</td>
<td>50 cm</td>
</tr>
<tr>
<td>$M_{0.93}$</td>
<td>2x2x0.93</td>
<td>4.21x10$^6$</td>
<td>53 cm</td>
</tr>
<tr>
<td>$M_{0.88}$</td>
<td>2x2x0.88</td>
<td>4.12x10$^6$</td>
<td>50 cm</td>
</tr>
<tr>
<td>$M_{0.67}$</td>
<td>2x2x0.67</td>
<td>4.66x10$^6$</td>
<td>38 cm</td>
</tr>
</tbody>
</table>

Table 5.2: Electric parameters for 900 MHz and 1800 MHz [14].

<table>
<thead>
<tr>
<th>tissue</th>
<th>900 MHz $\epsilon_r$, $\sigma$ [mho/m]</th>
<th>1800 MHz $\epsilon_r$, $\sigma$ [mho/m]</th>
</tr>
</thead>
<tbody>
<tr>
<td>bone</td>
<td>20.9, 0.33</td>
<td>19.7, 0.55</td>
</tr>
<tr>
<td>skin</td>
<td>40.7, 0.65</td>
<td>38.4, 0.99</td>
</tr>
<tr>
<td>fat</td>
<td>10.0, 0.17</td>
<td>9.4, 0.25</td>
</tr>
<tr>
<td>muscle</td>
<td>57.4, 0.82</td>
<td>55.2, 1.30</td>
</tr>
<tr>
<td>brain</td>
<td>44.2, 1.00</td>
<td>42.3, 1.21</td>
</tr>
<tr>
<td>CSF</td>
<td>79.1, 2.14</td>
<td>77.8, 2.83</td>
</tr>
<tr>
<td>blood</td>
<td>55.0, 1.86</td>
<td>54.0, 2.27</td>
</tr>
<tr>
<td>eye:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vitreous humour</td>
<td>36.6, 0.51</td>
<td>34.7, 0.87</td>
</tr>
<tr>
<td>lens</td>
<td>51.6, 0.90</td>
<td>49.5, 1.33</td>
</tr>
<tr>
<td>connective tissue</td>
<td>54.9, 1.17</td>
<td>52.7, 1.67</td>
</tr>
<tr>
<td>air</td>
<td>1.0, 0.0</td>
<td>1.0, 0.0</td>
</tr>
</tbody>
</table>

significant differences in the electrical parameters of corresponding tissue types in adults and children would have a direct impact on the findings. No study addressing this question has been found in the literature. Nevertheless, possible differences are discussed in Section 5.4.

In addition, simulations with homogeneous phantoms equivalent in shape to the three heterogeneous phantoms were performed at 900 MHz by setting the parameters of all tissues to $\epsilon_r=43.5$ and $\sigma=0.90$ mho/m. These parameters are equivalent to those used in [8].

5.2.3 Scaled Phantoms

The developmental changes in the anatomy of the human head follow a course quite different to that of the remaining body. Table 5.3 shows the data of a statistical evaluation of head circumferences [15]. Thus, head growth is very rapid in the first 12 months of life, i.e., the head circumference of a one year old child is already circa
The thickness of the cranial bone generally shows strong linear growth during the first 6 years of life and slows down significantly afterwards. Hence, there is a much greater relative difference in cranial thickness between small children and adults than between their head circumferences [16].

Modeling children heads by merely scaling-down adult heads can at best only represent a tentative approximation. The method proposed by the authors of [1] uses height and weight data of the male volunteer from which the head phantom was derived. The average heights and weights of children of the appropriate age groups were used to obtain the scaling factors for the scaled-down head phantoms. The cell dimension parallel to the body's vertical axis was reduced by a factor corresponding to the ratios of their heights. In the plane orthogonal to the body's vertical axis the dimensions of the cell were reduced until the ratio of the cell volumes corresponded to the ratio of the weights. This resulted in a factor of 0.635 for a 5-year-old child along the vertical axis and a factor of 0.693 for the two orthogonal axes [1]. The first head in Fig. 5.1 was generated using approximately the same scaling factor of 0.67 for all three axes. Table 5.3 shows that the resulting head circumference corresponds more to that of a new-born than to that of a five year old child.

For this study the adult head was scaled down by the factors 0.93, 0.88, and 0.67. The head models $M_{0.93}$ and $M_{0.88}$ had the same head diameter in the ear-to-ear direction as the models of the two children of the ages of 7 and 3 years, described above. The scaling factors correspond well with the statistically averaged factors for children of this age in Table 5.3. Using the same scaling factor for all three dimensions is a good approximation, since the growth of the base of the skull is nearly uniform in all directions [15], [17]. For the scaled-down head phantoms the cell dimensions along the z-axis were changed according to the scaling factor, in order to preserve the sequence of tissue layers near the feeding point of the dipole (Table 5.1).

### Table 5.3: Average head circumference for different ages [15].

<table>
<thead>
<tr>
<th></th>
<th>female</th>
<th></th>
<th>male</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>adult</td>
<td>54.3±1.2 cm</td>
<td>100%</td>
<td>56.4±1.6 cm</td>
<td>100%</td>
</tr>
<tr>
<td>7 years</td>
<td>51.5±1.3 cm</td>
<td>95%</td>
<td>52.6±1.4 cm</td>
<td>93%</td>
</tr>
<tr>
<td>3 years</td>
<td>49.5±1.2 cm</td>
<td>91%</td>
<td>50.8±1.4 cm</td>
<td>90%</td>
</tr>
<tr>
<td>1 year</td>
<td>45.8±1.2 cm</td>
<td>84%</td>
<td>47.1±1.3 cm</td>
<td>84%</td>
</tr>
<tr>
<td>newborn</td>
<td>36.4±1.1 cm</td>
<td>67%</td>
<td>37.1±1.3 cm</td>
<td>66%</td>
</tr>
</tbody>
</table>

84% of its adult value.

5.2.4 **EM Source**

The objective of this study was to investigate possible differences in the absorption due to differences between the anatomy of adults and children. The use of a model of a mobile phone would involve many additional parameters specific to that model, such as different distances between the currents on the device and the skin, as well as the current distribution itself. Use of a dipole instead does entail a number of advantages:
• Few parameters define the excitation. Therefore, it is easier to attribute differences in absorption to differences in anatomy.

• A direct comparison with the results in [8] and [9] is possible.

• The SAR distribution is mainly determined by the square of the incident H-field [7], which is proportional to the square of the feedpoint current for a given distance. It is therefore reasonable to normalize all calculations to the same feedpoint current instead of the same antenna input power.

A 0.45λ dipole was positioned at a distance of 15 mm from the head on the z-axis and oriented parallel to the body axis. All values were normalized to an antenna current of 100 mA_{rms}.

5.3 Results

5.3.1 SAR Distribution at 900 MHz

Since the mass densities of the various tissue types are only known with a large degree of uncertainty, the results are compared in terms of the volume related value SAR_{V}^{V} = \rho \text{SAR}. The index V indicates that the unit of SAR_{V}^{V} is mW/cm³ instead of mW/g for the SAR. For wet tissues having a mass density of about 1 g/cm³, SAR_{V}^{V} and SAR are almost equivalent.

In Fig. 5.2 the SAR_{V}^{V} distribution (plane y=0) is compared for the anatomically realistic head phantoms of the adult and the two children. Fig. 5.3 shows the SAR_{V}^{V} distributions in the scaled phantoms (factors 0.93, 0.88, and 0.67). Despite the large differences in size, shape, and tissue distribution of the heads, the SAR distributions are quite similar. Significantly, no differences in the absolute in-depth penetration are discernible. The relative depth of penetration is larger for the smaller heads, a logical consequence of the smaller head diameter.

Figs. 5.4 and 5.5 show the quantitative distribution of the SAR_{V}^{V} on the z-axis, i.e., along the shortest line connecting the feedpoint and sagittal planes. The only difference observable between the differently scaled head phantoms is a shift of the maxima and minima. This was to be expected, since the scaling alters the thickness of the various tissue layers. The SAR_{V}^{V} distributions along the z-axis of the three anatomically realistic head phantoms in Fig. 5.4 show clear differences. These are caused by the differences in the anatomy of the heads at the height of the feeding point of the antenna, e.g., the seven year old child has a voxel of CSF on the z-axis, which causes the pronounced peak in the SAR_{V}^{V} distribution due to its high conductivity. The differences in the SAR_{V}^{V} values near the surface of the heads are not greater than those found in [8] between the three head phantoms of adults. The SAR_{V}^{V} distributions on the z-axis of the homogeneous head phantoms in Fig. 5.6 demonstrates that size and shape alone have only a very slight effect.

5.3.2 Averaged SAR_{V_{av}}^{V} Values at 900 MHz

The volume averaged spatial peak SAR_{V_{av}}^{V} values were determined by shifting a cube of side length 10 mm (1 cm³) and a cube of side length 21.5 mm (10 cm³) across the head volume and computing σ||E||² averaged over the cubes at every position.
These values closely correspond to the 1 g and 10 g averaged SAR values, since the maximum values in the cubes are mainly found in areas with wet tissue.

In Figs. 5.7 and 5.8 $\text{SAR}_{1cm^3}^V$ values averaged over 1 cm$^3$ and 10 cm$^3$ for the various heads and different modelings are compared. As expected, the $\text{SAR}_{10cm^3}^V$ values have a smaller variation than the $\text{SAR}_{1cm^3}^V$ values, due to the larger averaging volume. The results for the two children and for the scaled heads differ only slightly from those of the adult. The variations between the six head phantoms in Figs. 5.7 and 5.8 are not larger than those found in [8] between phantoms of different adults. Therefore, no indication of a systematic increase with decreasing size or age could be found at
5.3.3 Radiated and Absorbed Power at 900 MHz

Since the impedance of the antenna is affected by the scattered field from the head phantoms, keeping the feedpoint current constant results in different antenna input powers for different head phantoms. In Fig. 5.9 the antenna input power, the power absorbed in the non-homogeneous head phantoms and the power radiated are given for all head phantoms. The variations in the input power of the antenna are quite small, whereas the ratio of radiated to absorbed power varies to quite an extent. As expected the efficiency (defined in this context as radiated power divided by antenna input power) increases with decreasing head size.

5.3.4 Distance Dependence at 900 MHz

The distance between the antenna of a mobile phone and the head of the user may be smaller than 15 mm. To exclude the possibility that a difference in the absorption
Figure 5.6: The SAR\textsuperscript{V} distribution on the z-axis for the homogeneous modeling of the head phantom of the adult, the three scaled down models and the two head phantoms of the children at 900 MHz.

Figure 5.7: The SAR\textsubscript{1\text{cm}^{3}} values for the non-homogeneous and the homogeneous modeling of the head phantom of the adult, the three scaled down models and the two head phantoms of the children at 900 MHz.

between adults and children may occur at smaller distances, the distance was varied between 3 mm and 30 mm. Fig. 5.10 shows the dependence of the SAR\textsubscript{1\text{cm}^{3}} on the antenna distance for the head phantoms of the adult and the three year old child. For the dependence on the distance there is no significant difference between the two phantoms. Fig. 5.11 compares the dependence of the SAR\textsubscript{1\text{cm}^{3}} values on the antenna distance for the homogeneous and the non-homogeneous modeling of the head phantom of the three year old child. Both curves are nearly parallel. As expected, the homogeneous modeling overestimates the SAR\textsubscript{1\text{cm}^{3}}, but only to a small extent.
Figure 5.8: The $\text{SAR}_{10\text{cm}}^V$ values for the non-homogeneous and the homogeneous modeling of the head phantom of the adult, the three scaled-down models and the two head phantoms of the children at 900 MHz.

Figure 5.9: The antenna input power, the power absorbed and radiated as well as the ratio of absorbed power to the antenna input power for the different non-homogeneous phantoms at 900 MHz.

### 5.3.5 Absorption at 1800 MHz

As the results of previous studies have already shown, the absorption at 1800 MHz is similar to that at 900 MHz. The only important difference is that the absorption is even more localized at 1800 MHz [8],[9]. The simulations performed for this study confirm these findings. Figs. 5.12 and 5.13 show the $\text{SAR}^V$ distribution on the $z$-axis for the three non-homogeneous phantoms and scaled phantoms respectively. In Fig. 5.14 the volume averaged values are given. The values for the two children and for the scaled heads differ only slightly from those of the adult. The variations between the six head phantoms in Fig. 5.14 are not larger than those found in [9] between phantoms of different adults. These data do not give any indications for
Figure 5.10: The dependence of the $\text{SAR}_{1cm^3}$ from the antenna distance for the head phantoms of the adult and the three year old child at 900 MHz.

Figure 5.11: The dependence of the $\text{SAR}_{1cm^3}$ values on the antenna distance for the homogeneous and the non-homogeneous modeling of the head phantom of the three year old child at 900 MHz.

differences in the absorption between adults and children at 1800 MHz.

The results for the head phantom of the adult do agree well with those of the three head phantoms of adults in [9]. Incorporating these values, the averaged $\text{SAR}_{1cm^3}$ for all four adult heads are in the range from 7.3 mW/cm$^3$ to 8.3 mW/cm$^3$ in the range from 4.5 mW/cm$^3$ to 5.0 mW/cm$^3$ for the $\text{SAR}_{10cm^3}$. The values for the seven year old child, 8.0 mW/cm$^3$ and 5.1 mW/cm$^3$, and those for the three year old child, 8.7 mW/cm$^3$ and 5.3 mW/cm$^3$, agree well with the values for the adults. The values for the differently scaled head phantoms of the adult lay in the range from 7.8 mW/cm$^3$ to 8.6 mW/cm$^3$ for the $\text{SAR}_{1cm^3}$ and in the range from 5.0 mW/cm$^3$ to 5.3 mW/cm$^3$ for the $\text{SAR}_{10cm^3}$. These data do not give any indications for significant differences between adults and children at 1800 MHz.
5.4 Discussion

5.4.1 Comparison with the Results of Other Authors

A number of papers have been published by other authors on the dosimetry of MTE, e.g., [18], [19], [20], [21], [1]. In most of these studies different models of mobile telephones held in various positions were used for excitation, which hinders the comparison of results and makes the comparison of absolute SAR\tiny{f} values nearly impossible. In [8] and [9] however, the same excitation was chosen as here. The good agreement between those results and the results of this study have been mentioned in Section 5.3. As mentioned in the introduction, the authors of [1] draw the conclusion that there are distinct differences in absorption between adults and children. As these results clearly contradict the findings presented here, a detailed discussion is necessary.

1. The head circumferences of the phantoms referred to as “5-year-old child” and “10-year-old child” corresponded more to those of a new-born and a few month
old baby respectively [15].

2. The penetration depth is scarcely dependent on the size of the head. The increased penetration postulated by the authors of [1] might refer to the relative penetration with respect to the head diameter.

3. The authors of [1] also report considerably higher SAR values averaged over the entire brain. The SAR was increased by a factor of 2.2 for the “10-year-old child” and by 3.3 for the “5-year-old child” at 835 MHz. These factors, however, are nearly identical to the ratio of the volume of the full sized phantom to the volume of the scaled down phantom, i.e., 2.0 and 3.3. An increase of the brain average exposure can be expected with small brain volume, since the absorption is only local and nearly independent of head size.

4. The authors found higher peak SAR values at both frequencies. This they attribute to the fact that the scaled-down phantoms had thinner ears, causing a reduced distance of the telephone to the region of highest SAR. That means that the effect of higher peak SAR values is a consequence of the positioning of the model of the mobile phone.

5. The SAR value of the “5-year-old child” at 835 MHz was more than 50% higher than of the adult. No increase was found at 1900 MHz. This contradicts the findings of this study and may therefore well be an effect of the phone position and not of the anatomy.

5.4.2 Possible Differences Due to Electric Parameters

All simulations for this study were done using the same electrical parameters for corresponding tissues in adults and children. Any clear differences in the parameters for the same tissues in adults and children could lead to significant changes in absorption. Unfortunately, there are no measurements on this subject available in the literature. An attempt was made, however, to estimate the differences of the electric
parameters for 1) skin, 2) bone, and 3) brain, based on the physiological changes that take place during the development from the newborn to the adult.

1. No hints for differences in the skin of adults and children that could effect the electrical parameters were found.

2. The growth interstices in the bone tissue of the newborn are less ossified. The ossification of the cranial sutures is usually completed at the age of forty [22]. It seems reasonable to suppose that the greater the ossification of bone structure the smaller the electrical conductivity. However, quantitative statements are not possible without measurements. Since the growth and ossification of the skull is largely localized, it is unlikely that the overall electrical parameters of whole bone structures change drastically.

3. The brain tissue of children contains less fat and more water than that of adults. The reason is to be found in the myelization of nerve cells in the brain, which is incomplete at birth. For the newborn the water content of the grey matter of the brain is 89% and that of the white matter 87%, whereas the corresponding values for adults are 82% and 72% [23]. This higher water content of the brain could increase the conductivity of this tissue. Myelization starts in the embryo and is not completed before adulthood. However, it is quantitatively negligible after the first year of life. [23] [24]. Therefore, differences in the electrical parameters of brain tissue are not to be expected after the first year of life. During the first year the increase of the spatial peak SAR due to the variations in electrical parameters is estimated to be less 20%.

In summary, significant differences in the spatial peak SAR values due to varying electrical parameters of tissues are not to be expected after the first year of life. Since it is reasonable to expect that newborn babies will not be exposed for periods of 6 minutes or longer, special consideration is not deemed necessary.

5.5 Conclusion

The results show that there is no difference in the absorption of electromagnetic energy at 900 MHz and 1800 MHz between MRI based phantoms of adults and children, nor for various linearly scaled adult phantoms. This contradicts the findings of [1], but is consistent with [7], [8], and [9], where the authors conclude that the spatial peak SAR is hardly affected by the size and the shape of the human head for electromagnetic sources at a defined distance from the head. The differences that were found between the head phantoms of an adult and two children are all attributable to normal anatomical variations and are not larger than those found between the head phantoms of different adults. Since these anatomical variations between different adults must be taken into account for compliance testing and safety considerations in any case, special considerations for children are not necessary, i.e., it is sufficient to perform compliance tests with a shell phantom representing the worst-case situation of an adult head [25].
References


Part III

Setups for \textit{In Vitro} and \textit{In Vivo} Experiments
Chapter 6

Basis for Optimization of \textit{In Vitro} Exposure Setups for Health Hazard Evaluations of Mobile Communications

Abstract - The main objective of this paper is a careful study of the fields induced in flasks exposed to RF electromagnetic fields. The study focuses on the widely used 60 mm Petri dishes and rectangular T-75 flasks for the two following cases: 1) cells in homogeneous suspension and 2) cell monolayers. The dependency of the coupling and the homogeneity of the SAR distribution on frequency (0.7 GHz to 2.5 GHz), polarization (E-, H- and k-polarizations) and the amount of medium (1.9 mm to 4.7 mm medium height) is studied. In addition, the effects of the environment, meniscus and field impedance as well as the distortion of the incident field are discussed. Based on these results, advantages and disadvantages of different fundamental designs of setups applied in the past are compared. These are TEM cells, HF-chambers, radial transmission lines (RTL), waveguides and wire patch cells. Furthermore, the major optimization parameters are identified for the development of highly optimized exposure setups enabling the conduct of high quality experiments.

6.1 Introduction

In 1996, the World Health Organization (WHO) initiated a research program addressing concerns about possible health effects from exposure to electromagnetic fields (EMF). One of the major focuses of this program is the exposure posed by mobile communications [1].

In the quality guidelines for EMF experiments, WHO explicitly emphasized the importance of well defined and characterized exposure conditions as one basis for health risk assessments. Although this may seem a very obvious requirement, many of the experiments conducted in the past have provided insufficient information about the exposure of the tissue or cell cultures. In many cases, only information about the incident field has been provided and not about the field strengths induced at
the location of the tissue samples or cells. This is greatly insufficient, since the ratio between induced fields and incident fields can vary by factors larger than 1000 depending on the exposure conditions, e.g., [2][3] and the variations of the induced fields within the same sample can be enormous.

In [4] quantitative definitions for well characterized exposures have been proposed for experiments addressing the health risk concerns of wireless communications. Important requirements for in vitro experiments are a low inhomogeneity of the SAR distribution (standard deviation of less than 30%) and the possibility to perform experiments at SAR levels in the range of the current safety standards.

Although these requirements are not very tight at first glance, they are only achievable by highly optimized setups. Average amplitude and distribution of the induced field strongly depend on various parameters which include frequency, polarization, field impedance, flask shape and size, amount of medium, meniscus size as well as the immediate environment (e.g., metal walls or other flasks). As a consequence of this strong dependence, in general, different experiments also require different exposure setups. In order to enable the development of highly optimized exposure setups, the mechanisms underlying the coupling between induced fields inside the medium and incident fields must be understood and all parameters which can have significant influence on the performance of the setup must be identified.

The objectives of the studies presented in this paper were the provision of this information as well as to evaluate the fundamental designs of in vitro exposure setups used and suggested in the past with respect to their advantages and disadvantages.

6.2 Methods

6.2.1 Dishes and Flasks

The body of the data collected in this study is based on the commonly used medium sized 60 mm Petri dishes and rectangular T-75 flasks. The dishes and flasks were modeled with the dimensions shown in Fig. 6.1. The limitation to the parameter space summarized in Table 6.1 was chosen under the assumption that many findings can be generalized to other flasks containing aqueous medium with vertical dimensions much smaller than the horizontal dimensions. This was verified by cross-checking the findings with results for dishes of other dimensions.

The dielectric parameters used during the course of this study were those of a typical aqueous medium called DMEM [5]. The parameters were measured at 37°C with the HP 85070A dielectric probe kit and are given in Fig. 6.2. The plastic material of the Petri dish was modeled as lossless with a relative permittivity of 2.5 [6].

6.2.2 Numerical Methods and Modeling

The simulations were conducted with the tool MAFIA (CST GmbH, Lautenschlägerstrasse 38, D-64289 Darmstadt) which is based on the finite-integration (FI) technique. Artifacts at material boundaries (staircasen effect) [7] were avoided by comparison of results of simulations with different spatial grid resolutions.

The finest resolution used was 0.5 mm x 0.5 mm x 0.236 mm. With computational domain sizes of (240 mm)^3 (as used at 1.6 GHz) and a nonuniform mesh with a global grading ratio of 10, this resulted in a grid with approximately 5.5 million cells. For parameter studies (Fig. 6.5) a lower resolution of 2 mm x 2 mm x 0.471 mm was used to
Table 6.1: Initial configurations studied:

<table>
<thead>
<tr>
<th>Incident field:</th>
<th>plane wave</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polarization:</td>
<td>E-, H-, and k-polarization</td>
</tr>
<tr>
<td>Frequency:</td>
<td>0.7 GHz to 2.5 GHz</td>
</tr>
<tr>
<td>Geometry of flasks:</td>
<td>60 mm Petri dish and T-75 flask</td>
</tr>
<tr>
<td>Medium parameters: see Fig. 6.2</td>
<td></td>
</tr>
<tr>
<td>Medium height:</td>
<td>1.9 mm to 4.7 mm</td>
</tr>
<tr>
<td>Location of cells: monolayer at the bottom or uniform suspension</td>
<td></td>
</tr>
</tbody>
</table>

Figure 6.1: Dimensions of 60 mm Petri dishes and T-75 flasks as used throughout the paper.

reduce computation time. Although this course resolution is not suited for deriving as precise numbers on the SAR distribution as the high resolution (used in Figs. 6.3 and 6.4), it is sufficient for studying parameter dependencies.

To assess the influence of menisci on the absorption in the medium, menisci of different sizes were modeled. The small meniscus had a maximum height of 0.75 mm.
and a maximum width at its bottom of 1.5 mm. It contained 0.14 ml of medium. The corresponding numbers for height, width and volume were 1.5 mm, 1.5 mm and 0.24 ml for the meniscus of medium size and 2.1 mm, 1.5 mm and 0.35 ml for the large meniscus.

The excitation was done with a plane wave oriented in E-, H- or k-polarization. E-polarization (respectively H- or k-polarization) means that the E-vector (respectively H- or K-vector) of the incident field is orthogonal to the largest surface of the medium (see Fig. 6.3). For the modeling of the standing wave, an electric boundary condition was used at the border orthogonal to the propagation vector of the incident plane wave. The electric boundary was positioned at a distance of $\lambda/2$ from the center of the medium to have the Petri dish in the H-field maximum.

### 6.2.3 Experimental Methods

The experimental results were obtained with the DASY near-field scanner (Schmid & Partner Engineering AG, Zeughausstrasse 43, CH-8044 Zürich) equipped with the latest generation of electric, magnetic and dosimetric probes [8] [9].

### 6.3 Coupling Mechanisms

#### 6.3.1 Basic Considerations

Some important qualitative characteristics of the coupling can be derived from basic principles without lavish calculations, e.g., [2]. If the dimensions of the medium are much smaller than the wavelength of the incident field, the total electric field inside the medium can be separated into the capacitively coupled electric field $\vec{E}_{cap}$ proportional to the incident electric field $\vec{E}_{inc}$ and to the inductively coupled electric field $\vec{E}_{ind}$ proportional to the incident magnetic field $\vec{H}_{inc}$. At first approximation, the specific absorption rate (SAR) can then be written as

$$SAR = \frac{\sigma}{\rho} \left( |\vec{E}_{ind}|^2 + |\vec{E}_{cap}|^2 \right)$$  \hspace{1cm} (6.1)
where $\sigma$ and $\rho$ are the conductivity and the density of the medium respectively, and $|E|$ is the rms amplitude of the electric field.

Some conclusions can be derived from the boundary conditions for the tangential component ($E^t$) and normal component ($E^n$) of the electric field between medium and air as well as from Faraday's law:

$$E^t_{\text{medium}} = E^t_{\text{air}}$$

$$E^n_{\text{medium}} = \frac{1}{\epsilon_{\text{medium}}} \cdot E^n_{\text{air}} \tag{6.2}$$

$$\int_{S} E_{\text{inc}} \, d\vec{l} = -\mu_{\text{medium}} \int_{S} \frac{\partial H_{\text{inc}}}{\partial t} \, dS \tag{6.3}$$

with the relative permittivity $\epsilon_{\text{medium}}$ and the magnetic permeability $\mu_{\text{medium}}$ of the medium and with $S$ being an arbitrary cross section of the medium while $\partial S$ is the boundary of $S$.

Based on the knowledge summarized in Equations (6.1) to (6.4) one can formulate the following qualitative principles which make predictions on the relative size of the induced fields in the medium, i.e. on the size of the coupling:

1. $|\vec{E}_{\text{cap}}|$ is larger if $\vec{E}_{\text{inc}}$ is tangential to the boundary of the medium and smaller if $\vec{E}_{\text{inc}}$ is normal to the boundary of the medium, since the relative permittivity $\epsilon_{\text{medium}}$ is typically about 75 for aqueous media in the frequency range of interest.

2. $|\vec{E}_{\text{ind}}|$ increases for increasing cross section of the medium perpendicular to $\vec{H}_{\text{inc}}$.

3. $|\vec{E}_{\text{ind}}|$ is proportional to the frequency of the incident field.

For dishes with horizontal dimensions which are considerably larger than their vertical dimensions (but still considerably smaller than the wavelength), the coupling can therefore be expected to be strongest for H-polarization (largest cross section of $\vec{H}_{\text{inc}}$ with the medium and $\vec{E}_{\text{inc}}$ parallel to the largest dimension of the medium), intermediate for k-polarization and weakest for E-polarization (small cross section of $\vec{H}_{\text{inc}}$ with the medium and $\vec{E}_{\text{inc}}$ parallel to the smallest dimension of the medium). The part of the SAR caused by $\vec{H}_{\text{inc}}$ is proportional to the square of the frequency.

Equations (6.1) to (6.4) also allow some general statements on the orientation of the inductively and capacitatively coupled field vectors:

1. $\vec{E}_{\text{ind}}$ at the surface of the medium is parallel to that surface according to Equation (6.4).

2. Equations (6.2) and (6.3) show that the capacitively coupled electric field $\vec{E}_{\text{cap}}$ is normal to the surface if the incident electric field $\vec{E}_{\text{inc}}$ is normal to the surface. If the incident electric field $\vec{E}_{\text{inc}}$ is parallel to the surface, $\vec{E}_{\text{cap}}$ is also parallel to the surface.

These basic considerations provide some useful general information about the coupling mechanisms and are valuable for the interpretation of simulation results and the derivation of optimization strategies.
6.3.2 E-polarization

As discussed above, the coupling is expected to be weak for E-polarization. This was reinforced by simulations for the two types of flasks, 60 mm-Petri-dishes (Fig. 6.3) and T-75 flasks (Fig. 6.4). The results of the simulations are summarized in Table 6.2. The simulations demonstrated that the flasks are almost transparent for the incident field in this polarization even at 1.62 GHz. Consequently, the ratio \( \left( \frac{|E_{medium}|}{|E_{inc}|} \right)^2 \), which is a good measure for the coupling, is as small as 0.5% at the bottom of flasks with 3.8 mm medium height. This translates to about 0.004 W/kg per W/m². The homogeneity of the induced field distribution is poor for cells in suspension but excellent for a cell monolayer at the bottom (standard deviation (SD) <20% for 60 mm Petri dish). In [10] a practical approximation formula was derived from equations (6.1) to (6.4) for E-polarization which was verified by numerical and experimental means:

\[
SAR(z) = \frac{\sigma}{\rho} \left( |\mu_0 2\pi f z|H_{inc}| \right)^2 + \frac{|E_{inc}|^2}{|\epsilon_k|^2},
\]

with \( \epsilon_k = \epsilon_{medium} - j\sigma/(\epsilon_0 2\pi f) \) and the frequency \( f \).

With the impedance \( Z \) of the incident field this can be written as

\[
SAR(z) = \frac{\sigma}{\rho} |E_{inc}|^2 \left( \frac{\mu_0 2\pi f z}{Z} \right)^2 + \frac{1}{|\epsilon_k|^2}.
\]

This equation gives the vertical SAR distribution in the medium at the center of the dish depending on the vertical coordinate \( z \), which ranges from \(-h/2\) to \(h/2\) whereby \( h \) is the medium height. The capacitively coupled contribution is not dependent on the medium height, while the inductively coupled part has a quadratic dependence on the medium height. This means that the incident H-field induces an inhomogeneous SAR distribution with its maxima at the top and the bottom of the medium and the minimum in between, as can be seen in Figs. 6.3 and 6.4.

The approximation formula (6.5) demonstrates the dominance of the inductive coupling (see also [11]) which contributes about 90% of the SAR at the bottom of the dish at 900 MHz and about 97% at 1800 MHz for a medium height of 3.8 mm and electric parameters according to Table 6.2.

Fig. 6.5 shows the dependence of homogeneity and induced SAR on frequency and medium height for the cell monolayer at the bottom. These figures as well as Equation (6.6) underline the fact that the frequency as well as the amount of medium are important parameters for increasing the coupling, whereas homogeneity is only marginally affected by these parameters.

E-polarization satisfies the requirements of [4] for homogeneity of the exposure in the case of monolayers. The strongly inhomogeneous field distribution with respect to the vertical axis results in a medium averaged SAR which is only about 30% of the SAR level at the bottom and top. This is advantageous, since the temperature load is proportional to the medium averaged SAR. The poor coupling, especially for small medium heights, requires significant input power if no resonating structures are applied.

Based on Equation 6.6 and on symmetry considerations, it can be seen that the coupling can be increased by approximately a factor of 4 for floating cell cultures (monolayer at the top of the medium) by placing the cell dish on a metal plate. This
Table 6.2: Simulated SAR values in a 60 mm Petri dishes and a T-75 flasks exposed to a plane wave with a power density of 1W/m².

<table>
<thead>
<tr>
<th>Polarization</th>
<th>60 mm Petri dish</th>
<th>T-75 flask</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>whole medium</td>
<td>bottom</td>
</tr>
<tr>
<td><strong>E</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean SAR</td>
<td>0.0019</td>
<td>0.0042</td>
</tr>
<tr>
<td>standard deviation</td>
<td>68%</td>
<td>13%</td>
</tr>
<tr>
<td>voxel count</td>
<td>136896</td>
<td>8556</td>
</tr>
<tr>
<td>minimum</td>
<td>0.00026</td>
<td>0.0016</td>
</tr>
<tr>
<td>maximum</td>
<td>0.013</td>
<td>0.0069</td>
</tr>
<tr>
<td><strong>H</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean SAR</td>
<td>0.34</td>
<td>0.30</td>
</tr>
<tr>
<td>standard deviation</td>
<td>41%</td>
<td>40%</td>
</tr>
<tr>
<td>voxel count</td>
<td>136896</td>
<td>8556</td>
</tr>
<tr>
<td>minimum</td>
<td>0.010</td>
<td>0.016</td>
</tr>
<tr>
<td>maximum</td>
<td>0.78</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>k</strong> (wave from top)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean SAR</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>standard deviation</td>
<td>39%</td>
<td>31%</td>
</tr>
<tr>
<td>voxel count</td>
<td>136896</td>
<td>8556</td>
</tr>
<tr>
<td>minimum</td>
<td>0.010</td>
<td>0.035</td>
</tr>
<tr>
<td>maximum</td>
<td>0.27</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>k</strong> (wave from bottom)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean SAR</td>
<td>0.12</td>
<td>0.11</td>
</tr>
<tr>
<td>standard deviation</td>
<td>38%</td>
<td>45%</td>
</tr>
<tr>
<td>voxel count</td>
<td>136896</td>
<td>8556</td>
</tr>
<tr>
<td>minimum</td>
<td>0.009</td>
<td>0.028</td>
</tr>
<tr>
<td>maximum</td>
<td>0.26</td>
<td>0.226</td>
</tr>
</tbody>
</table>

would also improve the thermal stabilization. However, for the usual situation with monolayers at the bottom of the flask, such a metal plate would drastically reduce the coupling.

6.3.3 H- and k-polarization

The simulation results visualized in Figs. 6.3 and 6.4 demonstrate that H- and k-polarizations indeed provide a significantly larger efficiency than E-polarization. Fig. 6.5 indicates that the medium height and frequency used for Figs. 6.3 and 6.4 are near optimum to reach low inhomogeneity with the given parameter. The homogeneity of the SAR distribution is considerably worse for a cell monolayer at the bottom of the flasks for H- and k-polarizations than for E-polarization due to stronger implications of the boundary conditions of \( E_x \) and \( E_y \). Neither polarization is suited for achieving SAR distributions with sufficient homogeneity.

The shape of the distribution for k-polarization in Fig. 6.4 is in good agreement with the data presented in [3] for T-25 flasks exposed at 2.45 GHz.
Figure 6.3: E-field amplitude and SAR distribution in a 60 mm Petri dish (3.8 mm medium height). The dish was exposed to a plane wave with a power density of 1 W/m² at 1.62 GHz. The figure demonstrates that low inhomogeneity is only possible for cells located at the bottom of a Petri dish exposed in E-polarization. However, the efficiency is very low for E-polarization compared to H- and k-polarization. The oscillation in the histogram for E-polarization is an artifact caused by the vertical resolution of 16 voxels for 3.8 mm in the numerical modeling.

6.4 Other Parameters

6.4.1 Interaction between Dishes

Generally, the placement of flasks within the scattering field of other flasks can result in significant changes of the conditions even in cases in which the magnitude
Figure 6.4: E-field amplitude and SAR distribution for E-, H-, and k-polarization at 1.62 GHz and for a medium height of 3.77 mm in T-75 flasks. One can see clearly the large similarities to the absorption patterns in the 60 mm Petri dishes shown in Fig. 6.3. The simulations for Fig. 6.3 and this figure used a voxel size inside the medium of 0.5 mm x 0.5 mm x 0.236 mm.

of the scattering field is small, especially in multimode setups. These effects must be carefully studied. Often it might be preferable to place dummy flasks at the edges of the flask arrays to reach maximum similarity between all flasks with exposed cells.

The poor coupling for E-polarization enables exposure of the flasks in three-dimensional arrays without significant impairment of the exposure performance. This is an important feature, since many biological protocols require the simultaneous
Figure 6.5: The two diagrams at the top show the dependence of homogeneity and efficiency of the SAR at the bottom of a 60 mm Petri dish filled with 8 ml medium (corresponds to 3.77 mm medium height) on the frequency. For the two diagrams at the bottom, the medium height was varied whereas the frequency was fixed at 1.62 GHz. The values are normalized to a power density of the incoming wave of 1 W/m². For the diagram at the bottom right the second scale gives the ratio of the average of the square of the electric field in the medium to the square of the incoming field. For the parameter studies the plastic of the flasks was not modeled and the voxel size inside the medium was 2 mm x 2 mm x 0.471 mm. Due to the course resolution and the steep SAR gradient in vertical direction for E-polarization, it was necessary to extrapolate the SAR values for E-polarization to the bottom of the medium according to the parabolic SAR distribution described by Equation 6.6.

exposure of various flasks in order to achieve sufficient statistical power. For H- and k-polarizations only two-dimensional arrays should be utilized, due to the strong distortion of the incident field.

6.4.2 Environment

The material used in the vicinity of the flasks can significantly alter the coupling as well. This is not only significant for metallic objects as already discussed but also in the case of materials with low conductivity. Careful evaluation, i.e., simulations of the entire setup including all elements, is indispensable.
Table 6.3: Increase of the SAR inside the medium in E-Polarization caused by the presence of menisci of different sizes.

<table>
<thead>
<tr>
<th>model of meniscus</th>
<th>( \text{SAR}_{\text{medium}}^{\text{const. medium height 3.77 mm}} )</th>
<th>( \text{SAR}_{\text{bottom}}^{\text{const. medium height 3.77 mm}} )</th>
<th>( \text{SAR}_{\text{bottom}}^{\text{const. medium volume 8.0 ml}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>small (0.75 mm x 1.5 mm)</td>
<td>9%</td>
<td>7%</td>
<td>3%</td>
</tr>
<tr>
<td>medium (1.5 mm x 1.5 mm)</td>
<td>25%</td>
<td>15%</td>
<td>8%</td>
</tr>
<tr>
<td>large (2.4 mm x 1.5 mm)</td>
<td>55%</td>
<td>26%</td>
<td>12%</td>
</tr>
</tbody>
</table>

*due to the quadratic dependence of the SAR on the medium height, it makes a considerable difference whether the medium height or the medium volume is held constant.

6.4.3 Meniscus

When an aqueous medium is used for *in vitro* experiments, a meniscus will occur at the edge of the flask where the medium touches the flask material. The size of the meniscus depends very much on the medium and the flask used [12]. Based on basic considerations on the absorption mechanisms, one expects that a meniscus will affect the SAR most when the flask is in E-polarization. In this case, the electric field vector is parallel to the thin liquid layer of the meniscus, causing a high electric field amplitude in the meniscus.

The simulations with 60 mm Petri dishes showed that the influence of the meniscus is smallest for H-polarization. The averaged SAR values for the whole medium and for the bottom of the dish increased by only 2% when a meniscus with a width and height of 1.5 mm was added. For k-polarization the corresponding values increased between 5% and 9%. For E-polarization, the effect of the meniscus on the induced SAR is considerably larger (see Table 6.3). A detailed discussion on the dependence of the SAR on the meniscus and the underlying mechanisms is given in [12].

6.4.4 Field Vector Orientation

Some researchers have emphasized the orientation of the induced field vector. For cells in suspension this issue is irrelevant. For monolayers it might be necessary to distinguish between fields induced normal or parallel to the monolayer. Special considerations should be given in the planning phase of the experiments.

6.4.5 Plane Wave Versus Other Incident Exposures

Many investigators prefer TEM exposure conditions since the reference limits of the safety standards [13] are defined for this exposure condition. However, this rationale is incorrect for choosing the exposure for bio-experiments, since the only relevant parameter is the induced field at the location of the tissue or cell culture. Most experiments today are evaluated with respect to the induced SAR (i.e., \(|E|^2\)) and not with respect to the induced H-field. Since the ratio of induced field to incident field can be fundamentally different between dishes and the human body, any conditions...
can be applied which satisfy the requirements for the locally induced field strengths and orientation.

Therefore, it may be necessary to use structures which enhance the efficiency (e.g., resonators) and/or increase the homogeneity (e.g., by changing the ratio between $E_{\text{inc}}$ and $H_{\text{inc}}$, i.e., by changing the field impedance). For resonating structures the amplitude of the incident field varies in the same way as for a standing wave. Therefore, these structures are only suitable if the variation of the incident field over the area with the cell cultures is sufficiently low. At the higher end of the frequency range considered in this paper, $\lambda/2$ is as small as the diameter of a 60 mm Petri dish, which means that resonating structures cannot be used in this frequency range for flasks of this size in E- and H-polarization.

Fig. 6.6 shows the SAR distribution for a 60 mm Petri dish exposed in the H-field maximum of a standing wave at 1.62 GHz. The comparison with the top of Fig. 6.3 demonstrates the increase of efficiency but also the higher inhomogeneity.

A field sensor for the control of the field amplitudes is indispensable for a resonator setup, while power meters may be used for setups with travelling waves.

6.5 Performance Evaluation of Different Designs

Different designs of setups have been used for the exposure of Petri dishes and flasks. Most of them belong to one of the following basic design ideas: TEM cells, RF chambers, radial transmission lines (RTL), waveguides or wire patch cells. This section gives an overview of the performance (summarized in Table 6.1) of the different designs and identifies parameters which can be optimized during realization of the setups.

6.5.1 TEM Cell

The most used setup in the past has been TEM cells, since they are small self-contained setups and fit in common incubators. For example, [14] and [15] exposed up to eighteen 60 mm Petri dishes with 8 ml of medium at 835 MHz in a TEM-cell.
Table 6.4: Qualitative comparison of the performance of five designs for the exposure of plated cells in 60 mm Petri dishes.

<table>
<thead>
<tr>
<th></th>
<th>TEM Cell</th>
<th>HF Chamber</th>
<th>RTL</th>
<th>Waveguide</th>
<th>Wire Patch Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>&lt;1 GHz</td>
<td>up to several GHz</td>
<td>&lt;3 GHz</td>
<td>0.7 - 2 GHz</td>
<td>0.7 - 2 GHz</td>
</tr>
<tr>
<td><strong>Number of Dishes</strong></td>
<td>2</td>
<td>&gt;20</td>
<td>≈20</td>
<td>4-10</td>
<td>8(1)</td>
</tr>
<tr>
<td><strong>Preferred Polarization</strong></td>
<td>E(2)</td>
<td>K(3)</td>
<td>E</td>
<td>E(2)</td>
<td>E</td>
</tr>
<tr>
<td><strong>Efficiency</strong></td>
<td>low</td>
<td>medium</td>
<td>medium</td>
<td>high</td>
<td>high</td>
</tr>
<tr>
<td><strong>Power Requirements</strong></td>
<td>high</td>
<td>high</td>
<td>medium</td>
<td>low</td>
<td>low</td>
</tr>
<tr>
<td><strong>Inhomogeneity</strong></td>
<td>low</td>
<td>high</td>
<td>medium</td>
<td>medium</td>
<td>medium</td>
</tr>
<tr>
<td><strong>Complexity</strong></td>
<td>low</td>
<td>high</td>
<td>medium</td>
<td>low</td>
<td>low</td>
</tr>
<tr>
<td><strong>Size</strong></td>
<td>small</td>
<td>large</td>
<td>medium</td>
<td>medium</td>
<td>small</td>
</tr>
<tr>
<td><strong>System Cost</strong></td>
<td>high</td>
<td>high</td>
<td>moderate</td>
<td>moderate</td>
<td>moderate</td>
</tr>
<tr>
<td><strong>Environmental Control</strong></td>
<td>incubator</td>
<td>self- built</td>
<td>self- built</td>
<td>incubator</td>
<td>incubator</td>
</tr>
<tr>
<td><strong>Electromagnetic Shielding</strong></td>
<td>self- contained</td>
<td>self- built</td>
<td>self- contained</td>
<td>self- built</td>
<td>self- built</td>
</tr>
<tr>
<td><strong>Exposure Control</strong></td>
<td>power</td>
<td>power</td>
<td>power</td>
<td>power</td>
<td>field probe(4)</td>
</tr>
</tbody>
</table>

(1) 35 mm Petri dishes placed into 60 mm Petri dishes with same medium height
(2) K- and H-polarization lead to poor homogeneity and are not further considered
(3) E-polarization leads to excessive power requirements and is not further considered
(4) Field probe must be used for control in resonating structures

They employed E-polarization resulting in an efficiency of about 0.04 W/kg per 1 W input power [10]. If only two dishes are used per cell, the homogeneity is excellent (SD ≈ 15%) but for larger numbers of dishes the inhomogeneity increases drastically, since the E-field amplitude decreases rapidly towards the wall of the cell (Fig. 6.7). Therefore, the TEM cell can only be recommended for studies with a very low number of dishes.

k-polarization, as used for the exposure of T-25 flasks at 835 MHz by [16], results in non-uniform exposures and standing waves in the TEM cell which must be carefully quantified with respect to the location of the dishes within the TEM-cell. Due to the expected strong dependence of the standing waves on even small changes in the location of the flask, the provision of a reliable dosimetry is a very difficult task.
Figure 6.7: The figure shows two cuts through the E-field distribution inside an empty TEM cell (in110Ω) measured at 835 MHz with an input power of 100 mW. An arrangement of 40 dishes was drawn into the figure to demonstrate that a homogeneous SAR distribution can only be expected for dishes near the center of the cell.

6.5.2 HF Chamber

In an HF chamber an array of the flasks with a dimension of several wavelengths can be simultaneously exposed. K-polarization is normally employed due to the immense power requirements for E-polarization [17] [18]. However, solutions to reduce the inhomogeneity of this polarization should be found. [17] exposed yeast cells on Agar. The homogeneity could be increased by placing the flasks on a metallic plate. The same approach would not work for a monolayer of cells on the bottom of the cell dish. A brief study could show that improved homogeneity would be achievable by surrounding the flask with a matching box filled with liquid to the same level as in the medium in the flasks. Such an arrangement would allow excellent temperature control, although the complexity of the setup would increase significantly. Generally, it is more costly to achieve environmental control and sufficient shielding for an HF chamber than with the other setups discussed. On the other hand HF Chambers enable circular polarized exposures.

6.5.3 Radial Transmission Line

The Radial Transmission Line (RTL) exposure setup consists of a circular parallel-plate applicator, driven at its center by a conical antenna and terminated radially by microwave absorbers or a load. An interesting feature of this setup is that several dishes can be exposed at the same time and that it can be used for a wide frequency band up to 3 GHz. In [19] the flasks were positioned either directly on the metal
smaller distance to center results in higher efficiency; limited by number of cell dishes

existing reflections can be used to maximize efficiency

smaller height results in higher efficiency; limited by coupling of cell dishes to wall and dimensions of antenna

matching layer: minimization of reflections from cooling water

Figure 6.8: The sketch shows some parameters which can be varied to optimize the performance of the RTL setup.

bottom or on an aluminum oxid layer in the RTL. Since the exposure was in E-polarization, the efficiency of the latter was considerably larger for cell monolayers at the dish bottom as was discussed above. Fig. 6.8 shows some of the important parameters which can be tuned for optimization. For an optimized setup with twenty 60 mm Petri dishes, an efficiency of circa 0.2 mW/g per W input power and an inhomogeneity of circa ±30% would be achievable at 1.62 GHz for a medium height of 3.8 mm.

6.5.4 Waveguide Setup

Waveguide setups have also been widely used in the past, e.g., [21][20]. The flasks can be oriented in E-, K- or H-polarization. If E-polarization is employed to achieve low inhomogeneity for plated cells at the bottom of the flasks, it may be necessary to overcome the poor efficiency due to the weak coupling. One possibility to increase the efficiency by a factor of almost four is to terminate one end of the waveguide with a short circuiting plate as described in [22] and shown in Fig. 6.9. For an optimized setup with ten 60 mm Petri dishes inside an R14 waveguide at 1.62 GHz, an efficiency of 1.6 mW/g per W input power and an inhomogeneity of approximately ±30% was achieved. The efficiency of the setup could be further increased by tuning the waveguide to become a resonator.

6.5.5 Wire Patch Cell

The wire patch cell is a recently developed setup [24]. It is basically a parallel plate resonator fed in the center of the plate resulting in large E-fields between the plates. To reduce the inhomogeneity caused by the tangential E-field (Equation 6.2), the eight 35 mm Petri dishes with medium are placed inside 60 mm Petri dishes filled with medium to the same height as in the 35 mm dishes. The efficiency reported in [24] is 0.6 W/kg per W input power at 900 MHz. The deviations from the mean value were within ±12% when the evaluation was restricted to the area more than 3 mm away from the edge of each 35 mm Petri dish. Further studies are necessary to
determine the deviation from homogeneity for the entire medium as well as for cell monolayers at the bottom of the dish.

6.6 Conclusion

For plated cells, E-polarization is largely superior to H- and k-polarizations with respect to homogeneity. The low efficiency can be overcome by resonant structures. None of the discussed approaches enables the exposure of cells in suspension with reasonable homogeneity (SD <30%) for homogeneously suspended cells with 60-mm Petri dishes or T-75 flasks. The best results were achieved by wire patch cells and HF chambers with the appropriate matching boxes. For a reliable numerical assessment of the SAR distributions, the environment (standing waves, coupling, etc.) as well as details such as the meniscus must be carefully evaluated.

The qualitative results on the characteristics of the SAR distribution can also be expected to be valid for flasks of other dimensions and shapes as long as the vertical dimensions of the medium are much smaller than the horizontal dimensions.

The decision as to which design is best suited for a certain in vitro study depends on numerous biological and technical requirements. Therefore, no general recommendation for a design can be given. However, the listed advantages and disadvantages as well as the identification of parameters which can be optimized during realization are helpful during the process of evaluating various setup designs for a planned in vitro experiment.

Figure 6.9: The sketch gives an overview of some parameters which can be optimized during the realization of a waveguide setup terminated by a short circuiting plate.
References

[1] WHO. Detailed information on the International EMF Project of the WHO can be found at http://www.who.int/peh-emf.


Chapter 7

Design, Optimization, Implementation and Analysis of an In Vitro Setup for the Exposure of Embryonic Stem Cells at 1.71 GHz

Abstract - The aim of this study was the development of an exposure setup which enables in vitro experiments to be conducted under variously modulated radio-frequency exposures. Based on the evaluation of different possible setups it was decided to realize a system based on rectangular waveguides. The setup was optimized for the following parameters: 1) homogeneity of the cell exposure, 2) simultaneous exposure of several Petri dishes, 3) efficiency, 4) strict environmental control, 5) quick and easy access to the Petri dishes, 6) cost and 7) simple-operation by non-engineering personnel. The implemented control software enables investigation of a wide spectrum of amplitude modulation schemes between 0.1 Hz and 1 kHz, including the modulation schemes of current and future digital mobile communication systems as well as different exposure protocols. The system described has been initially utilized for a study on the differentiation and cell functions of embryonic stem cells. Detailed numerical and experimental dosimetry and environmental tests have demonstrated that it meets all target objectives. The entire setup including the sham exposure setup fits into a single incubator. It enables the carrying out of various experiments designed to test biological responses to RF exposures in the frequency range from 1.2 GHz to 1.7 GHz using various modulation schemes and long-term exposure protocols as well as simultaneous data logging.

7.1 Introduction

In view of the exponential increase of the exposure of the general public to the electromagnetic fields emitted by digital mobile communication systems, health agencies
and user groups are asking for the conduction of a sound risk assessment. Under the aegis of the World Health Organization (WHO), a group of leading experts has worked out a priority list of *in vitro*, *in vivo* and epidemiological studies to be conducted in order to clarify the issue [1].

In this context, a set of experiments investigating the influence of modulated electromagnetic radiofrequency (RF) fields on the differentiation and cell functions of embryonic stem cells will be conducted during the next two years. Embryonic stem cells cultured *in vitro* retain their undifferentiated pluripotent state. Differentiation is induced by the aggregation of embryonic stem cells to form embryonic bodies from which the cells differentiate spontaneously into a wide variety of cell types (e.g., [2], [3], [4]). Embryonic stem cells have therefore become the favored system for analyzing the influence of chemical and physical agents on differentiation and cell communication. In particular, cell differentiation and communication is a current focus in bioelectromagnetics. This project, funded by the VERUM Foundation (Verhalten und Umwelt), is a joint effort between the research group 'In Vitro Differentiation' at the Institute of Plant Genetics and Crop Plant Research in Gatersleben, Germany, and the BIOEM/EMC group at the Swiss Federal Institute of Technology.

The initial objectives are to test various modulation schemes with particular emphasis on those of current and future mobile communication systems [5], and those schemes for which positive effects have been reported in the literature (e.g., [6], [7], [8]). It was decided to restrict the study to a single carrier frequency which should be within the frequency bands of one of the two most important European cellular systems, i.e., GSM or DCS.

In the first step an exposure setup fulfilling all the technical and experimental requirements was developed, optimized and tested. This is the subject of this paper.

### 7.2 Requirements for the Setup

#### 7.2.1 General Requirements for In Vitro Exposure Setups

An *in vitro* exposure setup must fulfill a number of general requirements (see also [9] and [10]):

- The signal characteristics must be well defined. In particular this requires a signal source that is well defined with respect to the frequency, modulation scheme, power stability and noise level.

- Signal characteristics and field strengths inside the medium must be relevant for risk assessment. Therefore, the setup should allow for field strengths that are at least as high as the relevant limits defined by the regulatory bodies [11], [12], [13] or the highest exposure occurring in real life situations.

- The field distribution at the location of the cell culture should be as homogeneous as possible. The target value shall be better than ±30% [10].

- The environmental requirements (e.g., stabilized temperature, atmospheric control, sterility) must be strictly fulfilled.

- All relevant technical and biological parameters must be monitored during the experiment. The most important technical data should be logged in order to track possible malfunctions of the system.
• All controlling and monitoring devices should be rigorously checked for interference under worst-case considerations. Non-disturbance of commercial services must be ensured.

• The costs for design, construction and maintenance of the setup should be reasonable.

• The system should be easy-to-use and as fool-proof as possible.

### 7.2.2 Special Requirements Imposed by the Experimental Protocol

In general, conducting a biological experiment under RF exposure involves a departure from the standard procedure or protocol. However, the extent of this departure should be minimal, which in turn imposes strict constraints on the design of the setup.

Details on the biological protocol of the experiment can be found in [14]. In the following, some aspects of the protocol which are relevant for the design of the exposure setup are presented. Fig. 7.1 provides a schematic overview of the various cultures to be exposed. For the formation of embryoid bodies of a defined size, embryonic stem cells are cultivated in droplets of 20 μl volume hanging from the lids of Petri dishes (in the following referred to as 'hanging drops'). Approximately 30 to 40 droplets hang from the lid of a single 60 mm Petri dish, and the dish itself contains 3.7 ml water in order to ensure a high degree of humidity inside the dish. Within 2 to 3 days embryoid bodies form. Each embryoid body nestles within the curvature of its droplet. The diameter of the bodies is circa 0.2 mm to 0.3 mm during the first 3 days.

Two other methods of cultivation employ 8.0 ml of aqueous medium, which is equivalent to a medium height of 3.8 mm in a 60 mm Petri dish. In the first method, the embryoid bodies are suspended in the medium according to a given protocol (referred to as 'suspension cultivation'). The embryoid bodies immediately settle at the bottom of the dish whereby almost no embryoid bodies are found further away from the center than half the radius of the dish. Hence, the dosimetric assessment can be restricted to this inner part of the Petri dish bottom for suspension cultivation. The second method consists of plating the inner bottom of the Petri dishes with the embryoid bodies (referred to as 'plated cultivation'). The embryoid bodies are distributed uniformly on the bottom of the Petri dish. This means that the embryoid bodies are located at the very bottom of the Petri dish for plated as well as for suspension cultivation. The two means of cultivation differ only with respect to the distribution of the embryoid bodies at the bottom.

Depending on the biological protocol, the medium in which the cells are cultivated is either DMEM or Iscove [14]. The measured dielectric parameters are listed in Table 7.1. The protocols require tight environmental conditions for the Petri dishes, i.e., strictly controlled CO₂ atmosphere at 37.0°C with a relative humidity of more than 90%. Any unavoidable disruptions of these conditions during the cultivation process should be kept to a minimum.

This imposes the following additional requirements:

• The setup must be suitable for the exposure of stem cells and embryoid bodies using all of the mentioned cultivation methods.
Table 7.1: Measured electric parameters of the media at 1.71 GHz. The biological experiments are performed inside an incubator at 37°C, whereas the measurements for validation were performed at room temperature (24°C).

<table>
<thead>
<tr>
<th>medium</th>
<th>Temperature</th>
<th>$\varepsilon_r$</th>
<th>$\sigma$ [S/m]</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMEM</td>
<td>24°C ± 1°C</td>
<td>75±5%</td>
<td>2.2±5%</td>
</tr>
<tr>
<td>DMEM</td>
<td>37°C ± 1°C</td>
<td>72±5%</td>
<td>2.4±5%</td>
</tr>
<tr>
<td>Iscove</td>
<td>37°C ± 1°C</td>
<td>72±5%</td>
<td>2.1±5%</td>
</tr>
</tbody>
</table>

Cultivation:

'**hanging drops**'
Embryoid bodies form in hanging drops of 20µl DMEM or Iscove, 3.7ml H2O at the bottom

'**suspension**'
Suspension culture of embryoid bodies, 8ml DMEM or Iscove

'**plated**'
Growing of adherent embryoid bodies or stem cells, 8ml DMEM or Iscove

Figure 7.1: Schematic overview of the various means of cultivation of embryoid bodies according to the biological protocol.

- Several 60 mm or 100 mm Petri dishes (a minimum of 10) shall be exposed simultaneously. It is possible to limit this to 60 mm dishes without endangering the biological relevance of the investigation.

- Rapid and convenient access to the Petri dishes must be ensured.

Further constraints are imposed by the exposure protocol, since the setup should enable testing of a broad range of extremely low frequency (ELF) amplitude modulation schemes. These should consist of at least sinusoidal and pulse modulation schemes, ranging from sub-Hertz frequencies up to 1 kHz. Different sequences of such signal strings should be programmable to last for periods as long as 20 days.

### 7.3 Design of the Exposure Setup

#### 7.3.1 Basic Design

In previous studies [15], [16], [17] four fundamental designs (quasi-plane-wave exposure, TEM-cell, radial transmission line (RTL) and waveguide) were compared with respect to their performance for the exposure of cell layers either located at the top or bottom of the medium in Petri dishes. The first outcome of these studies was that the polarization of the incident electric field parallel to the cylindrical symmetry
axis of a Petri dish (E-polarization) provides the best degree of homogeneity but the
lowest efficiency. In addition, this polarization pattern causes the lowest amount of
disturbances to the incident field, i.e., allowing several Petri dishes to be positioned
in the same setup. Among the four setups, a waveguide setup based on commercial
waveguides was found to be the most suitable with respect to efficiency, size and
cost, if the carrier is restricted to the frequency band between 1.5 GHz and 2.5 GHz.

A feasibility study also showed that the dominant interaction mechanisms differ
fundamentally for the various methods of cultivation. Whereas inductive coupling
is dominant in the case of the suspension and plated cultivations [15], capacitive
coupling is the dominant factor for hanging drops. Therefore, the efficiency can
be increased by terminating the waveguides with a short-circuiting plate and by
placing the Petri dishes in the maxima of the standing wave’s magnetic field for
the suspension and plated cultivations and in the maxima of the standing wave’s
electric field for the hanging drops cultivation. However, one condition for sufficient
homogeneity of the SAR distribution is that the distance between neighboring field
maxima of the standing wave is considerably larger than the diameter of the Petri
dishes. The dimensions of the 60 mm Petri dish, with an actual inner diameter of
52 mm (i.e., \( \approx \lambda/2 \)), are already at the upper limits for usage in this setup. A
significant advantage of terminating the waveguide with a short-circuiting plate is a
reduction of the overall length of the setup. Additionally, a removable short-circuiting
plate allows easy and fast access to the Petri dishes.

7.3.2 Details of the Design Determined by the Requirements of the
Experiment

In order to meet the demands listed in Section 7.2, the following waveguide system
was chosen. The optimization and system integration is described in the following
two Sections.

- R14 waveguides (cross-section 165.10 x 82.55 mm\(^2\)) were chosen because all
  standard parts are commercially available. The frequency range (1.12 GHz to
  1.73 GHz) encompasses the carrier frequencies used by the PHS, IRIDIUM and
  DCS systems. The current experiment will be performed at a carrier frequency
  of 1.71 GHz, which is at the lower end of the DCS band.

- The wavelength inside the waveguide is about 200 mm at 1.71 GHz, which
  means that neighboring maxima of the standing wave’s electric (respectively
  magnetic) field are separated by approximately 100 mm. Therefore, sufficient
  homogeneity of the SAR distribution can only be achieved with 60 mm Petri
  dishes (actual inner diameter 52 mm) but not with 100 mm dishes.

- In order to maintain the strict environmental control requirements at a reason¬
  able cost, a commercial incubator is used. The inner dimensions of the largest
  available incubator are 620 x 545 x 700 mm\(^3\) (height x width x depth). This
  limits the maximum length of the waveguides but allows several waveguides to
  be stacked in the same incubator.

- Since the biological protocol of the experiment requires quick and easy access
to the Petri dishes, it was decided to position the waveguide with the remov¬
able short-circuiting plate towards the door of the incubator. Given the avail¬
able depth of the incubator of 700 mm, the dimensions of the co-ax-waveguide
adapters and the approximate wavelength at 1.71 GHz, it can be calculated that up to four Petri dishes can be positioned along the longitudinal axis of a waveguide.

- Closed RF systems such as waveguides have the additional advantage that problems due to interference (e.g., disturbance of the controlling circuit of the incubator) are eliminated. Additionally, the waveguides with exposed and sham exposed Petri dishes can be placed in the same incubator.

7.4 Optimization of the Setup

7.4.1 Modeling and Numerical Techniques

The setup has been optimized using numerical techniques. The simulations were performed using MAFIA [18], a commercially available tool which is based on the FI technique and the EMLAB FDTD kernel, developed in a joint project between the Laboratory of Integrated Systems and the BIOEM/EMC group at ETH. Fig. 7.2 shows the numerical model used for the dosimetry of the suspension and plated cultivation methods. For the dosimetry of the hanging drops a similar model was used. The droplets were simulated as half spheres of radius 2.12 mm. The dimensions of the computation domain were 700 mm in the longitudinal direction and 82.55 mm in the two other directions. This means that only half of the inside of the waveguide was modeled, since the setup and the field distribution are symmetric with respect to the central vertical plane. This exact symmetry was modeled by using a perfect magnetic boundary which forces the tangential magnetic fields to zero in this plane. All other boundaries, except the front side where the field is coupled into the waveguide, were modeled with perfect electric boundaries.

The smallest voxel size used was 0.106 x 0.106 x 0.106 mm$^3$ for the modeling of the cultivation hanging drops and 0.50 x 0.50 x 0.157 mm$^3$ for the modeling of suspended and plated cultivations, resulting in up to 8 million cells for the whole computation domain. The use of much smaller dimensions of the mesh cells in the vertical than in the horizontal directions is appropriate for the plated and suspended cultivations, since the field gradients inside the medium are much larger in vertical direction than in horizontal direction (see Figs. 7.8 and 7.13). To save computer time, models of the setup with reduced resolution were used for part of the optimization process, while searching for the precise location of the field maxima. Since the experimental validation of the numerical model had to be performed in a slightly altered setup, the numerical model also had to be changed accordingly (see Section 7.7). Only the TE$_{10}$ mode was used for excitation, since this is the only mode which can propagate at the target frequency and the first dish is located about 20 cm from the probe of the coax-waveguide adapter. Steady state was always reached before the 30 periods chosen as computational time.

The maximum meniscus height at the walls of the Petri dishes was assessed to be less than 1 mm. This changed the total liquid height of the medium less than 2%. Increased SAR values may be caused by the meniscus [19] while a reduced medium height reduces the SAR [15]. However, simulations showed that the effect of the meniscus on the SAR distribution within a monolayer of cells located at the bottom of the dish is negligibly small (<4%). Locally increased SAR values in the meniscus itself are not of interest, since the embodi bodies are located at the bottom of the
7.4.2 Optimization of the Material Distribution inside the Waveguide

The number of Petri dishes per waveguide can be increased by stacking the dishes on top of each other. The numerical analysis showed that the homogeneity of the SAR distribution was greatly impaired in stacks of three dishes, whereas there was little loss in performance for stacks of two dishes. Consequently, it was decided to build a system with stacks of two dishes, thus increasing the number of Petri dishes per waveguide to eight. The design of the system holding the Petri dishes was guided by the requirement of minimal disturbance of the field distribution and air flow around the Petri dishes. Thus, a material with low relative permittivity ($\varepsilon_r$) should be used, and the amount of material utilized should be kept as low as possible.

Since the positions of the field maxima along the longitudinal axis of the waveguide depend not only on the frequency but also on the material distribution inside the waveguide, the precise positions of the field maxima were determined by simulations. Placing the dishes in the H-field maxima (for suspension and plated cultivation) respectively in the E-field maxima (for cultivation hanging drops) optimizes not only efficiency but also reduces inhomogeneity of the SAR distribution inside the medium, since the variation of the relevant field amplitude over the Petri dish becomes minimal for these locations. The optimized distances between the centers of neighboring Petri dishes $d_{pl}$ and the optimized distances between the short-circuiting plate and the center of the first cell dish $d_{sh}$ are listed in Table 7.2 for the supporting system described below. Because of the optimized design of the frames, only small corrections are necessary compared to the wavelength in the empty waveguide ($\lambda/2 = 103.6$ mm at 1.71 GHz).
Table 7.2: Optimized distances along the longitudinal axis of the waveguide at 1.71 GHz. A change of medium height, electric parameters of medium or construction of frames would result in different distances.

<table>
<thead>
<tr>
<th>cultivation</th>
<th>(d_{dd}) [mm]</th>
<th>(d_{sd}) [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>hanging drops (3.7 ml H₂O)</td>
<td>102</td>
<td>50</td>
</tr>
<tr>
<td>suspension &amp; plated (8 ml medium)</td>
<td>104</td>
<td>102</td>
</tr>
</tbody>
</table>

**Figure 7.3: Overview of the design and optimization of the setup.**

### 7.5 Realization of the Exposure System

#### 7.5.1 Hardware

Fig. 7.4 shows a sketch of the entire exposure system. The RF signal, generated by the signal generator (Hewlett Packard 8648B), is amplified to a maximum peak power of 40 W (Nucleotides S.A. M-25.45.65, Les Ulis Cedex, France) before being split in the 3dB power splitter (Mini Circuits ZA2CS-2G-20W, New York, USA, Symmetry: < 0.05 dB) and coupled into two of the waveguides (Flann Microwave R-14/WG06, Bodmin, Cornwall, UK) via two coax-waveguide adapters (Flann Microwave 06093-NF16). More than 90% of the power is reflected and directed into a 50Ω terminator via the circulator (included in the amplifier). Two waveguides of identical dimensions host the control groups. To reduce costs, the waveguides of the control group are not equipped with coax-waveguide adapters. A double-blind design of the experiment would require that all waveguides are equipped with coax-waveguide adapters.

The carrier is amplitude modulated utilizing the analogue input of the signal generator, whereby the ELF signal is generated by software using a digital-to-analog card (National Instruments PCI-MIO 16E-4, Austin, USA). The same computer controls the power using the feedback of the power meter (Hewlett Packard 437B with power sensor 8481A).

To guarantee sufficient air circulation, the waveguides are equipped with DC ventilators (Papst 612, St. Georgen, Germany) which take in air through two slots near the front end of the waveguide. The driving currents of the ventilators are continuously monitored in order to control their performance. The active and sham
waveguides are mounted inside a CO₂ incubator (New Brunswick Scientific BS-250/S, Nürtingen, Germany).

7.5.2 Materials

The frames of the supporting system for the dishes are made of low loss Eccostock0005 (Emerson & Comin, New York, USA) with εr=2.53 and a loss tangent of 0.0005. The design of the frames can be seen in Fig. 7.6. The lengths of the exchangeable spacers depend on the cultivation according to Table 7.2.

It was necessary to treat the surfaces of the brass waveguides in order to avoid toxicity problems due to oxidation. All brass parts are covered by a 20 µm amorphous layer of Nickel. This layer is very hard and corrosion resistant. The short-circuiting plates are screwed down in order to enable quick opening and good electrical contact.
7.5.3 Software

The exposure protocol can be implemented via a user friendly dialogue. The exposure protocol is characterized by the carrier frequency, modulation and periodically repeated on- and off-time of exposure, as well as the SAR level. The current implementation enables rectangular and sinusoidal modulation with depths between 0 and 100% and frequencies between 1 Hz and 1 kHz. The system continuously monitors the power level, which is adjusted according to the required SAR. Furthermore, the current flowing through each ventilator is monitored in order to detect any malfunction.

Knowledge of the thermal properties of the setup (see Section 7.8) is used to calculate the anticipated temperature profile. The maximum temperature increase inside the medium as well as the average temperature increase are calculated for the given exposure protocol. All relevant information, including the monitored values for the power and the current through the ventilators, is also logged. If any of the monitored values do not keep within an adjustable range, the software responds with optical and acoustic warnings.

7.6 Numerical Dosimetry

The results of the numerical dosimetry at 1.71 GHz are summarized in Table 7.3. The histograms in Fig. 7.7 give more detailed information on the SAR distribution for the cultivations suspension and plated shown in Fig. 7.8. The efficiency is excellent with 1.5 mW/g to 2 mW/g per W input power for the plated and suspension cultivations. Depending on the method of cultivation and the medium used, the standard deviation of inhomogeneity is between about 25% and 35%. The latter value does not meet the target value of less than ±30%. However, in the case of positive findings, the same setup could be utilized for conducting the experiments with enhanced homogeneity by grouping the two middle dishes of the top layer (d2top and d3top) and the bottom layer (d2bot and d3bot) for the biological analysis (see Fig. 7.7 and Table 7.3). The uncertainty of the average values was estimated to be below ±20% for the suspension
Table 7.3: Simulated SAR values at 1.71 GHz at the location of the stem cells respectively embryoid bodies. The SAR_{medium}, which is averaged over the whole medium volume is relevant for the temperature rise in the medium.

<table>
<thead>
<tr>
<th>SAR [mW/g] ±SD</th>
<th>medium</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>for 1 W input power</td>
<td>DMEM</td>
<td>Iscove</td>
</tr>
<tr>
<td><strong>Standard (all dishes)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hanging drops</td>
<td>0.63</td>
<td>0.55</td>
</tr>
<tr>
<td>suspension</td>
<td>2.3±22%</td>
<td>2.0±23%</td>
</tr>
<tr>
<td>plated</td>
<td>1.7±34%</td>
<td>1.5±35%</td>
</tr>
<tr>
<td><strong>Improved homogeneity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>suspension</td>
<td>d_2^{opp} &amp; d_3^{opp}</td>
<td>1.7±13%</td>
</tr>
<tr>
<td></td>
<td>d_2^{het} &amp; d_3^{het}</td>
<td>2.2±11%</td>
</tr>
<tr>
<td>plated</td>
<td>d_2^{opp} &amp; d_3^{opp}</td>
<td>1.5±25%</td>
</tr>
<tr>
<td></td>
<td>d_2^{het} &amp; d_3^{het}</td>
<td>2.0±23%</td>
</tr>
<tr>
<td><strong>SAR_{medium} (averaged over total medium volume)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hanging drops</td>
<td>0.60</td>
<td>0.52</td>
</tr>
<tr>
<td>plated &amp; suspension</td>
<td>0.92</td>
<td>0.82</td>
</tr>
</tbody>
</table>

and plated cultivations, since the numerical model represents the setup very precisely.

For the cultivation hanging drops the uncertainty of the numerical dosimetry is much higher. The SAR distribution inside a droplet is sensitive to variations in the number of drops, the distances between them and their exact shape. The uncertainty was evaluated by comparing the results of simulations for which the critical parameters were varied within a reasonable range. Using this method, the uncertainty of the average SAR given below was assessed to be approximately 50%. Fig. 7.9 shows that the simulated SAR distribution inside a droplet with the form of a half sphere is rather homogeneous. The standard deviation of the inhomogeneity of the SAR distribution at the location of the embryoid body inside one hanging drop was simulated to be circa 5% with a numerical model with improved local resolution. This inhomogeneity inside a certain drop can be neglected compared to the much larger contributions to the inhomogeneity caused by the variation of the electric field amplitude over the Petri dish and by the varying distances to neighboring drops. The square of the E-field is 40% lower at the edge of the Petri dish than at the center. Based on simulations of different arrangements of the drops on the lid of the Petri dish, the inhomogeneity caused by differing neighborhoods was roughly estimated to be circa ±30%. This means that the SAR values in the drops at the location of the embryoid body can be expected to vary circa ±50% around the average value. This average value, i.e., the efficiency of the exposure, is approximately 0.6 mW/g per W input power for the cultivation hanging drops.
Figure 7.7: Histograms of the SAR distribution at the bottom of the Petri dish for suspension and plated cultivation. The solid lines refer to the evaluation of all dishes. For the dotted black lines only the two middle dishes of the upper layer (d2top and d3top) were evaluated. For the dotted gray lines only the two middle dishes of the lower layer (d2bot and d3bot) were evaluated.

### 7.7 Experimental Validation

Any setup analyzed and optimized using simulations must be experimentally validated, which is the only reliable check to detect any possible shortcomings in the numerical model. The reason is that the latter always includes several simplifications of the physical setup. Since the chosen waveguide system is a closed system, mod-
Figure 7.8: Simulated SAR distribution at the bottom of the Petri dish for suspension and plated cultivations. The voxel dimensions are 0.5 mm in the shown plane and 0.157 mm in vertical direction.

Figure 7.9: Simulated SAR distribution in a drop with the form of a half sphere and a volume of 20 μl hanging at the lid of the Petri dish. The voxel size is 0.106 x 0.106 x 0.106 mm³.

ifications of the experimental setup were inevitable in order to enable reliable and accurate measurements. Obviously these changes should be kept as small as possible and must not alter the basic characteristics of the setup. If the required modification will alter the field distribution, then the corresponding alterations must be made to the numerical model as well. In the latter case the validation can only be considered as valid for the original setup if both of the following conditions are satisfied: (1) the agreement between simulation and measurements is within its uncertainty and (2) the modification enhances the complexity of the numerical model, i.e., its uncertainty.

7.7.1 Probes Used for Experimental Validation

All of the experimental validations were performed with the near-field scanner DASY3 (Schmid & Partner Engineering AG, Zurich, Switzerland) which is based on the concept described in [20]. For the assessment of the SAR inside the aqueous medium at the bottom of the Petri dish, the dosimetric E-field probe ET1DV1 with a tip diameter of only 1.5 mm was used (Fig. 7.10). Although the probe is equipped with only one sensor, it is constructed in such a way that an isotropic response can be achieved by rotating the probe in 120° steps around its axis. The DASY3 implemen-
tation enables the rotation of the sensor at a given location with a precision of better than 0.1 mm. The spherical anisotropy of the probe has been determined to be less than ±0.3 dB. Probe calibration was performed in the relevant medium, whereby the uncertainty was ±7% (k=2). A validation of the numerical results for the hanging drops was not possible due to the fact that the droplets are much too small to allow precise SAR measurements with the available tools.

The incident H-field was validated using the isotropic H-field probe H3DV5 (Fig. 7.10). The assessed uncertainty for the free space measurements using the H-field probe is ±7.2% (k=2). An additional uncertainty of ±2% is caused by the measurement of the input power to the waveguide.

7.7.2 Modification of the System for Validation

In order to provide access for the probes to the medium, the lids of the Petri dishes in the upper layer were removed and a slot of 14 mm width was milled into the waveguide. The slot was positioned in the middle of the waveguide parallel to its longitudinal axis to ensure minimal disturbance of the ground mode.

When the proximity of the E-field probe to a boundary is in the order of its tip dimensions, the measurement accuracy is impaired. In order to reduce the influence of such boundary effects, the amount of medium in the top layer of the Petri dishes was increased to 17 ml DMEM, which corresponds to a height of 8.0 mm when compared to 3.8 mm according to the biological protocol. The larger medium volume increases the SAR values and changes the wavelength inside the waveguide. Therefore, the Petri dishes of the modified system were no longer located in the standing wave's H-field maxima.
7.7.3 Validation of the Incident Field and SAR Distribution

The influence of the slot on the H-field distribution along the vertical line inside the empty waveguide is shown in Fig. 7.11. The figure demonstrates that the simulated H-field distribution, based on the modified numerical model which also models the slot, is in reasonable agreement with the measurements. Fig. 7.12 compares the simulated and measured H-field distributions along the longitudinal axis 4 mm above the upper layer of Petri dishes. Measurement and simulation correspond well with respect to the locations of the H-field maxima of the standing wave. However, the distortion of the H-field amplitude caused by the dishes is ±20% compared to the predicted ±10% by the simulations. Similar differences were found for SAR distributions (Fig. 7.13). Smaller disturbances and therefore better agreement between the actual induced field strength and the simulations can be expected for the closed waveguide and lower liquid height. All values of the validation were well within the predicted uncertainty of ±20% for the simulation results.

Since the modified setup only increased the complexity of the setup but preserved all important basic characteristics of the original setup, the performed validation places great confidence in the correctness of the performed analysis of the original setup.

7.8 Temperature Test

The exposure setup must guarantee that the induced electromagnetic fields are the only difference between exposed and sham exposed cells. Since energy is absorbed in the exposed Petri dishes, special attention must be paid to the temperature increases inside the medium.

While the SAR distribution in the medium is quite homogeneous inside the hanging drops and at the bottom of the cell dishes, it is highly inhomogeneous in the vertical direction for the suspension and plated cultivations, with maxima at the bottom and top and a value of almost zero in between (see Fig. 7.13). The heat transfer inside the medium across this steep gradient is much faster than the heat transfer to the surrounding environment. Additionally, the on- and offtimes of the exposure are in the order of several minutes for the planned protocols, which is also
much greater than the time scale of the heat transport inside the medium. It is therefore appropriate to use a temperature $T_{\text{medium}}$ and a medium averaged specific absorption rate $\text{SAR}_{\text{medium}}(t)$ (see Table 7.3) to describe the temperature increase. The temperature profile of the medium is then determined by:

$$\frac{\partial T_{\text{medium}}}{\partial t} = -\frac{T_{\text{medium}} - T_{\text{incubator}}}{\tau} + \frac{\text{SAR}_{\text{medium}}(t)}{c_w}$$  \hspace{1cm} (7.1)

with $T_{\text{incubator}}$ being the constant temperature of the air inside the incubator and with $c_w=4.18 \text{ kJ/kg K}$ for the specific heat capacity of the aqueous medium. $\tau$ is the time constant in s of the heat transfer and depends on many factors including air flow, humidity of the air and material and geometrical parameters of the synthetic material inside the waveguide.

For the measurements of the temperature course inside the medium a temperature probe was used (T5200, Schmid & Partner Engineering AG). The probe was inserted into the medium through the ventilation slot and a small hole drilled into the lid of the Petri dish. The temperature increase was measured with the waveguide outside as well as inside the incubator. The temperature of the atmosphere inside the incubator was kept constant at 37.0°C and the relative humidity was 98%.

For the given setup, $\tau$ was determined to be 330±50 s for the suspension and plated cultivations. Due to the small size of the droplets it was not possible to directly measure the temperature increase inside the droplets. Since the ratio of surface to volume is large for the cultivation hanging drops, the time constant for the heat transfer can be expected to be shorter than for the suspension and plated cultivations. Therefore, the value of $\tau$ measured for the suspension and plated cultivations can also be used for the hanging drops as a worst case estimation.

7.9 Conclusion

A flexible setup for conducting in vitro experiments under well controlled radiofrequency electromagnetic exposure conditions has been evaluated, analyzed, realized and tested. The waveguide-based setup allows the simultaneous exposure of several
60 mm Petri dishes containing cells located at the bottom or top of a liquid medium with good efficiency.

For the special means of cultivation used for the experiments with embryonic bodies, the target standard deviation for the homogeneity of < ±30% is easily met for the cultivation “suspension” but slightly exceeded (i.e., < ±35%) for the plated cultivation. However, considerably improved homogeneity of better than ±25% can be achieved for the latter case if the Petri dishes are grouped for analysis.

A main advantage of the waveguides is that they are closed and compact systems enabling the placement of both the active and sham waveguides in the same incubator. This considerably simplifies the fulfillment of the requirements regarding strict environmental control. In addition, these waveguides are commercially available, which results in cost and time savings. The carrier frequency of the setup is limited to the frequency range of the dominant mode of the waveguide (e.g., 1.2 - 1.7 GHz for the R14 waveguide).

In order to keep the system flexible, the ELF amplitude modulation scheme as well as the long-term exposure protocol is software generated, i.e., enabling a large variety of RF exposures with AM components of up to 1 kHz. The same software which controls the exposure can continuously monitor different sensor signals, e.g., the driving current of the ventilators. In addition, it computes the temperature profile within the medium in the petri-dishes and provides warning signals if the specified limits are transgressed.

The first system optimized for 1.71 GHz has been installed and tested at the Institute of Plant Genetics and Crop Plant Research in Gatersleben, Germany, in order to test the effects of modulated RF fields on the differentiation and cell functions of embryonic stem cells.
Figure 7.13: Comparison between measured and simulated SAB along the central vertical axis of the Petri dishes. Dish 1 is the Petri dish closest to the short circuiting plate. The medium height was increased from 3.8 mm to 8.0 mm for validation to reduce the influence of boundary effects on the measurements with the dosimetric E-field probe.
References


Chapter 8

Dosimetric Analysis of the Carousel Setup for the Exposure of Rats at 1.62 GHz

Abstract - The so-called carousel setup has been widely utilized for testing the hypotheses of adverse health effects on the central nervous system due to mobile phone exposures in the frequency bands 800 - 900 MHz. The objectives of this paper were to analyze the suitability of the setup for the upper mobile frequency range, i.e., 1.4 - 2 GHz, and to conduct a detailed experimental and numerical dosimetry for the setup at the IRIDUM frequency band of 1.62 GHz. The setup consists of a plastic ground plate upon which ten rats, restrained in radially positioned tubes, are exposed to the electromagnetic field emanating from a sleeved dipole antenna at the center. Newly developed miniaturized dosimetric E-field and temperature probes were used to measure the SAR inside the brain of three rat cadavers of the strain Lewis and two rat cadavers of the strain Fisher 344. Numerical analysis was conducted on the basis of three numerical rat phantoms with voxel sizes between 1.5 mm³ and 0.125 mm³ based on high resolution MRI scans of a 300 g male Wistar rat and a 370 g male Sprague Dawley rat. The average of the assessed SAR values in the brain was 2.8 mW/g per W antenna input power for adult rats with masses between 220 g and 350 g and 5.3 mW/g per W antenna input power for a juvenile rat with a mass of 95 g. The strong increase of the SAR in the brain with decreasing animal size was verified by simulations of the absorption in numerical phantoms scaled to sizes between 100 g and 500 g with three different scaling methods. The variation of the $SAR_{brain}$ due to changes in position was assessed to be in the range from +15% to -30%. A study on the dependence of the performance of the carousel setup for rats on the frequency revealed that efficiency (defined as $SAR_{brain}$ per W antenna input power) and the ratio between $SAR_{brain}$ and $SAR_{body}$ are optimal in the mobile communications frequency range.
8.1 Introduction

The carousel setup was developed for testing adverse health effects on the central nervous system (CNS) due to exposures of mobile communications signals in the frequency bands 800 - 900 MHz. During recent years, it has been utilized in a series of in vivo studies designed for testing the hypotheses of cancer promotion [1] [2] and genomic responses [3]. The important advantages of the setup are well defined exposure of the brain tissue, good handling and low stress levels for the trained animals. Since the animals are oriented with their snouts towards the central antenna, a high ratio of brain averaged SAR (specific absorption rate) to whole body averaged SAR is achieved with the setup.

The objectives of this paper were to analyze the suitability of the setup for the higher frequency band of wireless communications, i.e., 1.4 - 2 GHz and to perform a comprehensive dosimetric analysis at 1.62 GHz. The background was that the Battelle Institute in Richmond, USA received a contract to conduct a study on brain tumor promotion in Fisher 344 rats for the satellite based communications system IRIDUM (carrier frequency 1.62 GHz; TDMA with frame rate of 11 Hz, duty cycle 1:11).

In the last few years, several groups have conducted dosimetric evaluation of the carousel setup for the frequencies 835 MHz and 900 MHz using different experimental and numerical techniques. In [4] three fiberoptic temperature probes were included in a catheter which was inserted almost horizontally from the neck into the brains of 12 rats of the strain Sprague-Dawley, ranging in weight from 120 g to 520 g. A horizontal orientation has the advantage of minimal field coupling of the probe's lines. In [5] the analysis was performed numerically and validated using a fiberoptical temperature probe based on the cavity resonator. The probes were implanted vertically by stereotactic means and the temperature increase was measured in 10 positions on two different lines in the brain of an adult rat of the strain Wistar. In [6] radiation thermometry was employed for the dosimetric analysis of this setup.

However, the results of these studies revealed several shortcomings of the applied techniques and tools. For example, the resolution of the numerical rat phantom of $3 \text{mm} \times 1 \text{mm} \times 1 \text{mm}$ used in [5] turned out to be far too crude to resolve the fine anatomical structures of the rat. The uncertainties associated with insufficient resolution was expected to become more pronounced at higher frequencies. The experimental techniques employed lacked both sufficient dynamic and spatial resolution.

For this study improved rat phantoms were generated based on MRI scans with 0.5 mm slice separations. This resolution corresponds to current state-of-the-art MRI technology. The experimental dosimetry was conducted with the latest generation of temperature probes. Furthermore, a new E-field probe optimized for this kind of applications had been developed and was employed for this study. Measurements at more than 40 locations in the brains of five rat cadavers of two different strains were compared in order to assess the uncertainty and repeatability of the experimental techniques as well as to evaluate the appropriateness of the current numerical phantoms.
8.2 The Carousel Setup

8.2.1 Description of the Setup

The so-called carousel setup loaded with ten rats is shown in Fig. 8.1. The animals are restrained inside PVC tubes with an inner diameter of 62 mm, a length of 250 mm and a wall thickness of 5.5 mm. The front part of the tubes is triangularly cut to fit into the socket. The socket has a triangular ground shape which is cut in the front, so that a narrow slit is open. This stabilizes the position of the animals, since the rats tend to stick their nose into the air stream which is blown through the central part of the setup. The socket starts at a distance of 35 mm from the center of the setup and has a radial dimension of 98 mm. It is made of plexiglas with a thickness of 6 mm at the bottom and top and 4 mm at the side. The base plate has an inner diameter of 20 mm, an outer diameter of 110 mm and a thickness of 12 mm and is also made of plexiglas. The snouts of the rats are at a distance between 30 mm (nose sticked out into air stream) and about 37.5 mm (head drawn back, e.g., while sleeping) from the antenna. The last number depends very much on the method used to restrain the animals in their tubes. A sleeved dipole antenna developed and provided by Motorola Inc. is mounted in the center of the setup. The feedpoint of the antenna is positioned at the same height as the center of the tubes.

8.2.2 Numerical Modeling of the Setup

The setup has a tenfold rotational symmetry around the antenna in the center. Additionally, the setup has ten vertical symmetry planes running through the central antenna and the middle of the tubes respectively between the middle of neighboring tubes. The symmetry of the loaded setup is only perfect if identical animals in identical positions are used and the rats are symmetric to their midsagittal planes. Taking advantage of this symmetry, the simulations were performed either for only half a sector with an opening angle of 18° and half a rat or for a full sector with an opening angle of 36° and a complete rat. Both vertical walls of the sector were modeled as symmetry planes. Simulations showed that the two different modelings
result in almost identical SAR values (less than 3% difference for the brain averaged SAR and less than 1% for the whole body averaged SAR). All parts of the setup made of plexiglas or PVC were modeled in detail (see Fig. 8.2) with the parameters listed in Table 8.1.

The antenna was simulated as a simple filament dipole on a meshline having a length of 0.45λ. The feedpoint was at the same height as the center of the tubes which house the rats.

8.3 Rat Phantoms

8.3.1 Experimental Rat Phantoms

Three rats of the strain Louis were provided by the Institute for Brain Research at the University of Zurich and two Fisher 344 rats were delivered by BRL, Basel, Switzerland. All animals were killed by an overdose of a sleep inducing drug at the Institute for Brain Research, Zurich. The skin over the skull was cut and slightly moved apart. Three small circular holes were drilled into the skull (see Figs. 8.3 and 8.4). In most cases the cerebral membrane was not damaged and only opened immediately before the measurements. The position of the holes were controlled by comparison to the map of the rat brain shown in Fig. 8.3. The time between the death of the animals and the start of the measurements was kept as short as possible, and the skin over the skull was closed with a clamp during transport of the animals to the laboratory to reduce desiccation. During measurements small amounts of tissue simulating liquid were dripped into the measurement holes from time to time to reduce the effect of desiccation.

The brain of rat cadaver E2 was removed and replaced by tissue simulating liquid with well known parameters (see Table 8.1) since the electric parameters of biological tissues are only known with considerable uncertainty.

During the measurements in the rat cadavers, the other nine tubes of the setup were loaded with simply shaped experimental phantoms, since the absorption in the rats is largely affected by the neighboring rats [4] [5]. These simply shaped experimental phantoms were made of thin plastic and filled with an amount of tissue simulating liquid corresponding to the weight of the rat cadavers.
8.3.2 Numerical Rat Phantoms

The numerical rat phantoms used were derived from MRI scans of two different rats.

One model (called N1 in the following) is based on 71 lateral MRI scans taken of a male Wistar rat of circa 300 g at the Max-Planck-Institute for Neurological Research in Cologne, Germany at distances of 3 mm. The numerical phantom derived from
this series has a voxel size of $1.5 \times 1 \times 1 \text{mm}^3$ and distinguishes 14 different tissues. The model has already been described and used in [5].

A second series of 57 images of the brain region with a separation of 0.5 mm was used to refine the modeling of the head. The voxel size of the refined model (called N2 in the following) shown in Fig. 8.4 is $0.5 \times 0.5 \times 0.5 \text{mm}^3$ for the head region, whereas a voxel size of $1.5 \times 1 \times 1 \text{mm}^3$ was considered to be sufficient for the rest of the body.

To compare different methods of scaling numerical rat phantoms, a simplified rat phantom $N2_{simplified}$ was developed. Only the skull and brain of N2 were modeled inside the outline of rat phantom N2. The homogeneous tissue was modeled as muscle.

A further model used (called N3 in the following) was derived from 81 magnetic resonance images of a male 370 g Sprague-Dawley rat. The MRI slices are separated by 3 mm. Color coded slices with the discriminated tissues and voxel models of different resolutions were made available on the Internet by the EMF research group at the Air Force Base in Brooks, Texas, USA [7]. The model developed based on these slices distinguishes 30 tissues and has a voxel size of $1.5 \times 1 \times 1 \text{mm}^3$.

Tables 8.2 and 8.4 give an overview of the main characteristics and tissue distributions of the numerical phantoms. Most of the electric parameters of the tissues listed in Table 8.1 were calculated for $835 \text{MHz}$ according a 4-Cole-Cole analysis [8] and are based on the data in [9]. The densities of all tissues were set to 1.00 $\text{g/cm}^3$ throughout this study.

8.3.3 Scaling of the Numerical Rat Phantoms

The numerical phantoms were scaled to different sizes to study the dependence of the absorption on the rat size. The question of scaling numerical phantoms has been discussed in more detail in [11] and [12] with respect to human head phantoms.

Three different methods of scaling were used:

1. Uniform scaling: A very simplified method of creating phantoms of different sizes is uniform scaling by multiplying all dimensions of the original phantom with a constant factor. The numerical rat phantoms N1 to N3 and $N2_{simplified}$ were scaled to sizes between approximately 165 g and 450 g.

2. Transversal Scaling: Since adult rats can be expected to increase weight by getting wider but not longer, rat phantoms of different sizes can also be created by multiplying the transversal dimensions but not the longitudinal dimension of the original phantom with constant factors. Phantoms with masses between 200 g and 460 g were created with this method by scaling $N2_{simplified}$.

3. Transversal Scaling with constant brain size: The outline of numerical phantom $N2_{simplified}$ was scaled as described for the transversal scaling, while the brain and the skull were kept unchanged. This may be adequate, since the brain and the skull are not expected to grow for adult rats.

8.4 Methods

8.4.1 Experimental Methods

Minimal modification of the setup was required to enable access for the probes (see Fig. 8.5). A 14 mm wide slot was milled in one tube along the longitudinal axis.
The SAR measurements in the brain of the rat cadavers were performed in vertical steps of 0.5 mm with two different one-dimensional E-field probes both having a tip diameter of only 1 mm (0.8 mm sensor length). The probe ET1DV2 was optimized to achieve a deviation from spherical isotropy of less than 0.2 dB when three measure-
Table 8.2: Overview of the three numerical models used for this study.

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain</td>
<td>Wistar</td>
<td>Wistar</td>
<td>Sprague-Dawley</td>
</tr>
<tr>
<td>Size (g)</td>
<td>300</td>
<td>300</td>
<td>370</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Number of MR Images (head only)</td>
<td>74</td>
<td>57</td>
<td>81</td>
</tr>
<tr>
<td>Spacing between MR images (mm)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Voxel size (mm³)</td>
<td>1.5</td>
<td>0.125</td>
<td>1.5</td>
</tr>
<tr>
<td>Tissues discriminated</td>
<td>14</td>
<td>14</td>
<td>32</td>
</tr>
<tr>
<td>Distance antenna to line A (mm)</td>
<td>66.8</td>
<td>66.3</td>
<td>66.8</td>
</tr>
<tr>
<td>Distance antenna to line B (mm)</td>
<td>72.8</td>
<td>72.8</td>
<td>72.8</td>
</tr>
<tr>
<td>Distance antenna to line C (mm)</td>
<td>75.8</td>
<td>76.3</td>
<td>75.8</td>
</tr>
</tbody>
</table>

* MRI scans were performed by Max-Planck-Institute for Neurological Research, Cologne, Germany
** Model developed by the EMF Dosimetry research group at the Air Force Base in Brooks, USA [7]

...ments are taken by rotating the probe in 120° steps around its axis [13]. Accurate portioning (repeatability: <0.05 mm) and rotation (wobbling:<0.1 mm) was enabled with the latest implementation of the DASY3 near-filed scanner (Schmid & Partner Engineering AG, Zurich). The probes were calibrated with the most precise method [15] for media similar to brain tissue. The probe enables accurate measurement up to 0.5 mm from media boundaries (i.e., from the skull). The first prototype (ET1DV1) had the same performance parameters than ET1DV2 but a conical instead of the cylindrical tip, i.e., it had a less fragile tip but the disadvantage of disturbing the tissue slightly more.

The relative position within the brain was assessed by determining the brain surface from the step function when the sensor goes through the interface brain-air. This was necessary due to poor visibility of the brain surface.

8.4.2 Numerical Methods

The electromagnetic simulation tool MAFIA [16] was used for numerical dosimetry. This tool is based on the Finite-Integration-Technique (FIT), which is similar to the FDTD approach. First-order Mur-absorbing boundary conditions and magnetic boundaries were applied on the lattice truncation. The computation domain had a size of 410 mm in the vertical direction, 550 mm in the longitudinal direction and 550 mm·tan(18°) =178.7 mm orthogonal to the symmetry plane of the setup. A nonuniform mesh with a global grading ratio of 10 and a local grading ratio of 1.5 was used. Grid-conform symmetry planes were modeled as magnetic boundaries. The other symmetry planes were modeled with magnetic material forcing the tangential magnetic field to zero at their borders, which is equivalent to the symmetry.

The dipole is located in the corner formed by the magnetic material and the lattice truncation and was fed by a current source. Depending on the details of the modeling, the computation domain consisted of up to 6.7 million voxels. The
Figure 8.5: The setup with the modified tube enabling access with the E-field probe. For demonstration purposes, the tube opposite the one with the rat cadaver was removed to visualize the dummy rat used to simulate the neighboring rats.

simulations were performed on a Sun Sparc Ultra 2 workstation with a memory of 1.7 GByte and required up to 12 hours CPU time. Steady state was reached after approximately 6 periods. The electric and magnetic field vectors were recorded to calculate the SAR distribution inside the tissues and to determine the radiated power via the integration of the Poynting vector and via the feedpoint impedance.

8.5 Experimental Results for SAR in the Rat Brain

In Table 8.3 data of the animal cadavers as well as the positions of the animal brains (i.e., holes A, B and C) with respect to the dipole are given. Fig. 8.6 compares the SAR values measured in the brains of all rat cadavers on the vertical line through hole A. The SAR values measured in the brains of all four adult rat cadavers E1 to E4 agree surprisingly well and demonstrate a rather small dependence of the exposure on the animal's anatomy. The good correspondence with the measurements taken by the temperature probe strengthen the confidence in the absolute SAR assessments. This was supported even further by almost identical values measured when the brain was replaced with brain tissue simulating liquid of well known dielectric parameters ($\varepsilon_r = 42$, $\sigma = 1.55$ mho/m). An interesting observation is the small SAR variations within the brain, which is in contrast to the data found at the lower frequency bands by [5]. In Table 8.3 the averages of all measurement points inside the brain are given.

The variation within the brain as well as the average SAR value are much higher for rat cadaver E5, which was a juvenile rat of 95 g. More insight can be expected from the numerical analysis.
Table 8.3: Overview of the experimental protocol of the measurements with the experimental rat phantoms

<table>
<thead>
<tr>
<th>Rat cadaver</th>
<th>E1</th>
<th>E2</th>
<th>E3</th>
<th>E4</th>
<th>E5</th>
</tr>
</thead>
<tbody>
<tr>
<td>strain</td>
<td>Lewis</td>
<td>Lewis</td>
<td>Lewis</td>
<td>Fisher 344</td>
<td>Fisher 344</td>
</tr>
<tr>
<td>mass of animal</td>
<td>315 g</td>
<td>350 g</td>
<td>220 g</td>
<td>310 g</td>
<td>95 g</td>
</tr>
<tr>
<td>sex</td>
<td>male</td>
<td>male</td>
<td>male</td>
<td>male</td>
<td>male</td>
</tr>
<tr>
<td>diameter of holes</td>
<td>4-5 mm</td>
<td>4-5 mm</td>
<td>2-3 mm</td>
<td>2-3 mm</td>
<td>2-3 mm</td>
</tr>
<tr>
<td>time between death and first measurement</td>
<td>1.5 h</td>
<td>1.5 h</td>
<td>3 h</td>
<td>3 h</td>
<td>2 h</td>
</tr>
<tr>
<td>body temperature</td>
<td>23°C</td>
<td>24°C</td>
<td>24°C</td>
<td>22°C</td>
<td>22°C</td>
</tr>
<tr>
<td>dosimetric probes used</td>
<td>ET1DV1</td>
<td>ET1DV1</td>
<td>ET1DV2</td>
<td>ET1DV2</td>
<td>ET1DV2</td>
</tr>
<tr>
<td>distance antenna to hole A</td>
<td>61 mm</td>
<td>62 mm</td>
<td>68 mm</td>
<td>57 mm</td>
<td>57 mm</td>
</tr>
<tr>
<td>hole B</td>
<td>64 mm</td>
<td>67 mm</td>
<td>72 mm</td>
<td>61 mm</td>
<td>61 mm</td>
</tr>
<tr>
<td>hole C</td>
<td>70 mm</td>
<td>71 mm</td>
<td>77 mm</td>
<td>65 mm</td>
<td>65 mm</td>
</tr>
</tbody>
</table>

*distances were not measured for rat cadaver E1, but lay in the same range as for the rat cadavers E2, E3 and E4.

8.6 Numerical Results for SAR Distribution inside the Rats

In Fig. 8,8, the SAR distributions corresponding to lines through the holes A, B and C are plotted. The distributions are quite similar for the different phantoms N1, N2 and N3 but vary considerably in absolute value. However, both distributions and averaged values significantly deviate from the measurements. This is a clear indication that the currently achievable MRI resolutions are not sufficient to conduct absolute dosimetric evaluations in small animals based only on numerical analysis. The main limitations are seen in the appropriate modeling of those fine structures which have considerably different dielectric properties than wet tissues, e.g., scull (compare with Fig. 8,9). A further source of uncertainty might be the available dielectric parameters for the various tissues which were assessed using tissues of larger animals (e.g., sheep and pigs).

Although the numerical analysis fails to provide reliable information on the absolute values, it can provide valuable insight on the interaction mechanisms as well as on the dependence on various parameters.

8.7 Dependence of SAR on Position

The setup allows the rat to move its head up and down inside the tube as well as move slightly forward and backwards. The simulations predict a decrease of circa 5% of the SAR$_{brain}$ when the distance between the antenna and the nose of all rats...
Figure 8.6: Comparison of the SAR for a line vertical to hole A measured in the five different rat cadavers. In rat cadaver E2 the measurements were also performed with a temperature probe and with the brain replaced by brain tissue simulating liquid. The SAR distribution is very similar for all adult rat cadavers (E1 to E4), but is considerably higher for the small rat cadaver (E5). The step function at $z=0$ results when the probe goes through the boundary tissue-air.

Figure 8.7: SAR measured for the three lines in rat cadaver E4 (Fisher 344, 310 g) and E5 (Fisher 344, 95 g). The absorption is considerably higher in the juvenile rat. The SAR inside the brain is rather homogeneous. The brain average SAR was determined by averaging over all measured SAR values inside the brain.

is increased from 30 mm to 37.5 mm. Vertical movements of $\pm 10$ mm changed the $\text{SAR}_{\text{brain}}$ in the range of circa $\pm 15\%$, with the lowest values occurring for an animal.
Figure 8.8: Simulated SAR distribution on the three lines for the three numerical phantoms N1, N2 and N3. The SAR distribution differs considerably between the three models.

Figure 8.9: The upper part of the Figure shows the simulated SAR distribution in the mid-sagittal plane of the brains in rat phantoms N1, N2 and N3. The lower part shows histograms for the SAR distribution in the brains of the numerical models. The distributions are very different for the three models. The figure also demonstrates how coarse a voxel size of $1.5 \text{ mm}^3$ is compared to the fine structures in the head of a rat.

in the uppermost position. The SAR measured in the brain of rat cadaver 4 decreased by 20% when the cadaver was withdrawn by 7.5 mm. If the head of the animal was
moved up by 8 mm from the lowest position, the SAR in the brain decreased by circa 7%.

Based on the experimental and numerical results, the variation of the brain averaged SAR due to movements of the rat inside the tube can be estimated to be in the range of +15% to -30% compared to the standard position (head in the center of the tube in the foremost position).

### 8.8 Dependence of SAR on Size

The measurements showed only minor differences between the SAR in the four adult rat cadavers with masses between 220 g and 350 g. Considerably larger exposure values were measured for the small rat of 95 g weight (see Fig. 8.6). To gain sufficient knowledge for determining the exposure for different animal sizes, a number of simulations were conducted, the results of which are summarized in Fig. 8.11. It shows 1) the measured average SAR values in the brain of rat cadavers E1 to E5, 2) the simulated SAR$^{\text{brain}}_{\text{phantom}}$ for phantoms N1 to N3 scaled uniformly to different sizes and 3) the simulated SAR$^{\text{brain}}_{\text{phantom}}$ in the simplified numerical phantom E2$^{\text{simplified}}$ scaled with three different methods. Both measurements and simulations show a strong increase of the SAR$^{\text{brain}}_{\text{phantom}}$ with decreasing animal size at 1.62 GHz. Interestingly, the dependence on size is not sensitive for the applied approach, i.e., the exposure can be determined by simple interpolation.

### 8.9 Dependence of the Performance on Frequency

The performance of the carousel setup turned out to be considerably better at 1.62 GHz than for the lower frequency bands not only in terms of efficiency and brain-to-whole-body exposure but also regarding the homogeneity of the brain exposure. Fig. 8.12 shows the dependence of the brain exposure as a function of frequency. Below the mobile communications frequency range the absorption in the brain increases strongly with the frequency. This is consistent with an absorption mechanism of induced currents in a poorly conducting body which is small compared
Figure 8.11: Increase of the SAR in the brain with decreasing animal size. The results for phantom N2\textit{simplified} demonstrate that the size dependence is not sensitive to the method of scaling.

to the wavelength [17]. Above 2 GHz the absorption in the brain decreases with increasing frequency. The in-depth penetration becomes small compared to the size of the rat. The ratio of brain averaged SAR to whole body averaged SAR reaches its maximum of about ten in the mobile communications frequency range. At lower and higher frequencies, the setup is not suitable for reaching a reasonable ratio of \text{SAR}_{\text{brain}} to \text{SAR}_{\text{body}}. At low frequencies the ratio is just determined by the 1/r decrease of the magnetic field near the antenna, while the absorption becomes so local at high frequencies that the ratio tends to zero.

It is interesting to note that the opposite was found at the lower frequency bands, namely, a decrease of the \text{SAR}_{\text{brain}} with decreasing animal size [4] [5]. Simulations with models N1 to N3 at 835 MHz performed within this study confirmed this finding.

8.10 Efficiency

Table 8.4 gives the volume and the tissue averaged SAR values for the three numerical rat phantoms. The simulations predict that the setup is highly efficient since 1)
about 60% of the the emitted power is absorbed by the animals and 2) the SAR_{\text{brain}} is higher than the SAR_{\text{body}} by a factor of circa 7 to 9. This means that most of the power is absorbed in the head of the rat, which is also demonstrated by Fig. 8.10. The simulations show that averaging over three lines in the brain instead of averaging over the the total volume of the brain overestimates the SAR_{\text{brain}} by up to circa 20%. The precision of this ratio is poor, since the SAR distribution of the numerical analysis deviated considerably from the experimental data. For the adult animal, the efficiency is about $2.8 \pm 30\%$ mW/g per Watt antenna input power.

8.11 Discussion

The objective of the 2-year bio-assay as currently being conducted at Battele Laboratories is the application of a constant brain exposure level throughout the entire animal life span. In view of the uncertainties of the dosimetric analysis and the variations in the animal weight at a given age, only three power levels, i.e., three animal categories, were considered as being practical. They were selected as given in Table 8.5.

8.12 Conclusions

A detailed experimental and numerical dosimetry of the carousel setup for the exposure of rats at 1.62GHz was performed. Despite the improvements in numerical dosimetry, the results clearly demonstrate that the animal phantoms currently available are insufficient to perform reliable absolute dosimetric evaluation based only
Table 8.4: Volume and tissue averaged SAR values, fraction of absorbed power and ratio of brain averaged SAR to whole body averaged SAR for the three numerical rat models.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Volume average</th>
<th>Line average</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>volume [cm³]</td>
<td>SAR [W/kg/W]</td>
<td>[cm³]</td>
<td>SAR [W/kg/W]</td>
<td>volume [cm³]</td>
</tr>
<tr>
<td>brain</td>
<td>3.0</td>
<td>1.39</td>
<td>2.1</td>
<td>1.27</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>1.60</td>
<td>-</td>
<td>-</td>
<td>1.30</td>
<td>-</td>
</tr>
<tr>
<td>bone</td>
<td>14.4</td>
<td>0.33</td>
<td>12.4</td>
<td>0.28</td>
<td>26.0</td>
</tr>
<tr>
<td>digestive system</td>
<td>53.7</td>
<td>0.08</td>
<td>52.7</td>
<td>0.08</td>
<td>17.7</td>
</tr>
<tr>
<td>eyes</td>
<td>0.3</td>
<td>0.99</td>
<td>0.2</td>
<td>0.92</td>
<td>0.2</td>
</tr>
<tr>
<td>fat</td>
<td>53.0</td>
<td>0.05</td>
<td>43.2</td>
<td>0.03</td>
<td>32.8</td>
</tr>
<tr>
<td>heart</td>
<td>1.5</td>
<td>0.22</td>
<td>1.4</td>
<td>0.21</td>
<td>2.7</td>
</tr>
<tr>
<td>kidneys</td>
<td>3.0</td>
<td>0.14</td>
<td>2.9</td>
<td>0.11</td>
<td>2.2</td>
</tr>
<tr>
<td>lungs</td>
<td>3.6</td>
<td>0.11</td>
<td>3.5</td>
<td>0.12</td>
<td>4.0</td>
</tr>
<tr>
<td>liver</td>
<td>10.2</td>
<td>0.11</td>
<td>9.0</td>
<td>0.10</td>
<td>18.2</td>
</tr>
<tr>
<td>muscle</td>
<td>104.5</td>
<td>0.26</td>
<td>109.5</td>
<td>0.29</td>
<td>169.2</td>
</tr>
<tr>
<td>skin</td>
<td>104.2</td>
<td>0.14</td>
<td>97.8</td>
<td>0.14</td>
<td>39.2</td>
</tr>
<tr>
<td>testicles</td>
<td>5.7</td>
<td>0.06</td>
<td>5.7</td>
<td>0.08</td>
<td>4.8</td>
</tr>
<tr>
<td>whole body</td>
<td>330.8</td>
<td>0.18</td>
<td>328.4</td>
<td>0.19</td>
<td>300.8</td>
</tr>
<tr>
<td>absorbed power</td>
<td>61%</td>
<td>60%</td>
<td>60%</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>SAR&lt;brain&gt;/SAR&lt;sub&gt;Body&lt;/sub&gt;</td>
<td>7.6</td>
<td>6.9</td>
<td>9.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 8.5: Efficiency of the setup as a function of weight

<table>
<thead>
<tr>
<th>Animal Weight</th>
<th>SAR&lt;sub&gt;brain&lt;/sub&gt; per Watt</th>
<th>Dependence on Movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>70g - 120g</td>
<td>5.3 mW/g ±60%</td>
<td>+15%; -30%</td>
</tr>
<tr>
<td>120g - 180g</td>
<td>4 mW/g ±60%</td>
<td>+15%; -30%</td>
</tr>
<tr>
<td>&gt;180g</td>
<td>2.8 mW/g ±45%</td>
<td>+15%; -30%</td>
</tr>
</tbody>
</table>

upon numerical analysis. Since considerable progress has also been achieved in experimental dosimetry, the precision and reliability of dosimetric in vivo analysis show considerable improvement if both experimental as well as numerical techniques are utilized.

The analysis confirmed the high suitability of the carousel setup for studying the hypotheses of CNS effects in rats evoked by electromagnetic exposure in the frequency range of mobile communications, i.e., between 800 MHz and 2 GHz. The assessment revealed an even better performance of the setup at 1.62 GHz than at the lower frequency range.

Future dosimetric needs for in vivo studies are mainly seen in improved numerical phantoms of the animals and in new electric and temperature probes providing spatial resolutions in the submillimeter range.
References


[8] The tissue dielectric parameters can be found under http://www.fcc.gov/fcc-bin/dielec.sh


Epilogue

The objective of the studies performed during the term of this PhD was to provide input for improving quality and scientific rigor of the research programs focused on risk assessment of mobile communications by optimizing RF exposure setups. The importance of these studies was reflected by the analysis of WHO, which detected severe deficits in the design and characterization of previously applied exposure setups.

The guidelines developed within this thesis have become a valuable reference for every new research program. The setups for which the dosimetry was conducted within this thesis have been used for various experiments which are graded to be of high significance in the context of the WHO risk evaluations. The study about the exposure of children versus adults just lately gained new relevance by the publication of the report of the Independent Expert Group on Mobile Phone in UK (www.legmp.org.uk).

The research conducted by my colleagues in experimental and numerical near field technologies together with these contributions made Zurich to the most important center in this area. Since November 1999 this competence is concentrated under the roof of the new Foundation for Research on Information Technologies in Society (IT'IS).

Currently the IT'IS team is part of the collaboration conducting the large-scale toxicological studies supported by the 5th Framework Program of the European Union and the mobile telecommunication industry. IT'IS is responsible for the development and realization of the exposure setups which will be used by numerous partner institutions within the collaboration. This project will demand new approaches with improved efficiency and quality of dosimetry and new dosimetric tools. I am confident that the new team will successfully face these challenges and make major contributions to the enhancement of the quality of this ambitious research program.
Curriculum Vitae

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Dipl. Phys. (certified physicist), degree 1996
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