Exposure systems and dosimetry of large-scale in vivo studies

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Exposure Systems and Dosimetry of Large-Scale In Vivo Studies

A dissertation submitted to the
SWISS FEDERAL INSTITUTE OF TECHNOLOGY ZURICH

for the degree of
Doctor of Sciences

presented by
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Summary

Growth of the mobile communication market and the widespread use of wireless technologies has awakened public concern to the associated possible health risks and consequently the interest of health authorities to promote and demand careful risk assessment.

A look at the numerous contributions on risk assessment in the last decade from cell, animal and human exposure studies shows sometimes conflicting and controversial findings, which might be due to deficient exposure setup designs, the use of inadequate methods, poor documentation and insufficient dosimetric assessment.

This thesis focuses on the improvement of the exposure characterization and the enhancement of the dosimetry of RF-EMF large-scale in vivo animal studies. In Chapter 2, a description of the newest technological methods used in this thesis is presented. A universal methodology was developed in Chapter 3 to obtain comprehensive and detailed dosimetric information identified as the minimal requirements for in vivo experiments testing EMF potential hazards.

Relevant parameters for the comparison of animal studies involving RF-EMF exposure were investigated in Chapter 4. Significant uncertainty of the SAR values related to the discretization of the anatomical models was observed. Large variations of the whole-body averaged and peak spatial SAR were obtained at different frequencies and polarizations, and in particular for organ-specific averaged SAR.

Chapter 5 of this thesis presents the dosimetry results of the 1800 MHz DCS rat exposure setup, developed for the PERFORM A European project, and which is one of the most complete dosimetric assessments of its kind ever performed. It delivers high quality information about SAR strengths and distributions in all of the animals.
within the study and over their entire lifetime, a detailed uncertainty analysis, and the assessment of the SAR variations distinguishing between variations within one exposure session and variations over lifetime.

The last part of this thesis deals with reverberation chambers and their use as exposure setups for large-scale in vivo studies. Chapter 6 is an introduction to reverberation chamber theory. In the next four years NIEHS is performing a number of lifetime bio-assay experiments to evaluate the potential toxicology/carcinogenicity of cell phone RF radiation in unrestrained rats and mice. The performed research on the preliminary dosimetric study of these experiments, presented in Chapter 7, made NIEHS redesign the original exposure protocol in order to improve the animal exposure and reduce the cost. The research undertaken to determine a suitable implantable wireless transducer to monitor animal body temperature during its exposure in a reverberation chamber was the topic of Chapter 8. The challenge of designing and developing a water system to be used inside a reverberation chamber was successfully faced in Chapter 9.

Three different exposure setups for large-scale in vivo animal studies are compared in Chapter 10, in terms of efficiency, SAR variations, space requirements and cost.

The present thesis provides insights and methodology aspects to allow the good exposure design of future RF-EMF large-scale long-term in vivo experiments. This work presents guidelines to perform high quality dosimetric assessment which substantially enhances the relevance of the experiment results, allows their interpretation, and permits the replication of the studies by independent laboratories in a reliable manner.
Zusammenfassung

Der steigende Einsatz von Funktechnologien im täglichen Leben, insbesondere im Bereich der Mobilkommunikation, verbunden mit einem stetigen Wachstum der entsprechenden Märkte, wirft in zunehmendem Masse die Frage nach etwaigen Gesundheitsrisiken dieser Technologien auf. Gesundheitsbehörden reagieren auf diese Trends, indem sie eine sorgfältige Abschätzung der Gefahren durch verschiedene Institutionen fördern und von den Anbietern entsprechende Stellungnahmen verlangen.


In Kapitel 4 werden relevante Parameter für den Vergleich von Studien, bei denen Tiere mit RF-EMF bestrahlt werden, untersucht.

Kapitel 5 dieser Dissertation zeigt die Anwendung der bisher vorgestellten Methoden zur Auswertung der Dosimetrie der Bestrahlungseinrichtung 1800 MHz DCS für Ratten, die für das Europäische Projekt PERFORMA entwickelt wurde. Dabei handelt es sich um eines der kompletesten jemals ausgeführten dosimetrischen Bewertungssysteme. Es liefert hochwertige Informationen über die SAR Intensitäten und Streuungen in allen Tieren über deren ganzen Lebenszeitraum, eine ausführliche Analyse der Streuung, und die Bewertung der SAR Abweichungen, wobei zwischen Abweichungen innerhalb einer Bestrah lungssitzung und Abweichungen über die ganze Lebzeit unterschieden wird.


Drei verschiedene Aufbauten von Bestrahlungseinrichtungen für umfangreiche in vivo Tierstudien werden im Kapitel 10, in Bezug auf Effizienz, SAR Veränderungen, Platzbedarf und Kosten verglichen.
Die vorliegende Dissertation bietet Einblicke und methodologische Aspekte, um Bestrahlungseinrichtungen für langfristige und umfan-
reiche in vivo RF-EMF Experimente zu entwerfen. Diese Arbeit zeigt
Richtlinien, um eine hochwertige dosimetrische Auswertung durchzu-
führen, die die Zuverlässigkeit der experimentellen Resultate wesentlich
verbessert und ihre Interpretation und die Wiederholung der Studien
durch unabhängige Laboratorien auf zuverlässige Art ermöglicht.
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Part I

Introduction
Chapter 1

Background and Motivation
1.1 Introduction

An unprecedented rapid proliferation of wireless communication devices has taken place in the last two decades, especially in the area of mobile telecommunication equipment. Increasingly smaller devices with corresponding smaller antennas can be easily carried by the user (e.g., mobile phones) attached or implanted (biomedical monitoring applications) are being developed. Such small devices commonly establish communication with other antennas present in our environment (home, work place and leisure areas). The extensive and growing use of such devices has awakened the concern of individual users and consumer groups, in turn alerting health agencies and organizations, e.g., the World Health Organization (WHO), and governments to request and promote scientific investigation of the environmental and human effects of the wireless technology. In addition, mobile technology is using increasingly more complex modulation schemes. For instance, the fourth generation of mobile phones is currently being introduced, and further changes in the future are likely to increase the availability of wireless channels. Therefore, there is a continued need to research the interaction between biological bodies and radio-frequency (RF) signals. Numerous studies are currently being performed to assess and evaluate potential health risks or hazards due to electromagnetic field (EMF) exposure. Many others have been completed. Some of these published findings differ significantly or even contradict each other [1], [2]. Many of the studies involve a small number of experiments on a single biological system exposed to a specific set of field conditions. Some studies suffer from obvious methodological difficulties. Other apparently well done studies report bioeffects of unclear health significance. All this has given impulse to the scientific community to develop methodologies to perform well-designed studies [3], [4], [5], while regulatory bodies, e.g., the International Commission on Non-ionizing Radiation Protection (ICNIRP) and the European Committee for Electrotechnical Standardization (CENELEC) have been prompted to establish standards and safety limits for occupational RF users and the general public.

Studies for EMF exposure risk assessment can be divided into three main categories: *in vitro, in vivo* and human studies. *In vitro* studies
investigate possible effects of EMF exposure on cellular, sub-cellular and molecular levels. They are usually less expensive and time consuming than \textit{in vivo} and human studies, and higher exposure levels can be applied. However, the relevance of their findings for human health is relegated to clarify the mechanism of biological effects. \textit{In vivo} experiments are more expensive and resource intensive than \textit{in vitro} studies, and allow the assessment of potential long-term EMF effects in animals. Although findings from \textit{in vivo} studies are more relevant, their conclusions are not always applicable to humans. Human studies have the highest relevance, but they are limited to the use of low RF power level exposures. Experiments with exposure levels that cannot be applied to humans are performed with animals or cell cultures. Recent results can be found in [6], [7], [8]. \textit{In vivo} and human studies also permit the investigation of effects on subject performance in addition to toxicological effects [9], [10], [11]. Finally, there has been an increasing interest in studies focussing on the electromagnetic safety exposure of children because of the rapid proliferation of wireless phones among the young population [12], [13]. There are many reviews available about EMF and human health effects, e.g., [14], [15], [16], [17], [18] and most recently [19]. A very complete list of \textit{in vitro}, \textit{in vivo} and human studies can be found at the WHO website\footnote{http://www.who.int/peh-emf/research/database/en/}.

When an agent (physical or chemical) is being tested for its effects in a biological body for negative effects, it is implicit that the agent must be imparted to that body. Therefore, the agent dose and its units must be well defined and it is necessary to find parameters that quantify the interaction of EMF with the biological systems [20]. In the literature some proposals can be found such as the induced current density in tissue [21], the internal electric field, and the presently most accepted mass-normalized rate of power absorption, or dose rate. The dose rate started to become scientifically accepted in the 1970s, and was finally officially designated as specific absorption rate (SAR) by the National Council on Radiation Protection and Measurements (NCRP) [22]. The formal definition of SAR is the time derivative of the incremental energy absorbed by (dissipated in) an incremental
mass contained in a volume of a given density. It can be obtained from the expression:

$$SAR = \frac{dP}{dm} = \sigma \frac{E^2}{\rho} = c \frac{dT}{dt}$$

(1.1)

where all quantities are determined in the tissue/body exposed to the EMF radiation, with $P$ as the power absorbed, $m$ the mass, $\sigma$ the electric conductivity, $E$ the root mean squared (rms) of the electric field amplitude, $\rho$ the density, $c$ the specific heat capacity and $dT/dt$ the time derivative of the temperature at the onset of the exposure.

In order to interpret a biological effect, one must determine the internal field strength or the energy dose that can cause such an effect in the experimental subject. Defining the dose received by a body when exposed to EMF and determining the SAR distribution have proven to be complex tasks. Only a combination of advanced experimental and numerical methods allows reliable assessment of the actual level of exposure.

When radio-frequency (RF) radiation is incident on biological systems, part of the energy is absorbed producing a rise of the energy of the random molecular motion (temperature) in the tissues. Depending on the temperature increase, which is mainly related to the SAR, the exposure time and the thermal metabolism of the exposed system, two kinds of effects can be distinguished: thermal and non-thermal

[23]. The thermal effects lead to a rise in temperature of the irradiated system and are accompanied by physiological responses depending on the intensity and duration of the exposure. Non-thermal effects occur at exposure levels which neither stimulate thermoregulation nor produce any significant change in organism temperature. Thus, it is expected that these effects may be produced directly by the applied fields rather than indirectly as a result of heating. For the case of EMF risk assessment studies investigating potential non-thermal biological effects, exposure levels causing no significant increase in temperature anywhere within biological systems have to be chosen to avoid masking the results by thermal response.
The International Commission on Non-ionizing Radiation Protection (ICNIRP) has set human exposure limits with SAR values of 2 W/Kg for local absorption (averaged SAR over 10 g of contiguous tissue) and 0.08 W/Kg for whole-body average absorption, for the general public\(^2\) [24]. Well established studies have shown that no thermal effect is expected in humans if absorption levels are kept below these limit values. However, the risk evaluation of non-thermal effects is still controversial [25]. The power applied is generally low (to avoid thermal effects), and high sensitivity tools are required to measure and detect small power absorption levels and their variations. Studies and their exposure setups have to be designed to promote this high sensitivity and thus increase the likelihood of observing adverse effects, if there are any.

### 1.2 Motivation

Concern regarding the potential hazards of RF-EMF in human health has promoted risk assessment studies in biological systems. The interpretation of the results of these studies is not easy, since the RF energy interaction with biological materials is very complex. The controversial results of some studies in the last decades might be caused by the poor documentation of exposure data and conditions, deficient design of the exposure setups, and inadequate and insufficient dosimetry. Therefore, in order to provide the highest relevance to the results of \textit{in vivo} studies and to allow their clear interpretation, good definition of all RF-EMF exposure parameters as well as detailed experimental and numerical dosimetry have to be delivered together with the study results.

### 1.3 Objectives

This thesis focusses on \textit{in vivo} studies investigating RF-EMF risk assessment in the frequency range from 450 to 5000 MHz. Various \textit{in vivo} exposure systems were analyzed with respect to their feasibility for large-scale animal studies, power efficiency, uniformity of the SAR

\(^2\)These values are to be averaged over any six-minute period
pattern in the animal subjects, uncertainties and variations. The main objectives of this thesis can be summarized as follows:

- to develop a methodology to perform dosimetric investigation, assessment of SAR values and distributions, and treatment of uncertainties and variations,
- to assess relevant exposure parameters for the comparison of animal studies,
- to derive criteria for efficient, reliable and stable exposure in animals, evaluating three different exposure scenarios (Parts III, IV and V), and
- to improve the quality of dosimetric data which would in turn enhance the relevance of the experiment results and the quality of their interpretation and discussion, as well as facilitate replication studies.

1.4 Chapters Overview

The remaining chapters of this thesis are organized as follows:

- **Chapter 2**: A brief overview of the currently available and required experimental and numerical tools for RF dosimetry is presented, specifically the tools used within this thesis.

- **Chapter 3**: The development of a universally applicable method to obtain comprehensive and detailed dosimetric information for *in vivo* experiments is presented in this chapter. This methodology covers not only SAR assessment but also uncertainties and variations treatment, and gives higher relevance to the results of a study by providing high quality exposure information.

- **Chapter 4**: Under RF plane wave exposure conditions, relevant exposure parameters for the comparison of animal studies have been investigated. The use of various high resolution anatomical models was necessary to assess discretization uncertainties. SAR variations were evaluated for different frequencies and polarizations.
• **Chapter 5:** Within the European project PERFORMA, the dosimetry of an exposure setup developed to expose rats at 1800 MHz digital cellular system (DCS) signals was performed following the methodology described in Chapter 3. It is shown that high quality dosimetric data can be achieved with reasonable effort, given a well designed exposure setup.

• **Chapter 6:** An introduction to reverberation chamber theory is provided in this chapter, including the design of the chamber and stirrers, modal density, minimum operating frequency, effectiveness of the chamber, and $Q$-factor. The U.S. National Institute of Environmental Health Sciences (NIEHS) plans to perform a number of long-term large-scale *in vivo* studies to investigate the potential toxicity/carcinogenicity effects of RF radiation in rats and mice. Reverberation chambers were proposed as exposure setups for those studies. A description of a plane wave integral representation of the exposure of an object in a reverberation chamber is shown in this chapter, as well as the hypothesis that this exposure might be reproduced by a finite number of plane waves with different polarizations and incidence directions.

• **Chapter 7:** The numerical investigation of the feasibility of using a reverberation chamber as the exposure setup for the planned NIEHS studies is presented. An approximation of the minimum number of plane waves necessary to simulate the exposure of an animal in a reverberation chamber environment is assessed in the first part of this chapter. The second part comprises a preliminary characterization of the lifetime animal exposure including: efficiency, uniformity, whole-body and organ-specific average SAR, SAR distributions and variations.

• **Chapter 8:** The suitability of various implantable wireless temperature transponders to monitor animal temperature before, during and after exposure in a reverberation chamber was investigated. Based on the device properties, experimental and numerical SAR assessment of the best candidates as well as electromagnetic interference (EMI) measurements were performed, and the most suitable device was identified.
• **Chapter 9:** A novel system to provide water to rodents during exposure to high fields in a reverberation chamber was designed and developed. This water system (1) solves the problem of energy absorption in the water (comparable to animal absorption) thereby lowering power requirements, (2) does not significantly alter the SAR patterns in the animal when drinking, and (3) avoids peak SAR values at the animal mouth when drinking.

• **Chapter 10:** A comparison of three different exposure setups for large-scale *in vivo* studies is presented in this chapter, considering efficiency, uniformity, space requirements and cost.
Part II

Methods
Chapter 2

Experimental and Numerical Methods and Tools
2.1 Introduction

A biological body in a RF field constitutes a complex, poorly conductive scatterer. The induced and scattered fields have near-field characteristics and require full characterization of the E- and H-field distribution. This characterization can only be done by simulations representing the full complexity of the scatterer. However, as demonstrated in this thesis, the uncertainty of the numerical results can only be assessed via experimental validation. Therefore, the full exposure characterization consists of:

- detailed numerical analysis of E-field, H-field and SAR distributions
- experimental evaluation of the incident fields and scattered fields
- induced fields

Experimentally, there are two main methods to determine SAR in a body exposed to EMF radiation by measuring either the induced E-field or the temperature in the body. Both methods have advantages and disadvantages.

The E-field within an object can be mapped by moving a probe along a selected path/volume. Implantable E-field probes provide the most sensitive and direct means of SAR measurement. Probes with dipole sensor lengths of $<5\,\text{mm}$ can detect SAR of $<1\,\text{mW/kg}$. Although most E-field probes use three small orthogonal dipole antennas to provide isotropic measurements, they are still susceptible to isotropy errors. Therefore, full characterization of dosimetric E-field probes requires specialized equipment and complex procedures [26].

Assessing SAR by measuring the temperature in an object exposed to EM fields requires a high exposure level and short exposure duration in order to produce a linear temperature rise. In this way, accurate quantification of the temperature rise can be obtained in the absence of any significant thermal heat exchange process. Temperature sensors such as thermo-couplers and thermistors (with metallic sensors and leads) can provide very good sensitivity; however, they are not fully immune to RF fields. Optical probes provide high RF immunity but lower sensitivity. In general, SAR sensitivity using these
probes is lower than with dosimetric E-field probes (approximately a factor of 1000). These probes are suitable for single-point measurements rather than scanning or mapping biological bodies. Since temperature is a scalar quantity, temperature probes can be independently calibrated in non-RF conditions. These probes are often used to provide the bases for transfer calibration.

There are several numerical techniques being used in EMF theory [27], [28]. The finite-difference time-domain (FDTD) method introduced by Yee [29], is currently the leading technique for numerical mobile telecommunication equipment (MTE) exposure assessment and dosimetry. A review of publications related to FDTD is given in [30]. Chavannes analyzes this technique in detail [31]. The newest FDTD based implementations are increasingly robust [32], implement solid absorbing boundary conditions, which allows one to obtain results over a wide range of frequencies. They often incorporate conformal schemes that try to reduce stair-casing problems, [33].

Some of the limitations of FDTD techniques are associated with the use of fine wires or thin metallic sheets. Research in this field is ongoing [34]. FDTD-based programs generally use rectilinear grids. In order to reduce the impact of stair-casing errors, very fine grid steps must be used for the representation of complex structures whose boundaries are not aligned to the grid axis. The maximum stable time step [35] is another limiting factor when problems with electrically small geometries have to be solved. For such cases, the FDTD algorithm might be slower than other methods.

The total simulation time could recently be significantly reduced by means of dedicated hardware. Field programmable gate array (FPGA) implementations or parallelized graphics processing units with high memory bandwidth are used for the FDTD updating scheme [36]. These solutions yield a speed-up of one order of magnitude.

In spite of the remaining limitations listed above, FDTD is a very appropriate numerical method when largely non-homogeneous environments have to be investigated.
2.2 Experimental Instrumentation

The DASY4 system\(^1\) was used to scan incident fields and SAR distributions. The newest available probe technology was always employed, the specification of which are summarized in Table 2.1. Where DASY4 system could not be used as in a reverberation chamber, the EASY4 \(^1\) system was employed.

<table>
<thead>
<tr>
<th>Probe Type</th>
<th>Type</th>
<th>Manufacturer</th>
<th>Tip Diameter</th>
<th>Frequency Range</th>
<th>Dynamic Range</th>
<th>Linearity</th>
<th>Isotropy (in HSL(^2))</th>
<th>Calibration Uncertainty</th>
</tr>
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<tbody>
<tr>
<td>SAR Probe</td>
<td>ES3DV2, SN: 3005</td>
<td>SPEAG</td>
<td>3.9 mm</td>
<td>10 MHz to &gt;6 GHz</td>
<td>5µW/g to &gt;100 mW/g</td>
<td>±0.2 dB (30 MHz to 3 GHz)</td>
<td>±0.2 dB (axial)</td>
<td>±0.3 dB (spherical)</td>
</tr>
<tr>
<td>SAR Probe</td>
<td>EF3DP6, SN: 4004</td>
<td>SPEAG</td>
<td>3.9 mm</td>
<td>100 MHz to 5 GHz</td>
<td>2 V/m to 1000 V/m</td>
<td>±0.2 dB</td>
<td>±0.2 dB (axial)</td>
<td>±0.4 dB (spherical)</td>
</tr>
<tr>
<td>SAR Probe</td>
<td>H3DV6, SN: 2214</td>
<td>SPEAG</td>
<td>3.9 mm</td>
<td>100 MHz to &gt;6 GHz</td>
<td>2 V/m to &gt;1000 V/m</td>
<td>±0.2 dB (100 MHz to 3 GHz)</td>
<td>±0.2 dB (axial)</td>
<td>±0.4 dB (spherical)</td>
</tr>
<tr>
<td>E-Field Probe</td>
<td>H3DV6, SN: 6060</td>
<td>SPEAG</td>
<td>6 mm</td>
<td>200 MHz to 3 GHz</td>
<td>10 mA/m to 2 A/m at 1 GHz</td>
<td>±10% at 3 GHz (for plane wave)</td>
<td>±0.25 dB (spherical)</td>
<td>±6.0% (k=2)</td>
</tr>
<tr>
<td>T Probe</td>
<td>T1LAB, SN: 5101</td>
<td>SPEAG</td>
<td>1 mm</td>
<td>0 to 60°C</td>
<td>&lt;0.2°C</td>
<td>±2%</td>
<td>200µW/g in HSL</td>
<td>&lt;1 s</td>
</tr>
</tbody>
</table>

Table 2.1: Probes used for E- and H-field, SAR and Temperature measurements.

---

\(^1\)DASY4 and EASY4 systems from SPEAG.
2.3. **NUMERICAL TOOLS**

2.2.1 Animal Phantoms

Animal phantoms are simplified homogeneous models which represent the animals in terms of size and absorbed power. Several phantoms were developed to perform validation in the context of this thesis. These phantoms were filled with a tissue simulating liquid. Many different liquids and gels are manufactured with dielectric properties equivalent to a particular tissue or average of several tissues, for a single frequency and broadband. Recipes are available in the literature.

2.3 Numerical Tools

2.3.1 Simulation Tool

All simulations within this thesis were performed with SEMCAD, a FDTD-based simulation platform, developed within our research group. SEMCAD has been enhanced with specific dosimetry features: CAD phantom models, automatic evaluations of whole-body and organ-specific averaged SAR, as well as peak spatial averaged SAR values. Furthermore, this thesis could also profit from the hardware acceleration graphic card enhancement of SEMCAD (Accelware).

2.3.2 High Resolution Anatomical Models

Animal models with high anatomical resolution are a basic requirement to deliver quality dosimetric data. Experimental dosimetric measurements in animals are very limited. The methods are invasive: sometimes surgery is required; only specific points in the animals can be reached; stress is produced in the animals and might even provoke premature death. Even with the use of cadavers, the experimental methods are limited as it is impossible to obtain absorption values averaged over entire organs/tissues or localized absorption peak values in complex inhomogeneous bodies. On the other hand, numerical tools provide averaged and peak SAR values in every organ and tissue of the model as well as whole-body absorption and SAR distributions in and on the surface of the models. Therefore, the closer the anatomical models are to the real animals, the higher the quality of the results.
In addition, original size anatomical models covering the entire range of weights of the animals within the study should be generated, since scaling the animals might introduce uncertainties in the assessed SAR values [37].

Figure 2.1 depicts the 3-D anatomical models employed: four adult rats, three mice and one rat pup. All of them were generated following the method described in [38]. The anatomical data of these models are given in Table 2.2.

Figure 2.1: 3-D mouse and rat anatomical models.

The dielectric properties of the tissues determine the magnitude and distribution of the EM fields in the body, thus underscoring the relevance of assigning the right dielectric properties to the tissues of the anatomical models. Generally these properties, electric conductivity $\sigma$ and relative permittivity $\epsilon$, are dominated by the water content in the tissue. It is possible to divide tissues into those with high water content (eye, muscle, liver, skin) and those with low water content (fat, bone). The water content in the tissues varies over lifetime [39], and it is difficult to obtain realistic dielectric properties of the tissues. Measuring these quantities in living animals is very limited, and these parameters might change their values very quickly after death. In addition, the values also depend upon temperature and frequency, and
2.3. **NUMERICAL TOOLS**

<table>
<thead>
<tr>
<th>Species</th>
<th>Model</th>
<th>Size</th>
<th>Weight (g)</th>
<th>Length (mm)</th>
<th>No. of tissues</th>
<th>Slice thick. (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rats</td>
<td>Female SD (7-day old)</td>
<td>pup</td>
<td>14</td>
<td>body:67</td>
<td>43</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>Male SD</td>
<td>small</td>
<td>230</td>
<td>body:190</td>
<td>58</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Female SD (pregnant)</td>
<td>medium</td>
<td>250</td>
<td>body:160</td>
<td>55</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>Female SD</td>
<td>large</td>
<td>480</td>
<td>body:225</td>
<td>54</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Male SD</td>
<td>large</td>
<td>600</td>
<td>body:280</td>
<td>54</td>
<td>1.00</td>
</tr>
<tr>
<td>Mice</td>
<td>Male OF1</td>
<td>small</td>
<td>20</td>
<td>body:77</td>
<td>46</td>
<td>0.26</td>
</tr>
<tr>
<td></td>
<td>Female B6C3F1 (pregnant)</td>
<td>medium</td>
<td>30</td>
<td>body:77</td>
<td>43</td>
<td>0.36</td>
</tr>
<tr>
<td></td>
<td>Male OF1</td>
<td>large</td>
<td>40</td>
<td>body:100</td>
<td>46</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Table 2.2: Grid resolution employed in the simulations and anatomical data of the original sized animal models.

should be assessed over a wide range of both quantities. The dielectric parameters assigned to the tissues/organs of the models used here are those available for rodents [40], supplemented by data from human tissues [41].
Chapter 3

Methodology of Detailed Dosimetry and Treatment of Uncertainty and Variations for *In Vivo* Studies
3.1 Introduction

In vivo studies require optimized methodological approaches to test a hypothesis because of ethical, time, and cost limitations. Precise and well-defined dose delivery of the chemical or physical agent is essential. The delivery of precise doses of RF-EMF into specific tissues/organs is a complex and often underestimated task [42]. The locally induced fields or the locally SAR for a defined incident field strength depend on many extrinsic and intrinsic parameters such as frequency, polarization, field impedance, animal size, posture, age, sex, humidity, etc.

In many cases, only approximate whole-body absorption values are provided without uncertainty estimations, even when non-thermal effects are investigated. Imprecise or ambiguous analysis diminish the scientific value and significance of the studies, since the localized absorptions may vary by factors of several hundreds and the whole-body averaged values may vary by several factors. For example, an erroneous interpretation of two independent experiments conducted at the same time-averaged whole-body SAR, e.g., 1 W/kg, would inevitably show conflicting results of liver-related hazards if the liver-specific SAR of each study significantly differed, e.g., 1-5 W/kg in the first and 0.03 - 0.1 W/kg in the second study. In other words, detailed and accurate dosimetric information about the exposure is a basic precondition for accurate interpretations and validations of experimental results, especially if the evaluation is based on a detailed histopathology.

3.2 Minimal Dosimetric Data

Proper scientific practice requires precise and sufficient data for comparison with similar studies or potentially necessary replications. Ascertaining the uncertainties and variations inherent in the experiment is also crucial for ensuring and fostering a standard of good science. In RF dosimetry, however, uncertainties and variations can be very large and difficult to assess. In this context, the definition of the uncertainty is the description of the confidence interval of the assessed mean SAR values for all animals and the entire exposure duration of the study. Assessment of the relative uncertainty of the mean in multiple dose
3.2. **MINIMAL DOSIMETRIC DATA**

experiments is also recommended. In addition, information about the variations is needed, defined as the deviations from the mean value for individual animals in specific orientations with respect to the field due to position, orientation, posture, age, weight.

Particularly within RF dosimetry, the uncertainties can be larger than the variations, which can be substantial and in general vastly different either in the short-term or over the entire duration of the experiment. If macro-dosimetric data are available, micro-dosimetry can be derived at any time from the locally induced macro field values. In other words, the macro-dosimetric data constitute a complete exposure characterization.

Based on these considerations, the minimal requirements for RF dosimetry can be derived by dividing \textit{in vivo} studies into three categories of endpoints:

- **Studies to determine the EMF-induced thermal threshold of adverse health effects.** Such studies primarily require precise information about the thermal load, including the following minimal requirements: (1) total absorbed power, (2) metabolically generated heat, (3) heat exchange with the environment, etc. However, (4) local SAR distributions including estimations of local heat increases are also needed as long as biological responses caused by local hotspots cannot be excluded. The estimation of uncertainties and variations of thermal loads are difficult to determine, particularly for extrapolations. Thus, the validity and relevance of the safety guidelines formulated from insufficient data attained from past studies are questionable.

- **Studies to determine general biological responses, e.g., assessment of the general carcinogenic and toxic potential of RF below the thermal threshold.** As long as direct field effects cannot be excluded \textit{a priori}, determining the induced fields in each of the relevant tissues is necessary, e.g., all tissues examined in the histopathology. Hence the requirements include: (1) whole-body average exposure, (2) peak spatial SAR values, (3) tissue average SAR, including assessment of the uncertainties and variations. Additionally, assessment of the thermal loads as well as
information about the induced H-fields are valuable. If this information is not available, the usability for risk evaluations is very limited, particularly for negative findings.

- Studies to assess the biological responses of specific targeted tissues, e.g., brain tissues. Detailed dosimetry is primarily required for the targeted tissues but is also important for all other significantly exposed tissues. Hence, the minimal requirements are: (1) the whole-body average exposure, (2) peak spatial SAR values, (3) tissue average SAR for all tissues exposed more than -10 dB of the target tissue. Assessment of the uncertainties and variations is also necessary. In addition, assessment of the thermal loads and local hotspots as well as the induced H-field distributions would also be valuable information.

In conclusion, attaining precise and detailed whole-body as well as organ specific dosimetric information is imperative in all in vivo studies. Temperature assessment is equally necessary, especially if the exposure is close to the thermal threshold. The uncertainty and variations must also be determined for all values.

### 3.3 Objectives

One of the objectives of this thesis was to develop a universally applicable methodology to obtain comprehensive and detailed dosimetric information for in vivo experiments. In general, these are the mean SAR values for whole-body, peak spatial as well as organ-specific average SAR of the entire exposure group, averaged over the entire exposure duration. A substantial part of the analysis is the assessment of the uncertainty of the estimated mean value as well as the variations from this mean value for individual animals for different averaging time periods, e.g., instantaneous (few seconds), immediate (a week) or entire exposure period. This thesis does not address the methodology to determine the thermal load, some aspects of which had been addressed in [43].

The developed methodology has been applied to two large-scale in vivo studies:
3.4 Uncertainty Assessment for Dosimetry

Obtaining detailed RF dosimetric information is difficult because of the vast associated complexities and the large uncertainties. Therefore, an uncertainty assessment for dosimetry is essential to obtain precise results in any experiment. Since the required endpoints, namely the locally induced field strengths, can only be simulated, a statistical analysis cannot be performed. In addition, the parameter space for in vivo RF dosimetry is considerably larger than for other sources such as extremely low frequency (ELF), ionizing radiation, or chemical agents. The locally induced fields depend on many coupled parameters such as local tissue distribution, posture, polarization, wave impedance, etc.

Methodologies for determining the uncertainties of experiments involving quantities that cannot be assessed by statistical means were developed for electromagnetic compatibilities, as described in e.g., [44]. The methods are based on splitting the total uncertainty into various uncertainty sources that are independent or with limited interdependencies, determining their uncertainty from assumed statistical models and calculations of the total uncertainty as the root-mean-squared (rms) value. The adoption of such a methodology for the uncertainty assessment in dosimetry is proposed here. In some cases, uncertainties cannot be analyzed as truly independent parameters. Such combinations must be evaluated and treated accordingly, e.g., by considering the worst-case combination as a rectangular distribution.

A typical list of uncertainty parameters is:

- uncertainty of the exposure setup including
– numerical setup model including mechanical tolerances, material properties, antenna, coax-to-exposure system adapter, etc.
– transfer sensor calibrations (linearity, pulse modulation, etc.)
– numerical limitations, especially discretization;

• uncertainty of the animal model including
  – geometrical/anatomical representation of the animal
  – dielectric parameters assigned to the different tissues/organs
  – dielectric materials in direct contact with the animals (this uncertainty is dependent on the dielectric properties of the skin tissue)
  – uncertainty as a result of a deviation of the averaged weight dependent efficiency function applied and the actual dependency.

3.5 Assessment of Variations

The analysis of exposure variations requires the determination of the deviation around the mean SAR values. In general, many more parameters must be considered than for the uncertainty analysis. Even with a well-conceived concept, many of these parameters are interdependent.

A typical list of variations is:

• variations caused by the setup

  – variations of the input power or of the incident fields (due to drifts of amplifiers/measurement equipment, scattering caused by the animal, animal weight changes, load differences, calibration differences, non-linearities of the feedback loop, etc.)
  – variations of frequency (in general negligible)
  – mechanical and electrical differences between the setups (only if several setups are employed)
position occupied by the animal within the setup (only setups for several animals)

- dependence upon neighboring animals (only setups for several animals).

- variations caused by the animal

  - differences of size/weight as a function of age (should be compensated by applying a weight-dependent incident exposure)
  - differences of size/weight within exposure group
  - differences of anatomy (age, weight and sex)
  - differences of animal orientation in the field, changing the polarization type
  - differences of posture and position in the setup
  - losses in skin or fur (due to water, urine, etc.).

These parameters are analogous to those of the uncertainty analysis, and should be treated in the same manner as proposed for the dosimetric uncertainties. The complexity of the analysis greatly depends on the interdependence of these parameters. For example, if the exposure is strongly dependent on the neighboring animal, then this dependence will basically impact all parameters influencing the absorption/scattering of the field by the animal, i.e., all variations caused by the animal. The already complex matrix would be transformed into a multi-dimensional parameter space. Therefore, exposure setups must be carefully designed to minimize interdependent parameters.

3.6 Dosimetry Validation and Uncertainties

In most analysis, an interface exists between experimental evaluations and simulations, namely the technical exposure setup and the animal model. The setup can be experimentally and numerically evaluated,
whereas the internal field distributions in animal and human models are usually not accessible. The numerical model of the exposure setup generally has more unknown factors than the numerical model of the animal. Unexpected losses, reflections, resonant and multimode structures, etc. often occur in the setups, whereas the animal constitutes a lossy irregular body, yielding few surprises. Even small asymmetries in the setup can lead to significant deviations from the assumed setup that are not obvious and cannot be easily included in the uncertainty analysis. Examples are the Ferris-Wheel setup [43] or the radial transmission line (RTL) in vitro setups [45], where the performance, when experimentally evaluated, differed from what the numerical model would have suggested.

Thus, the most straightforward method to detect severe shortcomings of the dosimetric analysis is an experimental validation in which the setup operates close to its intended use. For example, an analysis with an empty setup might not show the same shortcomings as the loaded setup. Therefore, the setup should be loaded with animal phantoms that closely represent the load with animals in terms of size and absorption, but in which the field values can be easily assessed. This implies that an additional uncertainty analysis is necessary for the numerical setup including the phantom as well as for the experimental evaluation. The dosimetric analysis is reliable if the difference between experimental and numerical results is within the uncertainty boundary. This can be formally expressed as:

\[
E_n = \sqrt{\frac{(v_{\text{sim}} - v_{\text{meas}})^2}{[v_{\text{sim}}u_{\text{sim}}(k = 2)]^2 + [v_{\text{meas}}u_{\text{meas}}(k = 2)]^2}} < 1 \quad (3.1)
\]

whereby, \(v_{\text{sim}}\) and \(v_{\text{meas}}\) are the simulated and measured values, respectively, and \(u_{\text{sim}}\) and \(u_{\text{meas}}\) the uncertainties for assessing the quantities \(v\) by simulations and measurements (\(k=2\) corresponds to a 95% confidence interval). However, it must be noted that useful information can only be obtained if (1) the setup used for the validation approximately represents operation including the animals and (2) the uncertainty of the measurements can be maintained within the same range as that of the simulations.

Validation of the numerical uncertainty assessment using animals is very limited, as it can only be performed on specific organs in ca-
davers. An example is given in [46]. Alternatively, the validation can be conducted by inter-numerical comparison, e.g., by using different animals scaled to the same size or by changing parameters such as the discretization of the models and the dielectric parameters of all tissues. Determining whether the resolution is sufficient is a major obstacle, since limitations exist when discretization is based on slices without 3D-solid reconstruction of the organs. Although not all limitations can be detected, verification of the fine model using only every second slice may be possible. On the other hand, the effects of discretizations can only be significant between low and high permittivity tissues. Future work should be based on models with 3D solid reconstruction of the body, bones, and individual organs.

3.7 Requirement of Methods

The dosimetry and especially the assessment of uncertainties and variations require accurate and very effective tools. The anatomy of animals is highly complex, consisting of hundreds of different parts that the chosen simulation tool must be capable to handle. Furthermore, the simulation tool must allow the evaluation of the different tissues/organs separately, including organ average SAR and spatial peak SAR values, in addition to whole-body data.

Similar high requirements are placed on the measurement tools, preferably the incorporation of electric and magnetic field probes for free space with spatial resolutions of better than 5 mm, dosimetric probes with resolutions as low as 1 mm, as well as RF-transparent temperature probes. The scanning/position accuracy should be better than 10% of the probe diameter.

Detailed animal models with spatial resolutions of much less than 1% of their total length are essential. Since animals are usually not accurately scalable, animals of different sizes/ages as well as of different genders are preferred. In addition, simplified phantoms are needed and must be created to validate the simulation results. Such phantoms should represent the real animals in terms of size and absorption, while enabling the measurements.

It must be noted that the proposed methodology can only be applied with reasonable effort if the exposure setup is well designed and
carefully constructed such that most of the uncertainty and variation parameters will become independent.
Part III

RF-EMF Far-field Plane Wave Exposure
Chapter 4

Relevant Exposure Parameters for the Comparison of *In Vivo* Animal Studies
4.1 Background and Motivation

A wide range of agents are tested in in vivo studies to detect possible health effects related to the use of these agents. When the agent being tested is RF-EMF, the delivery of a well defined dose into a specific tissue/organ is a complex task. Therefore, the exposure setup needs to be optimally designed and composed based on a solid concept. Exposure setups may differ in concept, polarization and frequency. A brief review of some of the latest RF-EMF exposure systems for rodents can be found in [38]. Furthermore, scientific reviews of in vivo studies are grouped with respect to: animal strain, biological endpoint, frequency, whole-body SAR level.

In chapter 3, the relevance of detailed dosimetry has already been justified. In most cases, experiments with animals exposed to RF have the objective of either a histopathological examination (carcinogenicity/toxicology) or a behavioral study (e.g., cognitive performance). The interpretation of the findings from these experiments can be a difficult task if the exposure conditions and dose are not well characterized. Since the experiments to be compared might use different exposure setups and be done in different laboratories, using different methods and materials, etc., it is necessary to investigate which are the relevant exposure parameters for the comparison of animal studies.

4.2 Objectives

The objective of this study was to ascertain the dependence of SAR distributions and SAR values, namely whole-body SAR, organ-specific SAR and peak spatial SAR, on spatial resolution, frequency and polarization.

4.3 Methods

Simulation and Measurement Equipment

The simulations and numerical evaluations were realized with SEM-CAD. The experimental part, based on SAR measurements in animal
phantoms, was performed with the DASY4 system.

**Anatomical Models and Phantoms**

To determine the influence of spatial and anatomical resolution on SAR, high resolution anatomical models of a B6F3C1 pregnant mouse (~30 g, 15 days pregnancy) and a Sprague-Dawley pregnant rat (~250 g, 15 days pregnancy) were generated (Figure 2.1, Table 2.2). Laboratory plastic bottles of different size were used to represent the animal phantoms, mouse and rat, filled with tissue simulating liquid, appropriate for each frequency.

**Polarizations**

Various field polarizations were used in this study, namely E-, H- and k-polarizations, which correspond to the E-field vector, H-field vector and propagation direction vector parallel to the longest body axis of the animal, respectively (see Figure 4.1).

![Figure 4.1: Orientation of the animal body with respect to E-, H- and k-polarizations.](image)
Assessed Quantities and Averaging Volumes for Peak Spatial SAR

The quantities assessed were whole-body average SAR, organ-specific average SAR, peak spatial SAR and SAR distribution in the animal bodies. The color scale used to visualize the SAR patterns is in dB and goes from 0 to -20 dB, whereby 0 dB=0.3 W/Kg for an incident power density of 1 W/m². To assess the peak spatial SAR values, the considered averaging volumes were scaled from human averaging volumes (1 and 10 g), according to the average whole-body weight of the species, resulting in 5 and 50 mg for a rat and 0.5 and 5 mg for a mouse [47].

4.4 SAR Dependence on Resolution

Energy transported by the field waves going through the animal bodies will be unevenly absorbed by the different tissues. Therefore, in complex bodies, composed of various materials with different dielectric properties, the SAR distributions and the peak spatial SAR values are expected to be independent of the geometrical resolution if the discretization is sufficiently fine to determine this limit. To assess such a dependency, two different rat models were considered: a model with every single slice discretized, i.e., with a slice thickness of 0.6 mm (fine resolution model), and a model generated considering every second slice, i.e., with a slice thickness of 1.2 mm (coarse model). The resolution of the employed grid was also varied, leading to voxel sizes of 0.6x0.6x0.6 mm³, which generates a voxel volume of $\sim$0.22 mm³ (fine), and a 1.2x1.2x1.2 mm³ voxel size, or $\sim$1.7 mm³ (coarse).

Considering the model and grid resolutions, three different combinations were established in the simulations:

- coarse-coarse (CC): coarse animal resolution (1.2 mm) - coarse grid resolution (voxel size 1.7 mm³)
- coarse-fine (CF): coarse animal resolution (1.2 mm) - fine grid resolution (voxel size 0.22 mm³)
- fine-fine (FF): fine animal resolution (0.6 mm) - fine grid resolution (voxel size 0.22 mm³).
For each of these resolution combinations, simulations were performed at four different carrier frequencies: 450, 900, 1800 and 5000 MHz, and for each frequency, the E-, H- and k-polarizations of the incident plane wave were used, i.e., a total of 36 simulations were required.

4.4.1 Results

The evaluations of whole-body average SAR in the rat models for the three resolution configurations showed the maximum deviation between the coarse-coarse (CC) and the fine-fine (FF) configurations. Analogous results were obtained for peak spatial SAR over 50 and 5 mg. The deviations of these three quantities between the CC and FF configurations among the three used polarizations and for all four frequencies are shown in Figure 4.2. Deviations larger than 2 dB were obtained for peak spatial SAR; however variations in whole-body SAR were lower than 0.5 dB.

![Figure 4.2: Deviation of whole-body average SAR as well as peak spatial SAR over 50 and 5 mg, between coarse-coarse and fine-fine resolution configurations, among E-, H- and k-polarizations, and for all four frequencies 450, 900, 1800 and 5000 MHz.](image-url)
CHAPTER 4. RELEVANT EXPOSURE PARAMETERS

In addition, the largest SAR dependency on resolution was found for E-polarization at all frequencies. In Figure 4.3, the tendency of the SAR values versus resolution configuration is depicted for all four frequencies at E-polarization. This plot shows a significant increase of the peak spatial SAR values when increasing the resolution of the model by a factor of 2 and of the voxel size by a factor of 8. This is attributed to staircasing effects that have been overcome with the latest development of conformal cell modeling [33]. The issue of staircasing by the slices can only be overcome with 3D reconstruction currently in development.

4.5 SAR Dependence on Frequency and Polarization

To investigate the influence of varying frequency and polarization when exposing an animal to plane wave radiation, the employed rat
and mouse animal models were generated using every single slice. Only the fine-fine (FF) resolution configuration was used for this part of the study in order to avoid the inaccuracies coming from the resolution. This fine-fine configuration, already shown for the rat model, was chosen for the mouse model as follows:

- fine-fine (FF): fine animal resolution (0.36 mm) - fine grid resolution 0.40x0.40x0.36 mm$^3$ (voxel size 0.06 mm$^3$).

Exposure simulations for both the mouse and the rat were performed using the four different frequencies: 450, 900, 1800 and 5000 MHz, and for each frequency, the three field polarizations were used: E-, H- and k-polarizations, resulting in a total of 12 simulations per animal model. SAR values including whole-body and organ-specific average SAR, SAR patterns in the animals as well as in the surface of the animals, tail absorption versus whole body were the assessed quantities within this analysis.

### 4.5.1 Results

The whole-body average SAR for the mouse and rat was assessed and normalized to 1 W/m$^2$ incident power density, for each polarization and frequency. The results are plotted in Figures 4.4 and 4.5 for the mouse and rat, respectively.

As expected, the highest efficiency$^1$ was registered for both mouse and rat models when E-polarization was used, independent of the carrier frequency. Additionally, the mouse showed a significantly higher efficiency at 1800 MHz, as well as the rat at 900 MHz. These frequencies are close to the respective body resonance.

Further investigation of the SAR distribution in the animal bodies delivered results that confirm what was previously shown. Figures 4.6 and 4.7 depict the SAR patterns in the middle slice of a mouse and rat, respectively, for E-polarization, at all four frequencies. A higher efficiency for the mouse at 1800 MHz and rat at 900 MHz is again obvious in the pictures of the animal SAR distributions. In addition, similar absorption patterns are found exposing a mouse at 1800 MHz

---

$^1$Efficiency is here given in [(W/kg)/(W/m$^2$)], and in this context could also be expressed in [(W/kg)/(V/m)$^2$] by simple multiplication of the given SAR values normalized to power density times the impedance of free space, 377 Ω.
CHAPTER 4. RELEVANT EXPOSURE PARAMETERS

Figure 4.4: SAR of the mouse model versus polarization and frequency (normalized to incident power density unit).

Figure 4.5: SAR of the rat model versus polarization and frequency (normalized to incident power density unit).

and a rat at 900 MHz, with a maximum in the center of the body.
4.5. FREQUENCY AND POLARIZATION

Figure 4.6: SAR distribution in the middle slice of a mouse model exposed to plane waves, E-polarization at 450, 900, 1800 and 5000 MHz, from left to right, respectively.

Figure 4.8 illustrates the absorption differences in the SAR distributions in the middle slice of a mouse exposed at 1800 MHz using E-, H- or k-polarization. Higher absorption for E-polarization is well discernable. Equivalent conclusions can be extracted from Figure 4.9, which shows the SAR patterns for a rat model exposed at 900 MHz and three polarizations.

Since there is no indication in the literature that the carrier frequency might result in a different biological response, the similarity of the dose patterns between species is more relevant when comparing both species.

An assessment of the deviation of the organ to whole-body average SAR is crucial to know more about the level of exposure homogeneity in the bodies. The maximum deviation of organ to whole-body SAR among polarizations at each of the carrier frequencies used is shown in Figure 4.10 for a mouse and 4.11 for a rat, for a selection of representative and relevant organs and tissues. More information about the SAR in all organs and tissues of both species can be found in [48].

One of the parts of the animal body that requires special attention
is the tail. The tail is used by rodents for thermoregulation, and due to its shape (long and thin) and dimensions might be highly exposed at specific frequencies. It is very important to investigate the tail exposure and calculate its deviation to the whole-body level at each frequency and polarization of the experiment, since the body orientation in the field is expected to have a high influence on the SAR. If more than one polarization is used to expose a mouse or rat, the one with the highest tail to whole-body SAR deviation will determine and restrict the maximum whole-body absorption level.

In the data analysis, E-polarization resulted the polarization with the highest tail to whole-body SAR deviation. Figure 4.12 shows this deviation for E-polarization at all four frequencies for a mouse and a rat.

Exposing a mouse at 1800 MHz and a rat at 900 MHz, close to their respective body resonance frequencies, the deviation of tail to
4.5. FREQUENCY AND POLARIZATION

Figure 4.8: SAR distribution in the middle slice of a mouse model exposed to plane waves, at 1800 MHz, for E-, H- and k-polarization, from left to right, respectively.

whole-body SAR was the lowest among all four frequencies (<5 dB for both mouse and rat).

SAR patterns on the animal surface confirmed the overexposure of the tail with respect to the whole body, when the employed carrier frequency is not close to the animal resonance frequency. One example of this SAR distribution is shown in Figure 4.13, where a rat model was exposed at 450, 900 and 1800 MHz plane wave with E-polarization. The exposure at 900 MHz is more uniform.
Figure 4.9: SAR distribution in the middle slice of a rat model exposed to plane waves, at 900 MHz, for E-, H- and k-polarization, from left to right, respectively.
4.5. FREQUENCY AND POLARIZATION

Figure 4.10: Maximum deviation among polarizations of organ to whole-body average SAR at four different frequencies, for a selection of mouse organs.

Figure 4.11: Maximum deviation among polarizations of organ to whole-body average SAR at four different frequencies, for a selection of rat organs.
Figure 4.12: Deviation of tail to whole-body absorption for a mouse and a rat exposed to plane waves with E-polarization, at four different frequencies.

Figure 4.13: SAR pattern on the surface of a rat model exposed to plane waves with E-polarization and three different carrier frequencies: 400, 900 (close to body resonance frequency) and 1800 MHz.
4.6 Validation

For validation of these results, an experimental analysis was performed using a 900 MHz horn antenna to expose the rat and mouse phantoms in the far field. Figure 4.14 shows the mouse phantom filled with tissue simulating liquid and the probe introduced in it to perform the measurements, both in front of the horn antenna in the laboratory.

Two series of measurements were realized for each phantom, one for E-polarization and the other for H-polarization. SAR values were directly measured in the phantom with a dosimetric probe within a specific volume: 31.5x31.5x70 mm$^3$ in the rat with a distance between measurement points of 3.5 mm, and 9x9x30 mm$^3$ in the mouse with a separation of measurement points of 1 mm.

The measurements were then compared with the results of the simulations performed with the same phantoms at the same frequency and polarization. The deviations of SAR between experimental and numerical methods and their standard deviation are given in Table 4.1. These deviations and the comparison of SAR distributions showed very good quantitative and qualitative agreement between measurements and simulations, validating the numerical results.

<table>
<thead>
<tr>
<th>Phantom</th>
<th>Polarization</th>
<th>Deviation (dB)</th>
<th>Stand. Dev. (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>E</td>
<td>0.25</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>0.24</td>
<td>0.20</td>
</tr>
<tr>
<td>Rat</td>
<td>E</td>
<td>0.39</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>0.43</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Table 4.1: Deviation between simulated and measured SAR values obtained in a specific volume within the animal phantoms.
Figure 4.14: 900 MHz horn antenna used to expose the animal phantoms in the far-field, with mouse phantom filled with tissue simulating liquid and dosimetric probe to perform the SAR measurements.
4.7 Conclusions

Relevant parameters for the comparison of in vivo studies have been identified by assessing the SAR values and distributions in high resolution animal anatomical models which were exposed to plane wave, at different frequencies (450, 900, 1800 and 5000 MHz), polarizations (E-, H and k-polarization), and spatial resolutions.

It has been shown that both slice thickness and grid resolution have a significant influence on the numerical results, especially on peak spatial averaged SAR values. For whole-body averaged SAR, the uncertainty was <0.5 dB. The uncertainty at a grid resolution of 1.7 mm$^3$ was >2 dB for peak spatial SAR; however the uncertainty at a grid resolution of 0.22 mm$^3$ could not be assessed. The remaining uncertainty is expected to be mainly caused by insufficient resolution of the thin layers, with high variations in permittivity and conductivity. Therefore, the importance of utilizing conformal cells and 3D reconstruction of CAD based high resolution anatomical models is evident [49].

Absorption of electromagnetic field energy in the rat and mouse highly depends on the frequency and polarization. Regions of higher and lower absorption vary due to the exposure conditions and frequency. The coupling efficiency was at its maximum for E-polarization and 900 and 1800 MHz for a rat and mouse, respectively, frequencies which are close to body resonance. As a consequence of the variation of the absorption patterns, the organ-specific average SAR values also greatly depend on the specific exposure situation, i.e., the frequency and polarization. Due to the variation of these parameters, the deviation of organ to whole-body averaged SAR can be as large as 15 dB. This variation is expected to be even higher if more than one anatomical model per species is considered. Therefore, the evaluation of organ and tissue SAR values for all animals within the study is required for the interpretation and comparison of results from bio-assays. Based on the above research results, the dosimetry of animal studies must include:

- whole-body average SAR
• organ-specific average SAR
• whole-body peak spatial SAR
• organ-specific peak spatial SAR,

including the uncertainty and standard deviation of all assessed SAR values for all animals within the study.

Comparable SAR distributions in the animal bodies were found for a mouse at 1800 MHz and rat at 900 MHz. The overexposure of the tail was at a maximum for E-polarization at all frequencies and both models, but at a minimum close to the body resonance frequency, i.e., 900 MHz for a rat and 1800 MHz for a mouse. With the use of restrained animals or exposure systems that stir the incident field, e.g., in reverberation chambers, with respect to the polarization, a fixed ratio between organ and whole-body average SAR can be achieved.
Part IV

Standing Wave Exposure in Guided Radial Waveguides
Chapter 5

Dosimetry of the PERFORM A RF-EMF 1800 MHz Rat Exposure Setup
5.1 Introduction

The fifth Framework Program of the European Union included a large project involving an international interdisciplinary group of diverse investigation laboratories under the name of PERFORM A. Six different experiments (2-year bioassays) were conducted under good laboratory practice (GLP), combining toxicity and carcinogenicity studies of rats and mice of different strains exposed at either 900 MHz GSM or 1800 MHz DCS. Some of the the groups involved have already published their results. For instance, [6] reports results of some of the carcinogenicity studies in mice from PERFORM A, and [50] shows the results of a parallel study to PERFORM A, of carcinogenicity in rats using the same exposure system as in PERFORM A.

The IT’IS Foundation was responsible for the work package to develop, construct, install and test the exposure setups to these six experiments in addition to technical quality control, support and maintenance of the systems during the period of the experiments. Different exposure setups were needed for rats and mice. A description of the development of the exposure setup for rats at 902 and 1747 MHz is described in [38].

Another major task within this work package was to perform the numerical and experimental dosimetry. Since the final aim of the experiments was a histopathological examination of the animal cadavers, high quality of the dosimetry data was required.

5.2 Objectives

The aims of this work were:

- to obtain the final data of a complete dosimetric assessment of DCS exposure in rats using the PERFORM A exposure setup, for all animals within the study and over the entire study period (2 years),

- to demonstrate that high quality dosimetric information following the methodology in Chapter 3 can be delivered with a reasonable effort.
5.3 Exposure Requirements

The carrier frequency was selected as the mid-band of the uplink frequency for DCS, i.e., 1747 MHz. Four exposure levels (4, 1.33, 0.44 W/kg, and sham) with 65 animals per group were used, whereby the female and male groups were sequentially exposed. At 40 days of age, the rats were exposed for 104 weeks. Dead animals were replaced in the setups by phantoms during exposure periods. The goal was to provide a constant and uniform whole-body SAR distribution to all animals over the entire period of the study. The whole-body and organ averaged SAR as well as the peak spatial averaged SAR were included in the dosimetry. Averaging masses of 50 and 5 mg were selected.

Each exposure setup (illustrated in Figure 5.1) consisted of 17 circularly arranged waveguide cavities, exposing one animal each. All 17 isolated waveguides were excited by the same quarter loop antenna placed in the center (radius \( r = 0 \)). The feed of the waveguides was at \( r = 85 \) mm, constituting a mono-mode structure out to \( r = 392 \) mm radius, followed by a multimode cavity in which the animal was positioned (\( r = 444 \) mm). The electrical short was at \( r = 617 \) mm. Figure 5.2 shows the electrical mesh as well as the quarter loop antenna.

Figure 5.1: Front and back views of the 1800 MHz rat exposure setup.
Figure 5.2: The cavity was determined by a net of stainless-steel wires (<-50 dB), providing daylight and ventilation for the animals (A). The 17 waveguides are fed by a common quarter loop antenna (B) located in the center of the setup (isotropy <±0.5 dB).

Two redundant field sensors in the mono-mode section of the waveguides located at the E-field peak of the standing wave enabled accurate control of the incident fields. These sensors were calibrated by transfer calibration using a calibrated electrical near-field probe. The polarization (H-field) and distance from the short were optimized for maximum uniform exposure. In order to meet the National Toxicological Program (NTP) requirements, the only materials used were gold plated copper, stainless steel and polycarbonate. A detailed description of the setup and the exposure can be found in [38].

5.4 Methods

All simulations were conducted using SEMCAD. Resolutions up to 25 voxels/mm³ in a total volume of 65 million mm³ were needed. Four high-resolution rat anatomical models were developed to cover diverse sizes and both genders as well as provide high accuracy of all parts of the body (Figure 2.1, Table 2.2). Measurements were performed using DASY3/4 and EASY4 equipped with the probes listed in Table 2.1. Representative dummy phantoms (Figure 5.7A) were developed for experimental and numerical evaluation and filled with an appropriate tissue simulating liquid for the required frequency.
5.5 Uncertainty Assessment

Figure 5.3 shows a diagram with the considered uncertainty sources, whereby sources regarding the exposure setup are represented as plain ellipses and sources due to animal modeling are represented as hatched ellipses. Due to the concept of isolated mono-mode waveguides, the parameters could be treated as independent. In most cases, the uncertainty has been determined under worst-case considerations and assuming a rectangular distribution. Whenever another concept was applied, this has been explicitly stated.

Figure 5.3: Parameters composing the SAR uncertainties (setup: plain ellipses; animal modeling: hatched ellipses). Please note that the parameters can only be considered independent since the coupling between animals is negligible.

5.5.1 Setup Uncertainties

The uncertainty of the mechanical tolerances of ±2 mm has been numerically evaluated and found to be negligible, i.e., below 1%. The sensors are transfer calibrated, resulting in the parameter uncertainty of (1) probe calibration for k=2 (certificate), (2) probe position accuracy, which is better than ±2.5 mm (assessed based on numeri-
(3) sensor linearization (assessed by worst-case deviation from power scan), and (4) readout electronics (data sheet of Agilent 34970A). The main numerical uncertainty is due to the discretization; this has been assessed by increasing the spatial resolution with respect to the standard resolution (see Table 5.1).

<table>
<thead>
<tr>
<th>Uncertainty sources of setup</th>
<th>Tolerance (dB)</th>
<th>Distribution</th>
<th>Div.</th>
<th>$C_i$</th>
<th>STDEV (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical setup:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical and electrical tolerances</td>
<td>0.05</td>
<td>N</td>
<td>1.00</td>
<td>1</td>
<td>0.05</td>
</tr>
<tr>
<td>Variation of dose group setups</td>
<td>0.30</td>
<td>N</td>
<td>1.00</td>
<td>1</td>
<td>0.30</td>
</tr>
<tr>
<td>Transfer sensor calibration:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calibration of E-Field probe</td>
<td>0.25</td>
<td>N (k=2)</td>
<td>2.00</td>
<td>1</td>
<td>0.13</td>
</tr>
<tr>
<td>Position of E-field robe (± 2.5 mm)</td>
<td>0.11</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.06</td>
</tr>
<tr>
<td>Sensor:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensor linearity</td>
<td>0.25</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.14</td>
</tr>
<tr>
<td>Drift and offset of Schottky diode</td>
<td>0.10</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.06</td>
</tr>
<tr>
<td>Accuracy of data logger</td>
<td>0.05</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.03</td>
</tr>
<tr>
<td>Setup model:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discretization</td>
<td>0.95</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.55</td>
</tr>
<tr>
<td>Restrainer tube (polycarbonate) epsilon</td>
<td>0.13</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.08</td>
</tr>
<tr>
<td>Restrainer tube (polycarbonate) sigma</td>
<td>0.01</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td>Loading mechanism parameters</td>
<td>0.10</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.06</td>
</tr>
<tr>
<td>Weight variations:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incremental input weight (5 g steps)</td>
<td>0.02</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td>Combined standard uncertainty (K=1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.07</td>
</tr>
</tbody>
</table>

Table 5.1: Budget for the uncertainties contributed by the setup alone. Those for the animal are not shown since they are different from organ to organ.

### 5.5.2 Uncertainties of Animal Modeling

The average exposure was conducted for an animal with a weight of 420 g (scaled 590 g animal) and a length (nose to beginning of tail) of 220 mm, simulating an animal lying in the tube with its nose in the opening of the tube. The weight of the animal corresponds to the average weight of male and female adult rats from the twentieth week of the experiment to the end, and a male model was chosen to symbolize the average animal, since it is more representative for that weight. The weight development of male and female rats as a function of time is plotted in Figure 5.4. The anatomy uncertainty was tested by scaling the other three animal models to the same weight of 420 g. Because of the significant scaling, we received a reliable estimation of upper-boundary uncertainty due to differences in anatomy.

Another uncertainty source is the discretization. The discretiza-
5.5. UNCERTAINTY ASSESSMENT

Figure 5.4: Body weight development with standard deviation values, on average, of male and female rats, and over the whole study time.

tion has been changed from 1.2 mm to 0.6 mm along the animal body axis, while keeping the other two dimensions constant at 1 mm; 1.2 and 0.6 were the slice thicknesses when the model was generated considering every second slice and every single slice, respectively. Since the discretization is based on slices with a fixed resolution along the axis of the animal and only unconstrained resolutions are possible in the x-y plane, the reliability of the obtained uncertainty bounds is not guaranteed. However, the assessments are only in question for bone encapsulated structures such as the spinal cord or brain.

The tissue values considered were those of humans [41] combined with the tissue parameters available for rodents [40]. The uncertainty of tissue parameters was assessed for $\epsilon \pm 10\%$ and $\sigma \pm 10\%$, except for the skull bone, for which a variation of 20% was derived from the available data. The uncertainty due to the restrainer tube material was assessed by changing the relative permittivity of polycarbonate (PC) of 2.7 by $\pm 11\%$. The uncertainty due to the loading mechanism modeling (two plastic types of $\epsilon_r = 2.7$ and $\epsilon_r = 2.9$) was assessed by
comparing results after varying the relative permittivity of the loading mechanism plastics by ±11%.

The time- and weight-averaged deviation from the applied incident field as a function of the animal weight was assessed for the differently scaled animal models.

5.5.3 Validation

Validation was conducted as described in Chapter 3. The animal models were represented using two bottles of 500 ml (Figure 5.7A) and 250 ml volume filled with tissue simulating liquid \( (\varepsilon_r = 55, \sigma = 1.3 \text{ S/m}) \). Measurements were conducted with the setup completely loaded with animal phantoms. SAR values in the bottles were obtained using the dosimetric probe ES3DV2 (Table 2.1), scanning a fixed volume in the dummies of all 17 waveguides. The incident E- and H-fields were measured at several distances from the center of the sectorial structure where the antenna was located. The simulations were compared to the measurements of the E- and H-fields (Figures 5.5 and 5.6) and SAR patterns (Figure 5.7B), resulting in very good agreement. A comprehensive uncertainty analysis was also performed for this setup following the concept described in Chapter 3, the parameters of which are provided in Table 5.2. The evaluation of equation (3.1) gives a value of 0.44, indicating that the numerical setup model and its uncertainty estimation are adequate.

5.6 Variation Assessment

The variations from the averaged exposure were assessed by considering all parameters relevant for this setup as well as their interdependencies (Figure 5.8). Since all waveguides can be treated as electromagnetically isolated units, the interdependency of the parameters is small.

5.6.1 Setup

Evaluation of the data collected during the experiments has shown that the feedback loop had a maximum deviation of 0.25 dB for the
5.6. VARIATION ASSESSMENT

Figure 5.5: Comparison of the E-field between simulations and measurements. The values correspond to the middle point of the two parallel plates constituting the exposure setup at different distances from the antenna.

<table>
<thead>
<tr>
<th>Validation uncertainty sources</th>
<th>Tolerance (dB)</th>
<th>Distr.</th>
<th>Div.</th>
<th>C_i</th>
<th>STDEV (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Measurement dosimetry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incident field measurements</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calibration of E-Field probe</td>
<td>0.41</td>
<td>N</td>
<td>1.00</td>
<td>1</td>
<td>0.41</td>
</tr>
<tr>
<td>Probe spherical isotropy</td>
<td>0.40</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td>Position of E-field probe (± 2.5 mm)</td>
<td>0.11</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.06</td>
</tr>
<tr>
<td>Sensor linearity</td>
<td>0.25</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.14</td>
</tr>
<tr>
<td>Readout electronics</td>
<td>0.05</td>
<td>N</td>
<td>1.00</td>
<td>1</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Dosimetric measurements</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calibration of dosimetric probe</td>
<td>0.45</td>
<td>N (k=2)</td>
<td>2.00</td>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td>Probe spherical isotropy</td>
<td>0.30</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.17</td>
</tr>
<tr>
<td>Probe linearity</td>
<td>0.10</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.06</td>
</tr>
<tr>
<td>Readout electronics</td>
<td>0.05</td>
<td>N</td>
<td>1.00</td>
<td>1</td>
<td>0.05</td>
</tr>
<tr>
<td>Position of SAR cube within dummy</td>
<td>0.30</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.17</td>
</tr>
<tr>
<td>Position of dummy in the setup</td>
<td>0.00</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.00</td>
</tr>
<tr>
<td>Liquid parameters: ±5% epsilon</td>
<td>0.06</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.03</td>
</tr>
<tr>
<td>Liquid parameters: ±10% sigma</td>
<td>0.03</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.02</td>
</tr>
<tr>
<td>Liquid volume (± 2.5 ml)</td>
<td>0.10</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Combined uncertainty for measurement (K=1)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.61</td>
</tr>
</tbody>
</table>

| Numerical dosimetry                             |               |        |      |     |            |
| Setup                                           |               |        |      |     |            |
| Discretization                                  | 0.95          | R      | 1.73 | 1   | 0.55       |
| Mechanical and electrical tolerances            | 0.05          | N      | 1.00 | 1   | 0.05       |
| **Dummy**                                       |               |        |      |     |            |
| Model of the dummy                              | 0.10          | R      | 1.73 | 1   | 0.06       |
| **Combined uncertainty for numerical dosimetry (K=1)** |               |        |      |     | 0.55       |

Table 5.2: Uncertainty budget of the validation equipment.
Figure 5.6: Comparison of the H-field between simulations and measurements. The values correspond to the middle point of the two parallel plates constituting the exposure setup at different distances from the antenna.

incident E-field. All wheels were calibrated with the same probe at the same location, such that the differences in calibration are negligible, i.e., <0.1 dB. The linearity plays a role for only a relatively narrow range and is also estimated to be negligible. Variations between the setups were assessed experimentally using the temperature method described in [43], resulting in a standard variation of 0.5 dB. Since the subgroups were systematically rotated, the lifetime variation was 0 dB. The variation of position depends on the isotropy of the antenna and the incident polarization. The isotropy of the setup, including antenna, was assessed with the dosimetric measurements described above, resulting in 0.45 dB. Since the incident angle or pointing vector with respect to the animal varied with the position within the wheel, the effect was numerically estimated by evaluating the organ and whole-body averaged values for the positions which approximately correspond to the clock positions 12, 3, 6 and 9 (see Figure 5.1). The effect on neighboring animals was experimentally assessed to be 0.12 dB. Since a strict rotational scheme was applied,
5.6. VARIATION ASSESSMENT

Figure 5.7: A) Simplified 500 ml rat phantom (commercially available bottle) and its numerical model. B) Sectorial waveguide model and comparison of SAR distribution between simulations and measurements in the plane constituted by the bottle axis and the radial vector of the setup.

these variations were averaged out when comparing the life-averaged exposures (see Table 5.3).

<table>
<thead>
<tr>
<th>Variations sources of setup</th>
<th>Tolerance (dB)</th>
<th>Dist.</th>
<th>Div.</th>
<th>C_i</th>
<th>STDEV instant (dB)</th>
<th>STDEV lifetime (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deviation incident E-field (feedback loop)</td>
<td>0.25</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.14</td>
<td>0.14</td>
</tr>
<tr>
<td>Sensor linearity (small variation)</td>
<td>0.25</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.14</td>
<td>0.14</td>
</tr>
<tr>
<td>Weight variations in Group</td>
<td>0.63</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.36</td>
<td>0.36</td>
</tr>
<tr>
<td>Frequency</td>
<td>0.00</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Calibration differences</td>
<td>0.10</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.06</td>
<td>0.00</td>
</tr>
<tr>
<td>Mechanical/electrical var. between setups</td>
<td>0.50</td>
<td>N</td>
<td>1.00</td>
<td>1</td>
<td>0.50</td>
<td>0.00</td>
</tr>
<tr>
<td>Position of animal within the setup</td>
<td>0.35</td>
<td>N</td>
<td>1.00</td>
<td>1</td>
<td>0.35</td>
<td>0.00</td>
</tr>
<tr>
<td>Effect of neighboring</td>
<td>0.20</td>
<td>R</td>
<td>1.73</td>
<td>1</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>Combined standard variation (K=1)</td>
<td></td>
<td></td>
<td></td>
<td>0.80</td>
<td></td>
<td>0.43</td>
</tr>
</tbody>
</table>

Table 5.3: Budget for the variations contributed by the setup only. Those for the animal are not shown since they are different from organ to organ.
5.6.2 Animals

The variation of weight as a function of age was determined by assessing the variation from the applied incident field exposure. A major variation component is the different animal weights within the same group at a specific time of up to ±16\% (see Figure 5.4). The effect was assessed by comparing the SAR values for different weights with respect to the weight function. According to the dependence of SAR on weight variations, this resulted in a variation of 0.36 dB. The effect of anatomy changes was assumed to be negligible, as well as the effect of polarization since the animals were restrained in H-polarization.

The effect of position within the tube was estimated by evaluating the two extreme positions, i.e., front and back (38 mm total displacement), leading to a deviation of 1.6 dB. Figure 5.9 shows the SAR distribution in the middle slice of a rat at both front and back positions in the tube. Anatomy variations (organ/tissue shape, position,
5.6. VARIATION ASSESSMENT

etc.) were considered under the worst-case posture effect, which was evaluated by simulating a restrained (i.e., squeezed or stuffed) rat and a completely stretched rat (see Figure 5.10), leading to a maximum variation of 0.8 dB. The worst-case effect of urinated fur was estimated by replacing the skin with the parameters of urine, resulting in a deviation of 0.6 dB (standard variation of 0.35 dB).

Figure 5.9: SAR pattern in dB (0 dB = 5e-5 [W/Kg] for a field strength of 1 V/m) at the middle slice of the ∼230 g rat model situated at the front part of the restrainer (top) and back part of the restrainer tube (bottom).

Table 5.4 presents the results of the entire assessment. It should be noted that the brain averaged exposure was almost twice the whole-body SAR, i.e., about 8 W/kg for the high dose group. This is considerably above the maximum peak spatial SAR in humans for the GSM system of about 1 W/kg and close to the limit for occupational exposure. It should also be noted that the instant variation might range from 2 to 32 W/kg. The exposures of all organs in the high dose are above the peak spatial SAR limit for the general public [24].
Figure 5.10: Top: Rat model in the restrainer tube and loading mechanism. Bottom: Same model squeezed.
### 5.6. VARIATION ASSESSMENT

Table 5.4: Results of the combined uncertainty and variation assessment for the 1747 MHz PERFORM A rat exposure setup.

<table>
<thead>
<tr>
<th>Averaging mass or organ/tissue</th>
<th>$\text{SAR}<em>{\text{organ}} / \text{SAR}</em>{\text{wb}}$ (dB)</th>
<th>Uncertainty $k=2$ (dB)</th>
<th>Instant var. $k=1$ (dB)</th>
<th>Lifetime var. $k=1$ (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole body</td>
<td>0</td>
<td>2.1</td>
<td>1.3</td>
<td>0.8</td>
</tr>
<tr>
<td>50 mg (peak spatial)</td>
<td>9.5</td>
<td>3.8</td>
<td>1.6</td>
<td>1.0</td>
</tr>
<tr>
<td>5 mg (peak spatial)</td>
<td>10.3</td>
<td>4.3</td>
<td>1.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Bladder</td>
<td>-0.1</td>
<td>3.2</td>
<td>4.8</td>
<td>3.5</td>
</tr>
<tr>
<td>Blood</td>
<td>3.3</td>
<td>2.0</td>
<td>1.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>-3.3</td>
<td>2.6</td>
<td>1.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Bones</td>
<td>-6.3</td>
<td>2.5</td>
<td>2.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Brain</td>
<td>2.9</td>
<td>2.8</td>
<td>3.4</td>
<td>1.4</td>
</tr>
<tr>
<td>Cartilages</td>
<td>0.6</td>
<td>2.5</td>
<td>2.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Eyes</td>
<td>2.1</td>
<td>2.8</td>
<td>3.6</td>
<td>1.9</td>
</tr>
<tr>
<td>Fat</td>
<td>-7.7</td>
<td>2.3</td>
<td>1.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Gland, lacrimal</td>
<td>4.7</td>
<td>2.2</td>
<td>3.7</td>
<td>1.0</td>
</tr>
<tr>
<td>Glands</td>
<td>0.8</td>
<td>3.9</td>
<td>2.2</td>
<td>1.6</td>
</tr>
<tr>
<td>Heart</td>
<td>3.5</td>
<td>2.7</td>
<td>2.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Kidneys</td>
<td>2.1</td>
<td>1.8</td>
<td>1.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Large intestine</td>
<td>1.2</td>
<td>2.6</td>
<td>1.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Liver</td>
<td>1.4</td>
<td>2.5</td>
<td>1.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Lungs</td>
<td>2.6</td>
<td>2.3</td>
<td>1.7</td>
<td>1.1</td>
</tr>
<tr>
<td>Muscles</td>
<td>0.3</td>
<td>2.2</td>
<td>1.4</td>
<td>0.9</td>
</tr>
<tr>
<td>Nerves</td>
<td>2.5</td>
<td>2.2</td>
<td>3.0</td>
<td>1.6</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>3.3</td>
<td>2.0</td>
<td>2.6</td>
<td>0.9</td>
</tr>
<tr>
<td>Pharynx</td>
<td>6.8</td>
<td>3.7</td>
<td>3.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Skin</td>
<td>-0.1</td>
<td>2.2</td>
<td>1.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Small intestine</td>
<td>3.4</td>
<td>2.7</td>
<td>1.7</td>
<td>1.1</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>0.8</td>
<td>1.9</td>
<td>2.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Spleen</td>
<td>1.7</td>
<td>2.0</td>
<td>2.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Stomach</td>
<td>2.2</td>
<td>2.3</td>
<td>1.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Tongue</td>
<td>4.9</td>
<td>4.1</td>
<td>5.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Trachea</td>
<td>1.5</td>
<td>2.8</td>
<td>2.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>
5.7 Conclusions

A dosimetry study of DCS exposure in rats using the PERFORMA setup was realized. The obtained data included the whole-body and organ-specific averaged and peak spatial averaged SAR values of the animals, uncertainty of each assessed value and SAR variations distinguishing among instant variations, variations within one exposure session as well as the entire lifetime. This data provides a basis for high quality interpretations and valuations of the histopathological results.

Satisfactory dosimetric data have been obtained with reasonable effort, i.e., with less than 100 simulations following the methodology described in Chapter 3. The good quality of the dosimetry was largely possible due to the careful design of the exposure setup. Otherwise, several hundreds of simulations would be required.
Part V

RF-EMF exposure of free running animals in reverberation chambers
Chapter 6

Reverberation Chambers
6.1 Reverberation Chamber Basics

6.1.1 A bit of History

The appearance of reverberation chambers in the literature dates back to the end of the 1960s. In 1968 H. A. Mendes first proposed the use of reverberation chambers for electromagnetic compatibility (EMC) measurements in [51]. Reverberation chambers were slowly introduced into electromagnetic use. In the 1970s there were two main approaches, one derived from mode-tuned cavities (U.S.) and the other derived from thermodynamics (Italy). It has taken time for reverberation chambers to gain acceptance, and only in the last decade they have been introduced in EMC standards. A review of the most relevant work done on reverberation chamber investigation until the date of the publication (2002) is given in [52]; most of the papers relate to the use of reverberation chambers for EMC.

As early as 1976 [53], other uses for reverberation chambers were also predicted: *Besides the classical application, it is interesting to foresee some use in the biological field since it is possible to radiate isotropically specimens inside the chamber, obtaining a standard situation of irradiation not obtainable with a directive system.* Later, [54] showed that reverberation chambers are useful for bioelectromagnetic experiments.

The use of reverberation chambers has increased rapidly in the last 10-15 years, mainly for EMC testing; many studies have focussed on the characterization and measurement of the fields in the chamber. This rapid expansion was, and still is, due to the benefits of reverberation chambers. Notably, a wide range of techniques for EMC measurements exist in the frequency range up to 1 GHz, while new measurement techniques are required above this frequency. The use of reverberation chambers is one of these techniques. For instance, for radiated emissions testing, if the equipment under test (EUT) is several wavelengths in size, its radiation pattern can be very irregular, and determining the direction and magnitude of the maximum radiation becomes very difficult using open-area test-site (OATS) or anechoic chambers measurements. Reverberation chambers measure the total radiated power, regardless of the radiation pattern. For immunity measurements a similar argument can be made.
6.1. **REVERBERATION CHAMBER BASICS**

Reverberation chambers provide illumination of the EUT from all directions and so will always find the most sensitive direction without the need to rotate the EUT. In addition, reverberation chambers can also be used below 1 GHz.

Some of the advantages of reverberation chambers are:

- high versatility: radiated emissions (measures total radiated power), radiated immunity (illuminates in all directions and with all polarizations), absorber characterization, etc.,
- electrically isolated environment (free of ambient signals),
- reduced testing time, for instance of immunity tests (no need to rotate the EUT to ensure exposure to the field on each side),
- higher field strengths inside the cavity compared to an anechoic room with the same amount of input power,
- broad frequency capabilities,
- large working volume (effective volume).

Reverberation chambers also have some disadvantages:

- measurements must be averaged over many stirrer positions, and therefore statistical methods have to be employed to evaluate the obtained data;
- when performing immunity tests, the immunity dependence of the EUT on the aspect angle and polarization is not available;
- in radiated emission tests, only the total power radiated is measurable and not the electric field at a specific distance (required in many test standards);
- the directivity of the transmitter and receiver antennas are lost;
- their use is not yet present in many EMC standards, and it is not easy to compare emission/immunity measurements with other techniques.
6.1.2 Reverberation Chamber Theory

What is a Reverberation Chamber?

A reverberation chamber is an electrically large, highly conductive, resonant enclosure, where the electromagnetic field structure is continuously altered using paddles or stirrers (mode-tuning chambers are not considered here), such that they provide a statistically homogeneous field distribution and isotropic field within a specific volume in the chamber (effective volume).

In this closed cavity, many modes propagate and form 3-D standing wave patterns with a large number of resonant modes. This fact results in regions where fields can be large or small (e.g., variations of 40 dB are typical). Figure 6.1 illustrates an example of a standing wave field pattern in a chamber with one propagating mode (left) and four different modes (middle). The coupling between equipment and antenna might vary rapidly with position and frequency. The mode stirrer (or stirrers) alters the boundary conditions, changing the location of the maxima and minima of the field magnitude in every rotational position (Figure 6.1 right).

Figure 6.1: Standing wave patterns (E-field magnitude) in a rectangular chamber for one single propagating mode (left), for four propagating modes (middle), and for four propagating modes after changing the boundary conditions (right), which changes the relative phase of the modes (e.g., moving a stirrer in the chamber). Extracted from [55].

The typical shape of a reverberation chamber is rectangular (height, width and length should not be simple multiples or rational fractions of each other), although more important than the shape is the volume,
6.1. REVERBERATION CHAMBER BASICS

intimately related to various important factors such as the minimum operating frequency, the number of modes, the quality-factor of the chamber and the effective volume.

Mode Number, Modal Density and Minimum Operating Frequency

For a rectangular cavity, the resonant frequency at each mode is given by:

\[ f_{mnp} = \frac{c_0}{2} \sqrt{\left(\frac{m}{a}\right)^2 + \left(\frac{n}{b}\right)^2 + \left(\frac{p}{c}\right)^2} \]  \hspace{1cm} (6.1)

whereby, \( m, n \) and \( p \) are integer numbers (where only one of them may be zero at once); \( a, b \) and \( c \) are the dimensions of the cavity, and \( c_0 \) is the propagating velocity of the electromagnetic waves in the cavity (usually considered as free space). At frequencies above 3 times the lowest resonance frequency, more than 60 propagating modes are possible. This is used as a guide to obtain the lowest usable frequency of a stirred-mode reverberation chamber. Some examples of different volume chambers and their respective lowest useable frequency are given in Table 6.1.

<table>
<thead>
<tr>
<th>Chamber</th>
<th>Volume ( m^3 )</th>
<th>( f_{110} ) MHz</th>
<th>Lowest useable freq. MHz (empirical value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>17</td>
<td>71</td>
<td>300</td>
</tr>
<tr>
<td>B</td>
<td>29</td>
<td>69</td>
<td>300</td>
</tr>
<tr>
<td>C</td>
<td>80</td>
<td>43</td>
<td>150</td>
</tr>
<tr>
<td>F</td>
<td>170</td>
<td>31</td>
<td>150</td>
</tr>
<tr>
<td>G</td>
<td>290</td>
<td>24</td>
<td>3100</td>
</tr>
<tr>
<td>J</td>
<td>1360</td>
<td>15</td>
<td>30...50</td>
</tr>
</tbody>
</table>

Table 6.1: Volumes of different chambers and the associated lowest useable frequencies. Partially extracted from [55].

The total number of possible resonant modes (eigenmodes), \( N_s(f) \), inside a closed, lossless, rectangular chamber increases with frequency:

\[ N_s(f) = \frac{8\pi}{3} abc\left(\frac{f}{c_0}\right)^3 - (a + b + c)\left(\frac{f}{c_0}\right) + \frac{1}{2} \]  \hspace{1cm} (6.2)

The mode density, \( D_s(f) \), is also an important parameter for the chamber design, since it determines how many modes are present in a
small bandwidth about a given frequency, and it can be obtained by applying:

\[ D_s(f) = \frac{dN_s(f)}{df} \]  

(6.3)

**Stirring the Field**

In stirred-mode operating chambers, the stirrer (or stirrers) continuously rotates at a constant controlled speed, and a set of measurements are taken and averaged at each frequency. If field measurements in a reverberation chamber with a large number of modes (>60) are averaged over a certain number of stirrer positions (e.g., one entire rotation), the field is on average uniform throughout a large volume within the chamber. In addition the field has equal energy propagating in every direction and polarization.

There are not many sources in the literature regarding the optimum size and shape of the stirrer. In [56], a research group from the University of York published the results of a numerical optimization study of stirrer design (shape and size), concluding that the most important consideration when choosing a stirrer is its shape, finding the best performance for the most complexly shaped stirrer. Once the shape has been chosen, the stirrer can be improved by increasing its size, although this is obviously limited by the working volume. Figure 6.2 shows the reverberation chamber at the IT’IS Foundation with 2 bent plate stirrers, one vertical and one horizontal. The use of 2 stirrers is expected to provide better chamber performance than if only one stirrer is used, since 2 stirrers might be seen as an increase in the stirrer shape complexity and might optimize space requirements. In addition, the stirrers turn with different speeds in order to avoid continuously equal relative positions.

In order to assess the number of stirrer positions needed to average the field measurements and obtain this field value with a certain standard deviation, the repeatability of the E-field was assessed in the IT’IS reverberation chamber using 3440 different stirrer positions (combination of relative positions of both stirrers) and over 4 and 5 complete rotations of the horizontal and vertical stirrers, respectively. The standard deviation of the measurements performed at 900 MHz was <0.2 dB for the total field, and 0.2 dB at 1900 MHz. Figures 6.3
6.2 Stirred to Unstirred Energy

The ratio of the stirred to unstirred energy in dB is a measure of the effectiveness of the stirring. A manner to assess the ratio between the power received and the power transmitted in a stirred environment is

Figure 6.2: Reverberation chamber at IT'IS Foundation, with 2 mode-stirrers.

and 6.4 show the increase of the standard deviation and hence uncertainty with respect to the assessed values with 3440 stirrer positions versus the number of stirrer positions at 900 and 1900 MHz, respectively.
Figure 6.3: Increase in standard deviation of the E-field as a function of the number of samples or stirrer positions at 900 MHz.

Figure 6.4: Increase in standard deviation of the E-field as a function of the number of samples or stirrer positions at 1900 MHz.

the following:

\[
\frac{P_{rs}}{P_t} \propto \frac{1}{N} \sum_{N} |S_{21}|^2
\]  

(6.4)
6.2. STIRRED TO UNSTIRRED ENERGY

where the $S_{21}$ magnitudes are considered. To assess the same power ratio in an unstirred environment, the $S_{21}$ vectors are used, as given by:

$$
\frac{P_{r,us}}{P_t} \propto \frac{1}{N} \sum_{N} |S_{21}|^2
$$

(6.5)

Thus the stirred to unstirred energy can be calculated as the ratio of the expressions 6.4 and 6.5, expressed in dB, as a figure of merit.

**Quality Factor ($Q$)**

The quality factor is a number used to describe the ability of a cavity to store energy. The expression:

$$
Q = \frac{wU}{P_d}
$$

(6.6)

presents the $Q$-factor as the angular frequency $w$ times the stored energy $U$ divided by the dissipated power $P_d$ in the chamber, which for steady-state conditions is equal to the power transmitted into the chamber, $P_t$.

The most popular method of measuring $Q$ is based on the following expression:

$$
Q = \frac{16\pi^2V}{\mu_t\mu_r\lambda^3} < \frac{P_r}{P_t} >
$$

(6.7)

where $V$ is the chamber volume, $\mu_t$ and $\mu_r$ are the antenna efficiency factors for the transmitter and receiver, $\lambda$ is the wavelength, $P_r$ is the received power and $P_t$ the power transmitted. The measurement of $P_r$ must be performed over an integral number of rotations of each stirrer, with sufficient positions, to avoid the introduction of additional uncertainty.

Furthermore, the quality factor must be determined by considering all the losses present in the chamber. The components describing the $Q$-factor are:

- $Q_1$: losses in the chamber wall
- $Q_2$: losses due to the EUT (or animals, racks)
- $Q_3$: apertures and leakages
• $Q_4$: losses in the antenna loads

and follow the expression:

$$Q^{-1} = Q^{-1}_1 + Q^{-1}_2 + Q^{-1}_3 + Q^{-1}_4$$  \hspace{1cm} (6.8)$$

[57] describes the calculation of these $Q$ components. In an empty chamber without apertures, the $Q$-factor will only depend on $Q_1$ and $Q_4$, which may be calculated using the following expressions:

$$Q_1 = \frac{3V}{2\mu_{rel}S\delta}$$  \hspace{1cm} (6.9)$$

$$Q_4 = \frac{16\pi^2V}{m\lambda}$$  \hspace{1cm} (6.10)$$

where $S$ is the inner area of the chamber, $\mu_{rel}$ and $\delta$ the relative permeability and skin depth of the walls, respectively, and $m$ the impedance mismatch.

If the $Q$-factor is substantially reduced due to losses in the chamber, the field uniformity might be adversely affected. For continuous wave (CW) operation, the minimum $Q$ is determined by the operating frequency, as the excitation field needs to be sufficiently rapidly refreshed relative to the rate of decay of energy inside the chamber. Thus, the minimum permissible $Q$ is lower at high frequencies than at low frequencies. There are two metric methods described in [58] to assess effectiveness of a reverberation chamber, and one of these is based on the $Q$-factor. In [58], the expression to calculate the threshold value of the $Q$-factor of a reverberation chamber to be considered as effective is given as:

$$Q_{thr} = \left(\frac{4\pi}{3}\right)^{2/3} \frac{V^{1/3}}{2\lambda}$$  \hspace{1cm} (6.11)$$

The $Q$-factor also determines the field strength in the chamber for a given level of radiated power, which influences the sensitivity of the chamber for emission measurements as well as the maximum field strength that can be achieved for a given amplifier in immunity tests. This relation between $Q$ and the average electric field strength is given by:

$$\langle E \rangle = \sqrt{\frac{QP_{input}\mu_1Z_0c_0}{2\pi V f}}$$  \hspace{1cm} (6.12)$$
with $Z_0$ as the wave impedance in the propagating media (usually taken for free space in a reverberation chamber).

### 6.3 Plane Wave Integral Representation

Deterministic and statistical mode theories are useful methods to determine the properties of an empty cavity, but they might not be convenient for predicting the response of a receiving antenna or an EUT in a mechanically stirred reverberation chamber. In [59], a plane-wave integral representation for the fields in a mechanically stirred reverberation chamber is proposed. This representation automatically satisfies Maxwell’s equations in a source-free region and includes the statistical properties expected for a well stirred field. This statistical nature is introduced through the plane wave coefficients (angular spectrum), which are taken to be random variables with fairly simple statistical properties. Because this theory is based on propagating plane waves, it becomes easy to calculate the responses of test objects or reference antennas. The theory applies to single-frequency CW fields.

According to [59], the electric field $\vec{E}$ at location $\vec{r}$, in a source-free finite volume can be represented as an integral of plane waves over all real angles:

$$< \vec{E}(\vec{r}) > = \int_0^{4\pi} \int_0^\pi \vec{F}(\Omega) e^{i\vec{k}\cdot\vec{r}} d\Omega$$  \hspace{1cm} (6.13)

where $\vec{F}(\Omega)$ is the angular spectrum (considered as a random variable which depends on stirrer position), $\Omega$ is the solid angle (shorthand for the elevation and azimuth angles), and $\vec{k}$ is the vector wavenumber. The source-free volume considered here is spherical; for rectangular volumes the expression must be analytically continued outward from a spherical volume. The time dependence $e^{-i\omega t}$ is suppressed.

To model the exposure of animals within a reverberation chamber, a model using a reduced number of plane waves is proposed to be utilized without introducing significant errors.
6.4 NIEHS Planned Studies

The National Institute of Environmental Health Science (NIEHS), USA, plans to conduct NTP-like (National Toxicological Program) studies to identify potential toxicity and carcinogenicity of cell phone radio frequency radiation (RFR) associated with chronic exposure in rodents. Unconstrained and individually hosted Sprague-Dawley rats and B6C3F1 mice will be exposed to RFR, 900 MHz and 1900 MHz respectively using Global System for Mobile Communications (GSM) and IS95, a cellular phone system based on Code Division Multiple Access (CDMA) signals. The exposure should be as uniform as possible for all subjects. The characterization of a dose-response relationship with three different targeted whole-body average specific absorption rate (SAR) values is projected: 1, 2.5 and 6 W/Kg, plus a sham group. High efficiency is of particular relevance for this project to optimize the RF power requirements and associated cost, due to the large number of animals to be exposed in the experiments (~3000) and the high whole-body average SAR levels desired, up to 6 W/Kg. Moreover, the planned studies consider the entire animal life cycle from pup to senior, including youths, adults, pregnant subjects and their offspring.

The concept of an optimum exposure system for RF-EMF in vivo experiments is crucial and should include the most suitable exposure apparatus in terms of uniformity, efficiency, space and cost. Exposure uniformity and efficiency are factors that highly depend on the frequency and polarization of the incident radiation (see chapter 4). In comparison to exposure setup concepts designed for non-restrained animals, restrained animals setups can generally provide better control of the exposure uniformity and efficiency because:

- the animal can be positioned in an optimum place within the setup (a maximum of the electric field if using a standing wave concept, an area/volume where the measured field shows uniform distribution, etc.)
- the animal body orientation in the field can be optimally selected and will remain constant during exposure.

In such a setup, and when the concept is well developed, the cost can be held to a reasonable level through the simultaneous exposure
of several animals. In addition, when the animals are restrained, the space requirements can potentially be minimized compared to the case where the animals can freely move. However, these setup concepts do not have only advantages over non-restraining setups. For instance, the exposure time cannot be very long, in order to avoid stress in the animals (e.g., \( \sim 2 \) hours/day for rodents), which make these setups unsuitable for long exposure periods.

Exposing unrestrained animals implies that the body orientation in the field continuously changes over time. If for instance the plane wave incident field has a particular polarization, the animal might choose a body orientation in the field such that, for example, the brain exposure is lowest or the animal experiences fewer temperature increases. In this way, the efficiency and exposure uniformity can become very poor. There are also exposure setups for unrestrained animals which change polarization with time (e.g., a circularly polarized waveguide) or use more than one polarization. These setups enlarge the chance that the animal cannot choose a more comfortable orientation, thereby improving the exposure uniformity. Free-running animals are commonly exposed in cages which are placed in areas where the field has been proved to be homogeneous, to make exposure less dependent on the animal position in the cage. A uniform and homogeneous exposure eliminating the dependence between SAR and animal body orientation and position in the field is desired for the setup to be used in the NIEHS studies, which should also provide low space requirements per animal, high efficiency and low power cost.

The challenge to find the most appropriate exposure setup for the NIEHS experiments was first taken by the National Institute of Standards in Technology (NIST), USA, proposing the use of reverberation chambers for animal exposure to electromagnetic field radio frequency radiation (EMF-RFR). Reverberation chambers produce uniform exposure, with statistically homogeneous fields within a specific volume of the chamber, independent of the position within this volume. High efficiency can be obtained with reasonable cost, and the dimensions of the chamber can be chosen to expose a few hundred animals simultaneously, optimizing space requirements. In addition, animals can be exposed during long periods of time, since they are not restrained.

Although the idea of using reverberation chambers for bio-experiments is not new [54], a reverberation chamber has not as yet been used as
the exposure setup for a long-term in vivo study with a large number of unconstrained animals, exposed to RF-EMF.

NIST performed a preliminary study [60] involving experimental investigation of a reverberation chamber in the context of its utilization as an EMF exposure facility for the NTP-like NIEHS planned in vivo studies. This feasibility study included:

- assessment of electric field uniformity (spatial uniformity, consistency of statistical distribution, paddle position optimization, etc.) in an empty chamber as well as in a chamber with 255 500-g rat phantoms
- efficiency
- average SAR and absorption cross section (ACS) of the phantoms.

The study reported very encouraging results, for instance:

- total electric field uniformity with no phantoms of 0.67 dB at both 900 and 1900 MHz
- total electric field uniformity with 255 rat phantoms of 1.8-2.4 dB at 900 MHz and 1.5-2.1 dB at 1900 MHz
- efficiency with 255 rat phantoms of 89% at 900 MHz and 86% at 1900 MHz
- rat phantom average SAR uniformity of 0.5 dB at 900 MHz and 0.2 dB at 1900 MHz.

Figure 6.5 shows the NIST reverberation chamber loaded with racks of animal cages containing animal phantoms.

At the same time that NIST was delivering those results, a preliminary numerical dosimetric study was performed by the IT'IS Foundation to compliment the experimental evaluation realized by NIST.

Previous conclusions in this thesis have already shown that in a reverberating environment a statistically fixed relation of organ to whole-body average SAR could be achieved, and therefore the animal exposure would become independent of body orientation. This is a huge advantage if the homogeneous exposure of unconstrained animals
6.4. NIEHS PLANNED STUDIES

Figure 6.5: Reverberation chamber at NIST loaded with animal racks and cages containing animal phantoms.

is desired. The results of the IT’IS study are presented in Chapter 7. More recent measurements realized in the reverberation chamber at IT’IS [61], [62] have delivered better field uniformities than those reported by NIST, in both the empty and fully loaded chamber at 900 and 1900 MHz. Efficiency and SAR uniformity in the phantoms were also measured, showing very good performance of the chamber. Table 6.2 presents some of these results. A paper based on the final measurement results is in preparation.

6.4.1 Model of the Exposure in a Reverberating Environment

The modeling of electrically large, high-Q structures, such as reverberation chambers, is not a trivial exercise. In the literature, there are few methods and techniques for numerical electromagnetic model-
CHAPTER 6. REVERBERATION CHAMBERS

Field strength uniformity

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empty chamber at 900 MHz</td>
<td>0.59 dB</td>
</tr>
<tr>
<td>Empty chamber at 1900 MHz</td>
<td>0.48 dB</td>
</tr>
<tr>
<td>Chamber loaded with 90 rat phantoms at 900 MHz</td>
<td>0.74 dB</td>
</tr>
<tr>
<td>Chamber loaded with 180 mouse phantoms at 1900 MHz</td>
<td>0.70 dB</td>
</tr>
</tbody>
</table>

Field strength isotropy

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empty chamber at 900 MHz</td>
<td>≤0.84 dB</td>
</tr>
<tr>
<td>Empty chamber at 1900 MHz</td>
<td>≤0.70 dB</td>
</tr>
</tbody>
</table>

Efficiency of the loaded chamber

<table>
<thead>
<tr>
<th>Description</th>
<th>Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chamber with 90 rat phantoms at 900 MHz</td>
<td>74%</td>
</tr>
<tr>
<td>Chamber with 180 mouse phantoms at 1900 MHz</td>
<td>46%</td>
</tr>
</tbody>
</table>

Exposure uniformity in the setup (SAR measurements)

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>at 900 MHz</td>
<td>0.44 dB</td>
</tr>
<tr>
<td>at 1900 MHz</td>
<td>0.40 dB</td>
</tr>
</tbody>
</table>

Table 6.2: Preliminary results obtained with the reverberation chamber at IT’IS.

...
(1) the time and whole-body average absorption of the object considered is mainly caused by a small number of incident directions of plane waves; additional directions do not cause significant variations;

(2) the time average absorption pattern is also mainly determined by this reduced number of plane waves; additional directions do not cause significant variations.
Chapter 7

Preliminary Numerical Dosimetry of a Reverberation Chamber to expose Mice and Rats at 900 and 1900 MHz
7.1 Introduction

The encouraging results delivered by the NIST feasibility study of a reverberation chamber to be used as the RF-EMF exposure setup for unconstrained rodents [60] motivated the performance of a numerical dosimetric study to be carried out by IT’IS, almost in parallel to the NIST study.

7.2 Objectives

The principal aim of this study was to deliver reliable data about the performance of the reverberation chamber to be used as the exposure setup for the planned NIEHS studies, considering efficiency, uniformity, space requirements and power cost. With this intention, the main objectives consisted of:

- finding an approximation of the minimum number of plane waves necessary to represent the exposure in a reverberation chamber with low uncertainty, applying the chosen numerical model described in chapter 6
- characterizing the animal exposure over lifetime for each strain and carrier frequency
- providing guidelines for the load density and distribution, including data about proximity effects, different body postures and relative positions.

7.3 Methods

7.3.1 High Resolution Anatomical Models

Three rat models and three mouse models (small, medium and large), segmented in their original size were used in this study. The medium animal of both species was a pregnant subject, chosen to assess the exposure of the embryo during pregnancy. In addition, a 7-day-old Sprague-Dawley rat pup model was also used to study the exposure
7.3. METHODS

in pups. The main anatomical characteristics of these animals was presented in Table 2.2.

To assess energy absorption values in rodents over the entire lifespan, rat and mouse models were scaled up and down in order to cover a wide range of weights for each species (Table 7.1). The grid resolutions used in the simulations were chosen as the slice thickness of each animal model shown in Tables 2.2 and 7.1.

<table>
<thead>
<tr>
<th>Model</th>
<th>Original</th>
<th>Weight (g)</th>
<th>Scaling factor in all 3 direc.</th>
<th>Slice thick. (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD male rat small</td>
<td>~75</td>
<td>0.69</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>SD male rat small</td>
<td>~100</td>
<td>0.76</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>SD male rat small</td>
<td>~150</td>
<td>0.87</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>SD male rat small</td>
<td>~300</td>
<td>1.1</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>SD male rat large</td>
<td>~400</td>
<td>0.87</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>SD male rat large</td>
<td>~500</td>
<td>0.94</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>SD male rat large</td>
<td>~700</td>
<td>1.1</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Female mouse pup</td>
<td>rat pup</td>
<td>~4</td>
<td>0.58</td>
<td>0.29</td>
</tr>
<tr>
<td>OF1 male mouse small</td>
<td>10</td>
<td>0.79</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>OF1 male mouse large</td>
<td>55</td>
<td>1.1</td>
<td>0.84</td>
<td></td>
</tr>
</tbody>
</table>

Table 7.1: Data of the scaled animal anatomical models.

7.3.2 Homogeneous Phantoms

NIST utilized bottles of water (500 ml) as rat homogeneous phantoms in their feasibility study (approximate length=19.3 cm and width=6.5 cm). In addition to the rat phantom, a 50 ml bottle was modeled to represent a mouse (approximate length=9 cm and width=3 cm). These phantoms were modeled in SEMCAD and then used for the assessment of whole-body average SAR in certain scenarios as well as for validation of the numerical model. The phantoms used for the simulations were filled with two different kinds of liquid. When the purpose was to compare simulations and measurements, the liquids chosen were those used by NIST, which correspond to the values provided by the IEEE 1528 standard (2003) for tissue simulating liquids. When the phantoms were used to simulate animals in certain configurations, the liquid dielectric properties were chosen as the weighted average properties of all tissues in the mouse and rat bodies, shown in Table 7.2, in order to better represent the animal absorption.
### 7.3.3 Numerical Model of a Reverberation Chamber-Like Exposure

The method described in chapter 6 is applied in this study to simulate the exposure of animals in a reverberating environment. The method basically involves illuminating the animals with a finite number of plane wave excitations with the same magnitude but with different polarization and incident direction. The total SAR can be numerically assessed in each voxel as superposition of magnitudes (SAR) and normalizing according to the number of sources in terms of power or squared field strength. E-field superposition is not suitable in this case for total SAR assessment since the phases of the different plane waves are not correlated.

### 7.3.4 SAR Assessment

The quantities evaluated in the dosimetric analysis include averaged SAR values and SAR distributions in the homogeneous phantoms as well as whole-body and organ-specific averaged SAR values and SAR distributions in the anatomical models. Only the organs/tissues with masses larger than 1% of the total body were considered for the organ analysis. Furthermore, eyes, heart and spleen were also evaluated as being considered relevant. Tail to whole-body absorption was also assessed.

### 7.4 Results

Due to the large number of data generated during the performance of this study, the results were grouped into the following subsections.
7.4. RESULTS

7.4.1 Assessment of Minimum Number of Plane Waves

Plane waves are characterized by three vectors, namely the E-field vector (E), H-field vector (H) and propagation direction vector (k). As already mentioned in assumptions (1) and (2) (Chapter 6), the time whole-body averaged SAR and SAR pattern in a lossy body might be mainly caused by a certain group of incident plane waves with specific directions of these three vectors, and therefore additional plane waves could not cause significant changes. The aim here was to identify the minimum number of plane waves and the orientation of E-, H- and k-vectors for each of the plane waves necessary to accurately model the exposure in a reverberating environment. Five different sets of plane waves were investigated, varying the number of plane waves per set and the direction of the E-, H- and k-vectors. The medium rat and mouse anatomical models as well as the rat and mouse homogeneous phantoms were illuminated with all plane wave sets, at both 900 and 1900 MHz. Average SAR values of the whole body as well as of single organs/tissues were then assessed as a superposition of the solutions of all employed plane waves.

Except when otherwise specified, the anatomical and phantom models were positioned with their longest body axis parallel to the z-axis to perform the simulations (Figure 7.3 left). The five different sets of plane waves used are described in the following subsections, as well as the obtained results and conclusions.

Reference Set

In order to verify the mentioned assumptions, the number of plane waves used was first reduced to the main directions, i.e., the cases where all three E-, H- and k-vectors correspond each to one coordinate axis. Considering all possible combinations of these three vectors parallel to the coordinate axis, a total of 12 different plane waves are possible. Table 7.3 presents these twelve plane waves (labeled 1 to 12) in terms of the angles denoted in Figure 7.1. This set of 12 plane waves was tagged as reference. Figure 7.2 shows a rat anatomical model in the coordinate axis system as well as the E, H and k vectors for three of these plane waves (1, 5 and 9 in Table 7.3), which correspond to
E-, H- and k-polarizations, respectively.

<table>
<thead>
<tr>
<th>Plane waves</th>
<th>Label</th>
<th>θ</th>
<th>φ</th>
<th>ψ</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-polarization</td>
<td>1</td>
<td>90°</td>
<td>0°</td>
<td>0°</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>90°</td>
<td>90°</td>
<td>0°</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>90°</td>
<td>180°</td>
<td>0°</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>90°</td>
<td>270°</td>
<td>0°</td>
</tr>
<tr>
<td>H-polarization</td>
<td>5</td>
<td>90°</td>
<td>0°</td>
<td>90°</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>90°</td>
<td>90°</td>
<td>90°</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>90°</td>
<td>180°</td>
<td>90°</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>90°</td>
<td>270°</td>
<td>90°</td>
</tr>
<tr>
<td>k-polarization</td>
<td>9</td>
<td>0°</td>
<td>0°</td>
<td>0°</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0°</td>
<td>0°</td>
<td>90°</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>180°</td>
<td>0°</td>
<td>0°</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>180°</td>
<td>0°</td>
<td>90°</td>
</tr>
</tbody>
</table>

Table 7.3: Twelve plane waves with all E-field, H-field and propagation direction vectors parallel to the coordinate axis, in terms of the three angles in Figure 7.1.

Figure 7.1: Coordinate axis system showing the angles theta (θ), phi (φ) and psi (ψ) for the plane wave excitation used in SEMCAD, and the E-field, H-field and propagation direction vectors.

Tilted Plane Set

The anatomical models and phantoms were tilted 45° from the vertical (z-axis), towards the y-axis around the x-axis, in such a manner that they laid on the zy-plane. This scenario is represented in Figure 7.3 (middle) with a bottle phantom. By tilting the model in this...
7.4. RESULTS

Figure 7.2: Rat model in the coordinate axis. Orientation of E-field, H-field and propagation direction vectors with respect to the coordinate axis for an example of a) E-polarization, b) H-polarization and c) k-polarization

manner, and again using the reference set of plane waves (Table 7.3), the current orientations of the E-, H- and k-vectors with respect to the model are changed; neither the E- nor H- nor k-vectors are now parallel to the phantom or anatomical model longest body axis. This new situation corresponds to what was called the tilted plane set of plane waves.

**Combination Set**

Furthermore, the reference and tilted plane sets of plane waves were combined in one new set labeled as combination. In this case, the animal body axis remained parallel to the z-axis and, to represent the tilted plane set, fields and propagation direction vectors were appropriately tilted and rotated, with respect to the animal model. The uncertainty from tilting the fields and the direction of propagation vectors instead of the animal model (as done in tilted plane case) was assessed and can be neglected.
Figure 7.3: Rat phantom used by NIST in three different positions with respect to the coordinate axis, and corresponding to: a) reference, b) tilted plane and c) tilted diagonal sets of plane waves.

**Tilted Diagonal Set**

The anatomical and phantom models were now tilted 45° from the vertical (z-axis) towards the xy-plane, to finally lay parallel to the (1,1,1) direction (Figure 7.3 right). By again using the reference set of incident plane waves to expose the models, a new different scenario is achieved: tilted diagonal.

**Three Plane Waves Approach Set**

The reference set was composed of 4 plane waves with E-polarization, 4 with H-polarization and 4 with k-polarization. The approach here was to reduce the number of plane waves to only three, each corresponding to a different polarization. These three plane waves are labeled 1, 5 and 9 in Table 7.3.

**Results with Animal Phantoms**

Considering combination as the set of plane waves representing the most isotropic incident field from all the considered sets, the uncertainty of the averaged SAR values introduced by using the reference set was found to be <0.05 dB for both phantom sizes and both frequencies. With the number of plane waves further reduced to only three
as in the 3 plane wave approach set, i.e., 8 times less plane waves than in combination set, the uncertainty of the averaged SAR values was <0.1 dB in all cases. The SAR values in the phantoms using the other sets of plane waves were also investigated. Deviations found in averaged SAR with respect to reference are presented in Table 7.4, for the rat phantom at 900 MHz and mouse at 1900 MHz.

Results with Anatomical Models

Using the anatomical models, the same uncertainties as for the phantoms were assessed. Using the reference set, an uncertainty in whole-body average SAR of <0.1 dB was introduced with respect to the combination set, for the mouse and rat at both frequencies. The uncertainty using the 3 plane wave approach set was slightly higher, but still <0.2 dB in all cases. The SAR deviations with respect to reference found when other sets of plane waves were used are given in Table 7.4, for the rat at 900 MHz and mouse at 1900 MHz.

Organ-specific averaged SAR uncertainties were also assessed in the same manner. Uncertainties <0.5 dB were obtained for all considered organs using the reference set. However, these uncertainties increased up to 1.5 dB when the 3 plane wave approach set was used. The deviations assessed between the organ-specific average SAR using reference and the rest of plane wave sets are given in Table 7.5, for the rat at 900 MHz and mouse at 1900 MHz.

| Plane wave set | Deviation of SAR\text{\textsuperscript{\textit{w,b}}}, with respect to reference set in homogeneous phantoms | | Deviation of SAR\text{\textsuperscript{\textit{w,b}}}, with respect to reference set in anatomical models | |
|----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
|                 | rat @900 MHz | mouse @1900 MHz | rat @900 MHz | mouse @1900 MHz |
| Tilted plane    | 0.2         | 0.1             | -0.1         | -0.05           |
| Combination     | 0.02        | 0.04            | -0.1         | -0.1            |
| Tilted diagonal | 0.1         | 0.1             | n.a.         | n.a.            |
| 3 PW approach   | 0.05        | 0.04            | 0.1          | 0.02            |

Table 7.4: Deviation of whole-body averaged SAR values in the rat and mouse homogeneous and anatomical models using different sets of plane waves versus the reference set.

Analogous data for organ-specific average SAR are given in Table 7.5 for the mouse at 1900 MHz and rat at 900 MHz.

In conclusion, the assumptions (1) and (2) have been confirmed
and the reference set of 12 plane waves has been found well suited for the assessment of the whole-body as well as organ-specific average SAR values in both the mouse and the rat at both frequencies, with uncertainties lower than 0.1 dB and 0.5 dB, respectively. Furthermore, if only whole-body average SAR is relevant, the 3 plane waves approach set might be used with an assessed uncertainty of <0.2 dB, considerably reducing the computational effort. The uncertainty of the SAR values obtained using more than 24 plane waves has not been assessed. This uncertainty is not expected to be significant.

### 7.4.2 Efficiency and SAR Assessment

The aim of this section was to characterize the exposure of a medium mouse and rat at both 900 and 1900 MHz, using the 12 plane waves of the reference set, assessing the following quantities:

- efficiency (whole-body averaged SAR per squared field strength) and uniformity\(^1\)

- deviation of organ-specific averaged SAR with respect to the whole body

\(^1\)Standard deviation of the averaged SAR based on voxel data.

---

### Table 7.5: Deviation in dB of the organ-specific average SAR values obtained with the different sets of plane waves with respect to the reference set, for the mouse at 1900 MHz and rat at 900 MHz.

<table>
<thead>
<tr>
<th>Tissue/Organ</th>
<th>Mouse at 1.9 GHz</th>
<th>Rat at 900 MHz</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>tilt. plane</td>
<td>comb.</td>
</tr>
<tr>
<td>Blood</td>
<td>-0.02</td>
<td>-0.01</td>
</tr>
<tr>
<td>Bone M.</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
<tr>
<td>Brain</td>
<td>0.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Embryo</td>
<td>-0.2</td>
<td>-0.1</td>
</tr>
<tr>
<td>Eyes</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Fat</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Glands</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Heart</td>
<td>0.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Intestine</td>
<td>-0.2</td>
<td>-0.1</td>
</tr>
<tr>
<td>Kidneys</td>
<td>-0.1</td>
<td>-0.1</td>
</tr>
<tr>
<td>Liver</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Muscles</td>
<td>0.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Nerves</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Skin</td>
<td>-0.1</td>
<td>-0.1</td>
</tr>
<tr>
<td>Spleen</td>
<td>-0.2</td>
<td>-0.1</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>
• SAR patterns in the animals.

The efficiency and uniformity values for both rat and mouse models at both frequencies are shown in Table 7.6. The efficiency for the mouse exposed at 1900 MHz was 4 times larger than at 900 MHz, while the efficiency for the rat exposed at 900 MHz was 1.25 times larger than at 1900 MHz. Uniformity was also better for the mouse at 1900 MHz and rat at 900 MHz, showing smaller deviations.

<table>
<thead>
<tr>
<th>Models</th>
<th>Frequency (MHz)</th>
<th>Avg. SAR(_{WB}) ((\text{W/Kg}))</th>
<th>Uniformity (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>900</td>
<td>4.5e-5</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>1900</td>
<td>1.9e-4</td>
<td>2.8</td>
</tr>
<tr>
<td>Rat</td>
<td>900</td>
<td>9.2e-5</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>1900</td>
<td>7.3e-5</td>
<td>3.2</td>
</tr>
</tbody>
</table>

Table 7.6: Whole-body averaged SAR and uniformity for a medium rat and mouse at 900 and 1900 MHz.

Organ absorption at a specific frequency highly depends on organ size and shape as well as animal posture [67]. In a complex object, such as an animal body, the absorption in a single organ/tissue also depends on the organs/tissues around it, in terms of thickness, shape and dielectric properties. Organ-specific averaged SAR dependency on frequency is also expected (Chapter 4). The deviations of organ averaged SAR with respect to the whole body are given in Table 7.7 for the selected organs of a mouse and a rat. These deviations are within the range of +4.5 dB and -8 dB.

Figure 7.4 shows the SAR distribution in the middle slice of the medium mouse and rat models at both 900 and 1900 MHz. The tails of the animals were not included in this figure for model geometry reasons. For the mouse at 900 MHz, the exposure is mainly focused at the tail, whereas for the rat at 1900 MHz the exposure is localized at the head and at the region of the body to tail transition. Considering the SAR distribution within the animal as a relevant parameter, exposing mice at 1900 MHz and rats at 900 MHz would be most appropriate, since in these cases comparable SAR distributions are obtained, with the maximum absorption in the center of the animals. Tail exposure is represented in Figure 7.5, which depicts the SAR distribution on
CHAPTER 7. DOSIMETRY REVERBERATION CHAMBER

| Tissue/Organ  | Deviation organ vs. whole-body SAR (dB) |  
|---------------|----------------------------------------|---|
|               | mouse at 900 MHz | 1900 MHz | rat at 900 MHz | 1900 MHz |
| Blood         | 1.0            | 2.6      | 4.4            | 2.3      |
| Bone marrow   | -4.1           | -3.5     | -3.4           | -3.1     |
| Brain         | -2.5           | -0.9     | 0.9            | 3.4      |
| Eye           | -1.8           | -4.4     | -3.1           | 0.8      |
| Fat           | -5.4           | -7.5     | -7.9           | -6.8     |
| Glands        | -0.1           | 0.7      | 0.4            | 2.3      |
| Heart         | 0.2            | 2.0      | 2.4            | 0.2      |
| Intestine     | 2.0            | 3.7      | 2.6            | 0.3      |
| Kidney        | -0.1           | -0.3     | -0.0           | -0.7     |
| Liver         | -0.3           | 0.1      | 1.0            | -2.0     |
| Lung          | -0.5           | 1.1      | 1.7            | -0.5     |
| Muscle        | 0.8            | -0.4     | 0.2            | 1.0      |
| Nerve         | -2.0           | -0.6     | -0.6           | 3.5      |
| Skin          | 0.1            | -2.4     | -2.1           | -1.7     |
| Spleen        | 1.1            | -0.1     | -1.6           | -0.6     |
| Stomach       | -0.5           | 0.1      | 0.4            | -0.8     |

Table 7.7: Deviation of organ-specific average SAR versus whole-body averaged SAR of the selected organs of the medium mouse and rat at 900 MHz and 1900 MHz.

the surface of the animals. The SAR surface distributions clearly indicate an overexposure of the tail compared to whole body, which was quantified and showed deviations up to 6 dB for the rat at 1900 MHz and more than 9 dB for the mouse at 900 MHz. More moderate values, ∼2 dB, were obtained when the rat was exposed at 900 MHz and mouse at 1900 MHz.

The high exposure observed in the mouse tail at 900 MHz led to a deeper analysis of the influence of tail absorption on whole-body and organ averaged SAR, using a mouse model without tail and comparing this with the original mouse model (with tail). The results showed almost no difference in whole-body averaged SAR between the models, <0.1 dB at both frequencies. Organ SAR deviations between both models were not significant at either 1900 MHz or 900 MHz, <0.5 dB, with the exception of brain, fat and muscles at 900 MHz, with under-exposures of 1 to 2 dB.

In summary, all findings in this section suggest conducting the expo-
7.4. RESULTS

Figure 7.4: SAR distribution in the middle slice of both the medium mouse and rat models at 900 and 1900 MHz. (Scale in dB where 0 dB corresponds to 1.33e-3 \( \left( \frac{W}{Kg} \right) \left( \frac{V^2}{m^2} \right) \) for an isotropic incident field.)

Figure 7.5: SAR distribution on the surface of both the medium mouse and rat models at 900 and 1900 MHz. (Scale in dB where 0 dB corresponds to 1.33e-3 \( \left( \frac{W}{Kg} \right) \left( \frac{V^2}{m^2} \right) \) for an isotropic incident field.)

Sure of rats at 900 MHz and mice at 1900 MHz, in order to achieve higher efficiency, more uniformity, minimum overexposure of the tail, and comparable dose patterns between species.
7.4.3 SAR Lifespan Assessment

The weight and size of the animals are parameters that greatly vary over lifetime, and the absorption levels in an animal highly depend on these parameters, for a given frequency and field strength. In the planned NIEHS studies, a constant SAR in the animals over lifetime is a requirement. Therefore, field strength has to be varied according to animal growth.

This section had two main objectives:

- to assess the whole-body averaged SAR dependency on weight/age over lifetime for the animals in the study exposed at 900 and 1900 MHz
- to establish a relation between animal weight/age and field strength necessary to achieve a certain dose in the animals at a given frequency.

In this section the three plane waves set has been applied, since only whole-body average SAR values were assessed. Scaled and original sized models were used, covering a range of mouse weights between 10 and 55 g, and rats between 75 and 690 g.

Figure 7.6 shows the tendency curve of the efficiency versus weight for mice. These data were then added to the values obtained from the rat simulations, as if mice represented small rats. The efficiency data versus weight are depicted in Figure 7.7 for rats.

All mice exposed at 1900 MHz showed a higher efficiency than at 900 MHz. The tendency of the mouse efficiency at 1900 MHz was to decrease with animal growth, opposite to the tendency at 900 MHz. SAR variations of up to 4.6 dB and 3.6 dB were observed for mice at 900 MHz and 1900 MHz, respectively. For rats, the efficiency curve versus weight at 1900 MHz shows an exponential decrease with animal growth, as occurred for mice, with a maximum SAR variation along weights of $\sim 8$ dB. However, the efficiency at 900 MHz increases almost linearly with animal weight until a peak value (maximum exposure at body resonance frequency) for a weight of $\sim 100$ g, after which it reduces exponentially with animal growth. The maximum SAR variation found for rats at 900 MHz was 6.6 dB. All in all the efficiency in rats at 900 MHz is higher than at 1900 MHz for rats above...
Figure 7.6: Efficiency versus weight for mice at 900 and 1900 MHz.

Figure 7.7: Efficiency versus weight for rats at 900 and 1900 MHz.

∼75 g, and lower only for smaller rats.
In order to obtain an expression relating the SAR and the weight of the animals, the curves in Figures 7.6 and 7.7 were fitted, by convenience, to either exponential or polynomial functions.
Based on data from laboratory animal suppliers, a body-weight development curve versus age was generated for male and female mice and rats of the corresponding strains. These curves provided a conversion function between animal weight and age. With both the fit-
ted curves and the conversion function, it was possible to create Figures 7.8 and 7.9, which show efficiency versus age, between 1 and 406 days (highest age provided by the laboratory animal suppliers), for rats and mice at 900 and 1900 MHz, distinguishing between male and female subjects.

Figure 7.8: Efficiency versus age for male and female mice at 900 and 1900 MHz.

The efficiency curves versus age, separated by gender, showed equivalent tendency to those versus weight. Deviations of efficiency between male and female mice were close to 1 dB at 900 MHz, and close to 0.5 dB at 1900 MHz. For rats, deviations between male and female subjects were >1 dB at 900 MHz and 1 dB at 1900 MHz.

In summary, if rats will be exposed at 900 MHz, the separation of males and females might be considered, in order to achieve a more similar dose in all animals. However, if mice are exposed at 1900 MHz, males and females may be kept together without significant SAR deviation between genders, thereby reducing by half the number of chambers for mice.

The previous data reflected that important variations in animal whole-body average SAR occur over lifetime, depending on animal weight/age, for a given frequency. If a constant dose in the animal
over lifetime is a requirement, the field strength in the chamber has to change with animal weight/age variations. An expression that relates the necessary field strength for a targeted dose to the weight/age of the animals at a given frequency can be obtained from the fitting functions of the efficiency curves.

The expressions found for mice at 1900 MHz and rats at 900 MHz that relate field strength, targeted dose and animal weight are given as an example:

- for mice at 1900 MHz,

\[ FS = \sqrt{\frac{SAR_{target}}{(10^{-7} \cdot w^2) - (10^{-5} \cdot w) + (4 \cdot 10^{-4})}} \quad (7.1) \]

- for rats at 900 MHz with weight <100 g,

\[ FS = \sqrt{\frac{SAR_{target}}{(2 \cdot 10^{-6} \cdot w) + 10^{-5}}} \quad (7.2) \]
for rats at 900 MHz with weight ≥100 g,

$$FS = \sqrt{\frac{SAR_{target}}{2 \cdot 10^{-3} \cdot w^{0.6}}}$$  \hspace{1cm} (7.3)

whereby $FS$ is the field strength, i.e., the root mean square of the electric field per length unit, given in V/m; $SAR$ is the targeted whole-body dose in mW/g; and $w$ is the animal weight in g. Similar expressions can be obtained using age as a variable instead of weight. Table 7.8 shows the estimated field strength necessary to achieve a dose of 6 W/Kg in the original size mouse and rat models at 900 and 1900 MHz. Values up to 360 V/m were obtained.

<table>
<thead>
<tr>
<th>Models</th>
<th>Field strength at 900 MHz (V/m)</th>
<th>Field strength at 1900 MHz (V/m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small rat (228 g)</td>
<td>241</td>
<td>288</td>
</tr>
<tr>
<td>Medium rat (253 g)</td>
<td>255</td>
<td>289</td>
</tr>
<tr>
<td>Large rat (598 g)</td>
<td>316</td>
<td>348</td>
</tr>
<tr>
<td>Small mouse (20 g)</td>
<td>358</td>
<td>153</td>
</tr>
<tr>
<td>Medium mouse (30 g)</td>
<td>360</td>
<td>178</td>
</tr>
<tr>
<td>Large mouse (38 g)</td>
<td>292</td>
<td>189</td>
</tr>
</tbody>
</table>

Table 7.8: Estimated field strength necessary to achieve a dose of 6 W/Kg in the original sized rat and mice models at 900 and 1900 MHz.

To summarize, mouse efficiency trend curves showed higher values at 1900 MHz than at 900 MHz, over lifetime. For rats, the efficiency at 900 MHz is higher than at 1900 MHz for rats heavier than ∼75 g. If higher efficiency is desired for smaller rats, it might be considered to expose them at 1900 MHz. The exposure differences found between male and female rats at both frequencies suggest exposing them separately by gender. However, mice might be exposed mixed altogether at 1900 MHz with low deviations in whole-body averaged SAR, reducing the total number of chambers. The manner of how to obtain an expression relating the field strength of the incident radiation, targeted dose and animal weight has been described, and three examples were given. In addition, the estimated field strength for a dose of 6 W/Kg in the original sized animal models at both 900 and 1900 MHz show values up to 360 V/m.
7.4. RESULTS

7.4.4 Tail versus Whole-body Exposure over Lifetime

In general, when a lossy body is exposed to RF-EMF radiation, the absorbed power increases the body temperature. In living subjects, this process can be very complex, since organisms are able to auto-regulate their temperature (under a threshold value) by means of various mechanisms. The tail is a critical body part for rodents in their thermoregulation. If the tail is highly overexposed, and it has been seen that actually tail exposure may be very dominant at particular frequencies (see section 7.4.2), animals might have difficulty balancing their temperature and exceed the thermal regulatory threshold. Consequently, with steadily increasing body temperature, animals might reach the breakdown threshold and die [68]. The aim of this section was to analyze the exposure of the tail and its deviation to whole-body exposure, for rat and mouse models over lifetime and at both frequencies.

For mice exposed at 900 MHz, the deviations of tail to whole-body SAR were between 6 and 9 dB for a weight range of 10 to 55 g. Rats exposed at 1900 MHz showed tail overexposure between 5 and 7 dB for a weight range between 75 and 690 g. Figures 7.10 and 7.11 depicts the deviation of tail to whole-body absorption for mice at 1900 MHz and rats at 900 MHz, respectively, in the above mentioned weight ranges, including the pup model to see the expected tendency for small subjects (pup exposure is studied in detail in section 7.4.6). The values in Figures 7.10 and 7.11 are more moderate than those obtained at other frequencies. Excluding the pup, all deviations are below 4 dB for mice (at 1900 MHz), and below 5 dB for rats (at 900 MHz). The values corresponding to pregnant subjects deviate slightly from the trend curves due to their stuffed shape compared to non pregnant subjects (stretched).

7.4.5 Embryo Exposure

The question posed for pregnant subjects was whether they might be exposed under the same conditions as non-pregnant subjects, without risk of embryo overexposure. The aim of this section was to respond to this question by assessing the embryo exposure in the pregnant
Figure 7.10: Deviation of tail to whole-body averaged SAR for mice exposed at 1900 MHz, including mouse pup.

Figure 7.11: Deviation of tail to whole-body averaged SAR for rats exposed at 900 MHz, including rat pup.

models (pregnancy status of 15 days).
Results showed that in general, the exposure of the embryo remains
close to whole-body exposure of the dam, i.e., showing maximum deviations of $<1$ dB for a rat at 1900 MHz and mouse at both frequencies. However, a deviation $>1$ dB was found for the rat model at 900 MHz. Although no risk for the embryo is expected, further investigation might be necessary.

7.4.6 Exposure in Pups

Rodent pups are planned to be exposed with their mothers until weaning, which commonly occurs around the third week of life (21 days). It is thus important to estimate the absorption levels in pups in comparison with the exposure of their mother, in order to chose a suitable field strength for the exposure. The pup SAR analysis included different scenarios and configurations; therefore, up to three parts are distinguished in this section:

- efficiency assessment in a single pup
- relative exposure of one pup and mother
- influence of the complete litter in single pup and mother exposures.

In addition, the deviation of tail to whole-body exposure in pups was assessed.

Single pup

Single mouse and rat pups were exposed at both 900 and 1900 MHz. The assessed efficiency, uniformity and deviation of tail to whole-body exposure are given in Table 7.9.

The rat pup exposed at 1900 MHz showed the highest efficiency. Pup tails showed deviations with respect to the whole body of about 11 dB, with the exception of the rat pup at 1900 MHz, with 4 dB of tail overexposure. This lower overexposure occurs because the rat pup exposed at 1900 MHz is closer to body resonance frequency and therefore has a more uniform whole-body SAR absorption than the other scenarios. Some recommendations for pup exposure are given at the end of this section, 7.4.6.
Table 7.9: Efficiency, uniformity and deviation of tail to whole-body exposure of a rat pup and a mouse pup exposed at 900 and 1900 MHz.

<table>
<thead>
<tr>
<th>Models</th>
<th>Frequency (MHz)</th>
<th>Efficiency $(W/Kg)$</th>
<th>Uniformity (dB)</th>
<th>Dev. tail to WB (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat pup</td>
<td>900</td>
<td>3.5e-5</td>
<td>4.2</td>
<td>11.2</td>
</tr>
<tr>
<td></td>
<td>1900</td>
<td>3.4e-4</td>
<td>2.8</td>
<td>4.1</td>
</tr>
<tr>
<td>Mouse pup</td>
<td>900</td>
<td>5.8e-5</td>
<td>3.7</td>
<td>10.2</td>
</tr>
<tr>
<td></td>
<td>1900</td>
<td>9.0e-5</td>
<td>3.8</td>
<td>10.6</td>
</tr>
</tbody>
</table>

**Exposure of Pup and Dam**

Since pups will be exposed with their mother for the first days of life, the aim of this section was to assess the dose achieved in the pup bodies with respect to the dam, with the dam represented by the medium anatomical model. The SAR can be expected to be dependent on the relative position of the pup to the dam; therefore the following scenarios with both animals exposed at 900 and 1900 MHz were considered:

- pup and mother parallel to each other and facing the same direction

- pup and mother orthogonal to each other and with pup facing the mother’s body (representing pup suckling).

Pup exposure in the presence of the dam was highly dependent on the relative body orientation to the dam, especially for mice. Only the rat pup exposed with the dam at 1900 MHz presented an important higher exposure with respect to the dam, of more than 5 dB in both configurations. The mouse pup at 900 MHz in the perpendicular configuration presented an overexposure of more than 2 dB with respect to the dam. No pup overexposure was detected for rats exposed at 900 MHz and mice at 1900 MHz. However, these results only show whole-body averaged SAR values and do not refer to tail overexposure, which should be a priority factor for determining the applied field strength if pups and dam are exposed together.
7.4. RESULTS

Litter Clump

The members of a litter spend the largest part of their first days of life sleeping and resting, during which the pups tend to join in a clump, climbing on each other in a pile. This led to the representation of a clump of pups, with the pups occupying a random position with respect to each other, as shown in Figure 7.12 left. A second scenario was designed with the mother laying over the pups, as in Figure 7.12 right.

![Figure 7.12: Representation of a litter of rat pups in a clump (random relative position) in a resting/sleeping scenario (left), and same scenario with the dam over the pups (right).](image)

The results of the previous section indicate significant variations in SAR due to the relative orientation between the dam and a single pup. Here a similar effect can be expected among the pups in the clump.

Eight rat pups and six mouse pups are planned to be exposed with the dams in the NIEHS experiments (half male and half female), although litters are generally larger. In order to analyze the SAR levels in the dam and pups of a litter in random positions, as well as the dependency on the number of pups in the clump, the following configurations were considered:

- 12 rat pups in a clump
- 12 rat pups in a clump with the dam laying above
- 8 rat pups in a clump with the dam laying above
• 6 mouse pups in a clump with the dam laying above.

To perform this analysis the quantities assessed were:

• whole-body average SAR values of each pup in the litter,
• mean value of all pups,
• deviation of every pup to the mean value
• deviation of the pup mean value to a single pup
• deviation of the pup mean value to the dam,
• deviation of whole-body average SAR of the dam to reference dam (dam alone).

Simulations with the litter were performed at 900 MHz for rats and 1900 MHz for mice.

Clumping together significantly increases the whole-body exposure for all pups in the clump in comparison with single pup exposure. This increase is lower with fewer pups in the clump, and in the presence of the mother.

For the 8 rat pup configuration exposed at 900 MHz, the pup with maximum whole-body averaged SAR presented an overexposure of 5 dB with respect to a single pup. For the 6 mouse pup configuration exposed at 1900 MHz, the maximum pup whole-body averaged SAR was 3 dB above the single pup absorption. In spite of this increase, the mouse pup with the maximum absorption in the clump, still presented a whole-body average SAR 0.4 dB below the dam SAR. In a clump of 8 rat pups, the pup with the maximum absorption had a whole-body average SAR 0.1 dB higher than the dam. These results show that pups did not receive a higher whole-body dose when exposed with the mothers under the same conditions. However, tail absorption evaluation in the pups of the litter again showed large deviations to the whole body, between 2 and 11 dB. Once more, the maximum tail exposure should be used as a limiting factor when determining the appropriate field strength, to avoid harm to the pups. The exposure of the dam was only moderately enhanced by the presence of the
pups, i.e., by about 0.7 dB for rats at 900 MHz and 0.2 dB for mice at 1900 MHz.

Conclusions

The obtained results show high absorption in the pup’s tail in comparison to its whole body (>11 dB) when pups are exposed under the same conditions as the mother (same frequency and field strength). If a target dose of 6 W/Kg for the whole-body average in the dam is desired, the maximum exposure of a pup tail might achieve 70 W/Kg, i.e., ~11 dB higher. It is therefore recommended to use tail absorption to limit the maximum possible dose in the animals when pups and dam are exposed together. Since complex mechanisms are involved in the thermoregulation of rodents exposed at high-power RF radiation [69], [68], an experimental study is highly recommended to monitor the temperature increase in pups, to assess whether using high field strengths would imply a risk on a pup’s health or life. If necessary, a reduction of the whole-body dose should be considered during the pre-weaning exposure period.

7.4.7 Proximity, Relative Orientation and Posture

Assessment of the SAR variations due to proximity, relative orientation and posture was performed with homogeneous phantoms. For these evaluations, the reference set of plane waves was used.

Proximity

Since optimized use of the chamber room is desired, it is important to estimate the minimum separation between animals which does not imply significant SAR variations. Proximity of the animal phantoms was varied, first using only 2 phantoms and then using a 3-D array of 27 phantoms (3x3x3). In both configurations the phantoms were positioned parallel to each other, and separations were considered from the center of one phantom to the center of the other. To study the variations due to proximity effects with 2 phantoms, the distances between phantoms under investigation were 0.25λ, 0.375λ,
0.5\(\lambda\), 1\(\lambda\) and 1.5\(\lambda^2\), where \(\lambda\) is the wavelength of the field propagating in free space. The variations of whole-body averaged SAR with respect to the single phantom for all considered scenarios were within \(\pm0.5\) dB both phantom sizes and both 900 and 1900 MHz. When the 3-D array was used, the distances between phantoms were 1\(\lambda\) and 1.5\(\lambda^3\). The results for mice at 1900 MHz showed that the largest variation of the average exposure of all phantoms in the array with respect to the reference phantom was -1 dB for a separation of 1\(\lambda\). The standard deviation of averaged SAR of the mouse phantoms within the array was 0.4 dB. For rats, the most significant variation of the average exposure of all phantoms in the array with the respect to reference phantom was -1 dB and occurred for a separation of 1\(\lambda\) at 900 MHz. The standard deviation of the averaged SAR of the rat phantoms within the array was 0.3 dB.

In summary, the SAR variations using 2 phantoms were not significant at separation distances as short as 0.25\(\lambda\). The deviation of the mean SAR value of all 27 phantoms in the 3-D array with respect to the reference phantom and the standard deviation within the array were smaller for larger separations between the phantoms. No significant variation was found for distances as short as 1\(\lambda\) for both phantom sizes and both frequencies. Whether these results can be extrapolated to the case of a larger array, non homogeneously disposed array or shorter separation should be further investigated by experimental means in a reverberation chamber.

**Relative Orientation**

The influence of relative orientation on the SAR values was studied with two homogeneous phantoms separated at a constant distance of 1\(\lambda\) in three different scenarios:

- two phantoms parallel to each other and to the z-axis
- one phantom parallel to the z-axis and the other one tilted 90° around x-axis, towards the y-axis

\(^2\)Some separations could not be used due to frequency and phantom dimensions.
\(^3\)Shorter distances were not feasible because of the phantom height.
• one phantom parallel to the z-axis and the other one tilted $90^\circ$ around y-axis, towards the x-axis.

The SAR variations found with respect to a single phantom were within $\pm 0.3$ dB for both rats and mice and at both frequencies. In conclusion, no significant variation of the SAR due to relative position was observed in the considered phantoms at a distance of $1\lambda$ for the tested frequencies.

**Posture**

Significant variability of the exposure of non-restrained animals is expected due to different postures of the animal body, especially for organ-specific averaged SAR values. The assessment of SAR variability due to animal posture is a difficult task, since high resolution parameterized animal anatomical models enabling posture changes are not yet available. In order to achieve an estimation of the expected whole-body averaged SAR in the animals by changing their posture, homogeneous phantoms were used whose shape and posture are easy to manipulate. Two *capsule-phantoms*, i.e., cylinder phantoms terminated with two spherical caps, represented the mouse phantom (length=80 mm and diameter=24 mm) and the rat phantom (length=200 mm and diameter=48 mm). These original phantoms were then stretched, rammed and curled, maintaining the same volume and weight of the original phantoms.

The largest SAR variation with respect to the original phantom, $\sim 2$ dB, was found for a stretched mouse phantom exposed at 900 MHz. However, the SAR variations found between the stretched, rammed and curled phantoms with respect to the original phantom models, for the mouse at 1900 MHz and rat at 900 MHz, were all within a range of $\pm 1$ dB. Variations in real animals can be expected to be somewhat larger than for the phantoms, especially for organs. For the variation budget, it was assumed that this difference is not greater than $\pm 2$ dB for rats exposed at 900 MHz and mice at 1900 MHz.

**7.4.8 Uncertainty and Variation Assessment**

The main uncertainty sources according to Chapter 3 are (1) the numerical model of the exposure (number, direction and polarization
of the plane waves used), (2) the grid resolution and animal model discretization, (3) the animal model anatomy and weight, (4) the dielectric parameters assigned to the tissues/organs. The uncertainty from (1) was assessed within this chapter (experimental validation is described in the following section). The uncertainty from (2)-(4) were not considered here, although the determination of the uncertainty from these sources is of high relevance in the final dosimetry. In addition, uncertainties of the experimental dosimetry and the setup should be considered. An example of all these uncertainties and how to treat them in an in vivo study was given in Chapter 5.

Regarding SAR variations, the following sources must be considered (1) weight and size of the animal (strain, gender, age), (2) position of the animal in the working volume of the chamber (to be assessed experimentally), (3) proximity of the animals, (4) relative orientation and (5) posture. The SAR variation analysis within this study considered the parameters 1, 3, 4 and 5. Remaining SAR related to the experimental dosimetry and setup should be assessed in the final dosimetry following the methodology in Chapter 3.

### 7.4.9 Experimental Validation

To validate the results obtained by numerical means, a comparison with the measured values was realized. The SAR values in the phantoms (numerically assessed) could be directly related to the absorption cross section (ACS) of the phantoms (experimentally obtained), by this simple expression:

$$\text{SAR} = \text{ACS} \frac{P_d}{m}$$

(7.4)

with $P_d$ as the power density and $m$ the mass of the phantom. The absorption cross section (ACS) values obtained experimentally for a rat phantom at both 900 and 1900 MHz by different methods [60] are given in Table 7.10, as well as the values numerically obtained.

Good agreement was found between simulated and measured data, with standard deviations of 0.6 dB and 0.5 dB at 900 and 1900 MHz, respectively.
Table 7.10: Comparison of absorption cross section (ACS) values obtained by experimental and numerical methods of a rat phantom at both 900 and 1900 MHz.

<table>
<thead>
<tr>
<th>Method</th>
<th>ACS (m$^2$) 900 MHz</th>
<th>ACS (m$^2$) 1900 MHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insertion loss method</td>
<td>1.2e-2</td>
<td>1.1e-2</td>
</tr>
<tr>
<td>Temperature method</td>
<td>1.3e-2</td>
<td>0.95e-2</td>
</tr>
<tr>
<td>Numerical method</td>
<td>1.0e-2</td>
<td>0.86e-2</td>
</tr>
<tr>
<td>Mean result</td>
<td>1.2e-2</td>
<td>0.97e-2</td>
</tr>
<tr>
<td>Variability</td>
<td>±0.6 dB</td>
<td>±0.5 dB</td>
</tr>
</tbody>
</table>

More recent SAR measurements performed in animal homogeneous phantoms in the chamber built at IT’IS have been compared with new simulation results showing even smaller deviations of 0.3 dB for male rats at 900 MHz, 0.2 dB for female rats at 900 MHz and 0.4 dB for mice at 1900 MHz.

7.4.10 Requirements for Final Dosimetry

The final dosimetry of the reverberation chambers to be built for the NIEHS experiments should be done following the methodology described in Chapter 3, including SAR values of the whole-body and organs, at least of those relevant for the histopathological investigation as well as the peak SAR values; additional investigation must be performed focusing on the SAR uncertainty and variation assessment of all the animals within the studies, distinguishing among instant and lifetime variations.

7.5 Discussion and Conclusions

A numerical model representing the exposure of animals in a reverberation chamber-like environment was developed.

Rats exposed at 900 MHz presented significantly higher absorption efficiency than at 1900 MHz. Similar behavior was observed in mice exposed at 1900 MHz, with efficiency much higher than at 900
MHz. In addition, comparable SAR patterns were observed for rats at 900 MHz and mice at 1900 MHz, presenting the maximum absorption at the center of the body. Optimization of the exposure with respect to similar absorption patterns in both species might be preferable than utilizing the same carrier frequency.

Moderate overexposure of the tail with respect to the whole-body exposure occurred when rats were exposed at 900 MHz and mice at 1900 MHz. Based on these data, NIEHS changed their protocol and will conduct the experiments for GSM and IS95 modulation with rats at 900 MHz and mice at 1900 MHz.

The evaluation of the efficiency versus animal weight and age showed a generally higher efficiency for rats at 900 MHz and mice at 1900 MHz. Expressions that relate the weight of the animals, the targeted SAR level and the required exposure field strength were obtained.

Exposing male and female rats needs to be expected in different rooms due to large differences in body size leading to deviations >1 dB. This separation of rats by gender has also the advantage that the power required can be further optimized. However, male and female mice may be exposed together with expected variations of much less than 1 dB. This lower variation is a positive outcome, since it enables the reduction of the number of chambers by a factor of two, at least for mice.

For rats exposed at 900 MHz and mice at 1900 MHz, the obtained deviations were always smaller than 5 dB, much less than when rats and mice are exposed at 1900 and 900 MHz, respectively. Whether or not these overexposure values are acceptable at the field strengths necessary to achieve the required SAR levels during the periods of power on (10 minutes) should be experimentally investigated, assessing possible hot spots or thermoregulation difficulties.

The exposure of the pup is greatly dependent on its position with respect to the dam and other pups, presenting high SAR variations. In general, the pup whole-body averaged SAR increases with respect
to the single pup with the number of pups in the clump and decreases with the presence of the dam. When pups were exposed with the mother, at 900 MHz for rats and 1900 MHz for mice, whole-body averaged SAR levels in the pups were not higher than in the dam, but of the same order. The most outstanding finding from the pup exposure was the high tail absorption compared to the whole body. Absorption in the tail larger than 11 dB above the whole-body SAR were found for rats at 900 MHz and mice at 1900 MHz. This should be considered as a limiting factor when determining the appropriate exposure field strengths. Experimental investigations are recommended prior to the beginning of the final experiments, and if necessary, the target SAR level should be reduced while pups are exposed with their mother.

The SAR variations in homogeneous phantoms due to proximity and relative orientation were not significant when 2 phantoms were used at distances as short as 0.25\(\lambda\). The effect of the array was not large at distances as short as 1\(\lambda\). However, whether these results can be extrapolated to animal models in a larger array or at shorter distances should be experimentally verified.

The variations of whole-body averaged SAR upon posture, assessed with homogeneous phantoms, showed values in the range of \(\pm 1\) dB for rats at 900 MHz and mice at 1900 MHz. However, it must be expected that the variations for real animals will be larger.

The instant\(^4\) variations of whole-body averaged SAR estimated here are presented in Table 7.11. Long-term variations are expected to be smaller as shown in Chapter 5.

\(^4\)Integration over a time period of larger than one paddle rotation
### Table 7.11: Preliminary budget of variation for whole-body averaged SAR values.

<table>
<thead>
<tr>
<th>Variation description</th>
<th>Tolerance (dB)</th>
<th>Distr.</th>
<th>Div.</th>
<th>STD. DEV. (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>900 MHz</td>
<td>1900 MHz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incident Field</td>
<td>1.0</td>
<td>1.0</td>
<td>normal</td>
<td>1.0</td>
</tr>
<tr>
<td>Array Effect**</td>
<td>1.3</td>
<td>1.4</td>
<td>rect.</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>Sex</td>
<td>1.3</td>
<td>0.6</td>
<td>rect.</td>
<td>0.4</td>
</tr>
<tr>
<td>Weight</td>
<td>0.4</td>
<td>0.3</td>
<td>normal</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Proximity</td>
<td>0.5</td>
<td>0.5</td>
<td>rect.</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Rel. orientation</td>
<td>0.3</td>
<td>0.3</td>
<td>rect.</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td>0.2</td>
</tr>
<tr>
<td>Posture</td>
<td>2.0</td>
<td>2.0</td>
<td>rect.</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td>1.2</td>
</tr>
</tbody>
</table>

Combined std. variation: 1.9, 1.8
Expanded std. variation with k=2 (coverage 95%): 3.9, 3.6

* Variations of the local cartesian field, which is an overestimation for the integration.
** For an animal separation of λ.
Chapter 8

*In Vivo* Temperature monitoring in RF Experiments using Wireless Transponders
8.1 Introduction

The highest SAR exposure in the upcoming NIEHS lifetime bioassay NTP-like \textit{in vivo} studies is just below the thermal threshold, namely at 6 W/kg. Since an exposure level resulting in thermoregulatory problems in animals is a function of their weight, stress, health condition and environment [68], continuous monitoring of the animal body temperature is desired. Rectal measurements using optically based sensors or thermistors with RF transparent leads have been used in the past but are only applicable for short-term monitoring in anesthetized or restrained animals. Although wireless implantable thermal transponders have been developed for long-term surveillance and are commercially available, they had not been tested for usage in harsh electromagnetic environments.

8.2 Objectives

The objective of this study was to evaluate the performance and suitability of commercially available wireless implantable thermal transponders for \textit{in vivo} thermal monitoring of mice and rats in RF exposure experiments at 900 and 1900 MHz. The requirements for suitability are:

- small size of the implantable device (suitable for rats and mice),
- the access time for the required number of measurements should be as short as possible\(^1\),
- the transmission range should be as large as possible\(^2\),
- the presence of the transponder should not significantly alter the global and local absorption strength and pattern in the animals,
- the transponder should not result in any local temperature hotspots when exposed,

\(^1\)According to [68], mice are able to cool with a rate of approximately 0.3 \(^\circ\)C/min after RF is switched off.
\(^2\)The most preferred solution would be if the signal could be read remotely from outside the chamber.
8.3. **PROPERTIES OF THE FOUR EVALUATED SYSTEMS**

- the response of the transponder should not be altered by EMF after and/or during exposure by EMI.

## 8.3 Properties of the Four Evaluated Systems

Four different implantable temperature monitoring systems have been evaluated. Their main technical data are shown in Table 8.1.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Biotelemetry</th>
<th>BMDS</th>
<th>Mini Mitter</th>
<th>Transoma Medica</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temp. range</td>
<td>-</td>
<td>32-43°C</td>
<td>-</td>
<td>33-43°C</td>
</tr>
<tr>
<td>Temp. resolution</td>
<td>-</td>
<td>0.1°C</td>
<td>-</td>
<td>0.01°C</td>
</tr>
<tr>
<td>Accuracy</td>
<td>-</td>
<td>± 0.25°C</td>
<td>-</td>
<td>0.1°C (+drift over time)</td>
</tr>
<tr>
<td>Transmission</td>
<td>RF-FM telemetry</td>
<td>telemetry</td>
<td>telemetry</td>
<td>telemetry</td>
</tr>
<tr>
<td>Carrier frequency</td>
<td>88-150 MHz</td>
<td>power: 400 kHz; data: 40-80 kHz</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Access range</td>
<td>&lt;7 m</td>
<td>&lt;5 cm</td>
<td>max cage size: 25x50 cm²</td>
<td>max cage size: 33x33x14 cm³</td>
</tr>
<tr>
<td>Measurement time</td>
<td>- 1-5s/animal</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lifetime (battery, etc.)</td>
<td>133h/56h passive</td>
<td>passive</td>
<td>passive</td>
<td>6 months (warranted)</td>
</tr>
<tr>
<td>Size</td>
<td>7.8x7.8x2.5 mm³ + pins/antenna + battery + wires + coating</td>
<td>l: 14 mm; d: 2.2 mm</td>
<td>l: 22 mm; d: 8 mm</td>
<td>volume: 1.75 cc</td>
</tr>
<tr>
<td>Metallic parts</td>
<td>many</td>
<td>small</td>
<td>medium</td>
<td>medium</td>
</tr>
<tr>
<td>Complexity</td>
<td>high</td>
<td>small</td>
<td>small</td>
<td>medium</td>
</tr>
<tr>
<td>Integration</td>
<td>medium</td>
<td>high</td>
<td>high</td>
<td>high</td>
</tr>
<tr>
<td>Failure probability</td>
<td>high</td>
<td>small</td>
<td>small</td>
<td>medium</td>
</tr>
<tr>
<td>Application method</td>
<td>surgery</td>
<td>injection</td>
<td>surgery</td>
<td>surgery</td>
</tr>
<tr>
<td>Identification</td>
<td>carrier freq.</td>
<td>code</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>Add. freq. comp.</td>
<td>DC-10 kHz</td>
<td>none</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cost</td>
<td>$520</td>
<td>reader: $4'400; 100 items: $1'750</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 8.1: Technical data of the 4 implantable transponders evaluated.

After preliminary analysis of the data with respect to the requirements, the Mini Mitter was not further considered, because its large size reader (55x30x7 cm³) would have to be placed immediately below each animal cage in the reverberation chamber. This is not acceptable in an RF exposure study. Furthermore, the Transoma Medical device had to be rejected for similar reasons.

The implantable microchip transponder of BMDS is superior to the wireless implantable transmitter of Biotelemetrics with respect to size, metallic parts, lifetime and method of application. However, it requires manual reading of the temperature. Therefore it does not
allow the body temperature to be read during RF-on phases. The usefulness of the information acquired manually depends on the delay between RF-off and temperature measurement. According to a study on response, thermal regulatory threshold and thermal breakdown threshold of restrained RF-exposed mice [68], where the temperature of the animals was continuously monitored, mice are able to cool with a rate of approximately 0.3 °C/min after RF is switched off. However, a solution based on the Biotelemetrics System might enable automatic temperature measurements. Thus, the transponders from Biotelemetrics and BMDS were retained in the following detailed numerical and experimental analysis.

8.4 Numerical Evaluations

The aim of the numerical analysis was to evaluate the potential effects of the transponders on the absorption pattern in the animals. Since the transponder should be used during the entire study, it was decided to conduct the evaluation under worst-case considerations with respect to effects on the absorption pattern. For this purpose, the 20 g mouse model was selected. The models of the implants are shown in Figure 8.1. The BMDS transponder was numerically implanted in the mouse model in two different positions: rear part of the mouse neck and left rear side of its body. For size reasons, the Biotelemetrics was only tested implanted on the rear part of the mouse neck.

The results of the numerical evaluations are shown in Table 8.2 as deviations of the whole-body averaged SAR of the mice with an implant with respect to the mouse without implant. No significant effects on whole-body averaged SAR, i.e., deviations of ±0.01 dB, were observed using the BMDS transponder in both locations in the mouse. A small but slightly larger deviation, 0.2 dB, was determined using the Biotelemetrics device implanted in the mouse neck. The deviations assessed of the organ-specific averaged SAR between the mice with implants and the mouse without implant were found in a range of ±0.5 dB using the BMDS transponder and ±1 dB using the Biotelemetrics device. The effect on the animal SAR pattern produced by each implant is depicted in Figure 8.2. A zoomed view of the simulated SAR distribution distortions resulting from the Biotelemetrics
8.4. NUMERICAL EVALUATIONS

Figure 8.1: Models of the implants: (above) detailed model of the BMDS and (below) simplified model of the Biotelemetrics transducer.

A device implanted in the mouse model is shown in Figure 8.3.

<table>
<thead>
<tr>
<th>Mouse model</th>
<th>Dev. WB avg. SAR (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse with BMDS (neck)</td>
<td>-0.01</td>
</tr>
<tr>
<td>Mouse with BMDS (left side)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mouse with Biotele. (neck)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Table 8.2: Deviation of the whole-body averaged SAR in mice with an implanted temperature transponder with respect to a mouse without implant at 1900 MHz.

The evaluations showed, in conclusion, that the BMDS device is superior to the Biotelemetrics:

- small size of implantable device
- suitable for a 20 g mouse
- placement by injection vs. surgery
- passive vs. active operation
Figure 8.2: From left to right, SAR distribution pattern on the middle slice of a 20 g mouse without implant, a mouse with a BMDS device implanted in the neck, a mouse with a BMDS device implanted in its rear left side (not visible in the figure) and a mouse with a Biotelemetrics device implanted in its neck. Scale: \(0 \text{ dB}=5\times10^{-3} \left[\frac{\text{W/Kg}}{(\text{V/m})^2}\right].\)

- long usage time
- minimal local SAR distortions.

### 8.5 Experimental Evaluations

Based on the numerical evaluations, the BMDS transponder IPTT-300 was found to be the most suitable candidate for lifetime whole-body temperature assessments. The BMDS device was therefore experimentally evaluated with the dosimetric scanner DASY4. A flat phantom with tissue simulating liquid was used; the transponder was introduced in the liquid and laid at the bottom of the phantom mold. The excitation dipole used as the radiator was placed at a distance from the phantom surface of 15 mm at 900 MHz and 10 mm at 1900 MHz. The experimental evaluation included (1) SAR distributions, (2) EMI tests, (3) local temperature increase and (4) thermal hotspots.
8.6 Conclusions

Four different wireless transponders for \textit{in vivo} temperature measurement were evaluated based on the requirements: sufficiently small for implantation into mice, passive operation, no significant effect on the absorption pattern, no thermal hotspots under RF exposure and good immunity against EMI of induced pulsed RF fields. For the specified requirements, only the IPTT-300 transponder from BioMedic Data Systems proved suitable for long-term monitoring.

8.7 Recommendations

The IPTT-300 temperature transponders of BMDS are sufficient to periodically validate that the animals are not suffering any thermal

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Figure 8.3: SAR distribution pattern (zoomed) on the middle slice of a 20 g mouse with a Biotelemetrics transponder implanted in the neck and without implant.
stress, i.e., an increase of the whole-body averaged temperature of less than 1°C. However, a thermal study is recommended to monitor temperature with a cable system parallel to use of the BMDS transponders. This will enable determination of the thermal threshold as well as the thermal breakdown values with high precision. More importantly, it will allow derivation of the correlation of the temperature measured with the transponder after the exposure to the actual rectal temperature before the end of exposure.
Chapter 9

Novel Design of a Water System for Rodents
9.1 Introduction

The data delivered by NIST [60] and the IT’IS Foundation (see Chapter 7), of the suitability of reverberation chambers to expose unconstrained animals to RF radiation with high SAR efficiency and uniformity, led to the decision of NIEHS to utilize reverberation chambers for its toxicological/carcinogenical studies of mobile phone RF radiation in laboratory animals.

In the planned experiments, more than 3000 unconstrained individually hosted rodents will be chronically exposed to GSM and IS95 signals. Several important decisions regarding the design of the exposure were derived from the results obtained by NIST and the IT’IS Foundation. For instance, rats and mice will be exposed at 900 and 1900 MHz, respectively. Male and female rats will be exposed in separate chambers. Up to 112 rats and 216 mice will be exposed per chamber (volume $\sim 21 \text{ m}^3$), with a regime of 10 minutes power on - 10 minutes power off, 20 hours a day, 5 days a week over an entire life cycle in a period of 2 years. A total of 21 reverberation chambers of approximate inner dimensions of $2.2 \times 3.6 \times 2.6 \text{ mm}^3$ (width x length x height) are required for the study.

Further tasks in the NIEHS program were distributed; in addition to the construction of a reverberation chamber prototype including signal generation and RF equipment and software, one of the main engineering challenges given to IT’IS was the design, development and manufacture of a water system for the animals. Water is an electrically lossy material and attains SAR levels within the same range as the animals. Energy absorbed in this way would be wasted and would increase the RF power needed to reach the required whole-body average SAR level in the animals. In addition, animals might experience unpleasant sensations when in contact with water exposed to high fields.

A literature search produced only one paper reporting a detailed description of the water system used during rodent exposure to high RF field strengths [70]. Other studies either did not allow animals to access water during exposure [71], [72], or targeted very low SAR levels [73] or exposed animals for short intervals [74]. The water sys-
tem reported by [70] consists of a bottle of water and a sipper tube and is located outside the exposure waveguide. Only the very tip of the sipper is introduced in the setup through a wall of the waveguide. There is little or no absorption of power by the water in the metallic sipper tube. Unpleasant sensation in the animals when contacting the water in the high field environment is avoided by means of an external quarter wave choke structure connected to the wall of the cavity. The structure reported in [70] cannot be directly applied to the reverberation chamber case, as the animals are housed well away from the walls of the chamber.

The lack of information in the literature regarding water systems used during animal high field RF exposure as well as the unsuitability of the well documented system for the conditions of the NIEHS experiments were the motivation to design an innovative water system and to perform the following investigation.

9.2 Objectives

The aim of this study was to design a water system that can supply water to more than 3000 rodents (up to 216 animals per chamber) exposed to EMF-RF radiation in reverberation chambers at average field strengths of up to 400 V/m (rms), avoiding:

- elevated local peak SAR in the animal while drinking,
- significant variations in animal average SAR levels and distributions either whilst drinking or not,
- RF absorption in the water.

9.3 Methods

The following numerical methods were used to perform this study.

9.3.1 Anatomical Models

Two female models were used, a 250 g Sprague-Dawley rat and a 30 g B6F3C1 mouse. Both are of medium size and represent pregnant an-
imalls, such that the embryo exposure could also be assessed. General data of the anatomical rat and mouse models can be seen in Table 2.2.

The exposure in a reverberating environment was modeled as described in Chapter 7. The rat models were exposed at a carrier frequency of 900 MHz, the mouse models at 1900 MHz. In order to minimize computational effort, the tails of the models were not considered, based on previous tests of its impact on animal SAR which delivered no significant variations in the assessed quantities. Drinking animals were exposed with the sipper tube introduced in their mouths in such a way that their tongues were in contact with the water at the tip of the tubes.

The simulation grid was homogeneous, with a raster size of 1x1x1 mm$^3$ for both the rat and water system regions. For the mouse, a homogeneous grid of 0.5x0.5x0.5 mm$^3$ was utilized for the animal region and 1x1x1 mm$^3$ for the water system region. The use of grids with double resolution was previously tested, delivering no significant SAR variations with respect to the chosen resolution for the whole-body averaged SAR ($<0.1$ dB) and only ±0.5 dB for the assessed organ averaged SAR.

### 9.3.2 Water System Components

Various components of commonly available water systems were used. These mainly included standard plastic water bottles of different shapes and volumes, metallic sipper tubes of different lengths and shapes, more sophisticated metallic sipper valves and lixits, and water pipes. The bottles of water were modeled as high density polycarbonate with a density of 4444 Kg/m$^3$ and the dielectric parameters $\epsilon=3$, $\sigma=0.015$ S/m at 900 MHz and $\epsilon=2.7$, $\sigma=0.01$ S/m at 1900 MHz. All metallic parts, such as water pipes and sipper tubes (stainless steal), were modeled as perfect electrical conductors (PEC). The water dielectric parameters were measured at the IT’IS laboratories and are those of a commercially available mineral water ($\epsilon=79.4$, $\sigma=0.25$ S/m at 900 MHz and $\epsilon=78.3$, $\sigma=0.88$ S/m at 1900 MHz).
9.3.3 Dosimetric Assessment

The dosimetric assessment focused on the investigation of possible alterations in animal SAR levels and patterns as well as detection of any peak absorption value in the animals while drinking in comparison to non-drinking animals. With this intention, the assessed quantities were: whole-body average SAR, whole-body peak spatial SAR (averaged over 50 mg for the rat and 5 mg for the mouse) and organ-specific average SAR values. The organs considered as relevant due to their proximity to the water system and, therefore, included in the analysis were the brain, eyes and tongue in addition to the embryo, since the models used were pregnant subjects. The SAR in the rest of the organs/tissues was also analyzed but is not presented in this thesis. The numerical SAR values (W/Kg) in this study were normalized to the square of a 1 V/m field strength (root mean square E-field) given isotropic incident exposure.

To allow visual detection of changes in SAR distributions, a single cut through the middle of the anatomical model is presented for each case. These SAR distributions are depicted using a color scale between 0 dB and -25 dB, where 0 dB is 1 (mW/Kg)/(V^2/m^2) for isotropic incident exposure.

9.4 Standard Water Systems

Standard water systems for laboratory animals are not designed and manufactured for use in high RF field environments. For instance, standard bottles of water should be shielded from the EMF fields to avoid extra power cost, and additionally to prevent excessive heating of the water.

In line with the NIEHS experimental requirements, a water system based on the use of single bottles of water was first considered. The plastic bottles of this system had dimensions sufficient to provide more than enough water for a single animal during 2-3 days, i.e., 400 ml for rats and 20 ml for mice. The water was shielded from the EMF radiation by means of metallic sleaves (mesh sleaves are also applicable, since they allow visibility of the water level in the bottle) with the top open to allow insertion of the bottles. These shielded bottles were
placed outside of the animal’s hosting cage. The animals reach the
water via sipper tubes introduced through the cage walls. Metallic sip-
per tubes are widely used mainly because they prevent rodents from
gnawing them and they can be easily cleaned at high temperatures.
Stainless steel sippers also shield the water in the sipper from the RF-
EMF radiation (except at the tip). Figure 9.1a shows a rat drinking
from a standard bottle of water and Figure 9.1b depicts a possible sce-
nario where a rat in a cage is drinking from a shielded bottle of water.
Previous to any dosimetric analysis, a system like this has the main
advantage of low cost, but also has important disadvantages such as
(1) the need to shield the bottles, which rises the cost and introduces
many undesirable metallic structures in the chamber, (2) the regular
exchange of 3000 bottles (2-3 times a week), (3) the spillage of water
caused by bottle handling and (4) the space requirements to attach
the bottles to the racks and cages.

An interesting alternative to the standard bottles of water is an
automatic water system. This system, which can be attached to the
animal cage rack, consists of a metallic water pipe that meanders from
the bottom of the rack to the top, in the middle of each rack shelf with
drinking lixits branching off to each side. Water continuously runs in
this structure, driven by a pump placed outside the chamber. The
system supplies water to the animals by means of short valved sipper
tubes, orthogonal to the main central tube (Figure 9.1c). These short
tubes or pipes end in a sipper valve with a lixit, which can be opened
by the animals with just a simple movement of their tongues and auto-
matically closes when the animals stop pressing the lixit (Figure 9.1d).
Disadvantages of this system, prior to any dosimetric assessment, are
the higher cost in comparison with the system of single water bottles
and the introduction of metallic parts. The advantages are: (1) the
reduction of labor cost (exchange, washing and refilling ∼3000 bottles
2-3 times a week), (2) the space requirements in the chamber are lower
than for the water bottles and (3) the avoidance of water leakage dur-
ing animal husbandry.
Both systems were analyzed for use in a reverberation chamber envi-
noment with a rat model exposed at 900 MHz and a mouse model at
1900 MHz.
9.5 Results

9.5.1 Analysis of the Standard Systems in a Reverberating Environment

A dosimetric assessment was performed using the mouse and rat models drinking from the standard water systems in order to analyze their performance and identify potential weaknesses when these systems are used in a high field reverberating environment.

Water systems consisting of single bottles of water may differ from each other through many factors such as bottle size, material and position, the length, shape and materials of the sipper tube, bottle shielding, etc. These factors were varied in this study to verify that

Figure 9.1: Rat anatomical model drinking in four different scenarios: (a) with a standard bottle of water, (b) in a cage with a shielded water bottle, (c) with a part of the automatic water system including sipper and pipes, and (d) with the sipper valve and lixit of an automatic system.
the resulting differences in animal SAR values are very small in comparison to the relative difference between an animal drinking from a water system and an animal not drinking, for both rats and mice exposed at 900 and 1900 MHz, respectively. Thus, the results in this section show the values obtained using a common polycarbonate bottle of water (shielded) with a metallic sipper, as initially described. Table 9.1 contains the deviations of the SAR values assessed in an animal drinking with such a water system versus the reference animal (without water system) for a rat and mouse.

The rat model analysis showed a significant increase (∼7 dB) in tongue averaged SAR when the animal was drinking. This effect is due to conducted currents by the sipper tube. Furthermore, whole-body peak spatial averaged SAR of a rat drinking was about 4 dB higher than the reference case, and the location of the peak was shifted from the center of the body (in reference case) to the mouth. These differences can be seen in Figures 9.2left and 9.2center, which show the SAR pattern in the middle slices of the rat model in reference scenario and drinking from a water bottle. The deviations of whole-body, eye and embryo averaged SAR with respect to the reference animal were within ±0.5 dB.

The exposure changes in a mouse while drinking from a water bottle resulted in an overexposure of the tongue of >3 dB with respect to the reference mouse. On the other hand, the whole-body average SAR as well as the whole-body peak spatial SAR were lower than in the reference case, 0.6 dB and 1.2 dB, respectively. This is explained by the differences in resonance between the reference mouse and the mouse plus the water system. Brain, eye, and embryo SAR deviations remained within ±0.5 dB. The SAR distribution in the middle slice of the mouse model is shown in Figures 9.3left and 9.3center for the reference case and the mouse drinking from a water bottle, respectively.

An analogous analysis was realized for the automatic water system, obtaining similar findings. The numerical results, presented in Table 9.1, show the deviations of the assessed SAR values of the animals drinking from the automatic system versus the reference animals. The rat whole-body averaged SAR remained constant. The tongue averaged SAR as well as the whole-body peak spatial SAR of a rat drinking were more than 5 dB higher than in an animal not drink-
9.5. ANALYSIS WATER SYSTEM

<table>
<thead>
<tr>
<th>Standard system</th>
<th>Animal model</th>
<th>SARr,WB</th>
<th>SARs,WB</th>
<th>SARavg,tong</th>
<th>SARavg,eye</th>
<th>SARavg,emb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single bottle</td>
<td>Rat</td>
<td>-0.5</td>
<td>3.8</td>
<td>6.9</td>
<td>-1.7</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>Mouse</td>
<td>-0.6</td>
<td>-1.2</td>
<td>3.2</td>
<td>-0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Autom. system</td>
<td>Rat</td>
<td>0.02</td>
<td>5.3</td>
<td>5.3</td>
<td>0.6</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>Mouse</td>
<td>-0.7</td>
<td>7.2</td>
<td>7.4</td>
<td>-0.4</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Table 9.1: Deviation (in dB) of the assessed SAR values in an animal drinking from the standard water systems with respect to the reference animal.

ing, and the peak SAR moves again from the center of the animal (as in the reference case) to the mouth. Eye exposure was about 1 dB higher in the rat drinking. Exposure of the brain and embryo do not significantly change with respect to the reference case. Figure 9.2right shows the SAR distribution in the middle slice of a rat drinking from the automatic water system.

SAR assessment in the mouse model showed a tongue overexposure when the animal is drinking of more than 7 dB with respect to reference, and a whole-body peak spatial SAR of 1.2 dB higher. Whole-body, brain, eyes and embryo average SAR remained within a range of ±1 dB. Figure 9.3right shows the SAR distribution in the middle slice of a mouse drinking from this water system.

In summary, special attention must be paid to the high whole-body peak SAR values registered, specially in the rat’s mouth, and of tongue averaged SAR in all animals, while these are drinking from standard water systems, since values can be up to 7 dB higher in comparison with reference animals. These SAR levels, mainly caused by the induced currents at the sipper tube surface, are undesirable and should be avoided. Therefore, a solution is required.

9.5.2 Novel Design of a Water System

Due to cost reasons and the hustle to achieve NTP approval, a solution based on a modified standard water system was preferred. The solution found was inspired by [70]. From transmission line theory, a quarter wavelength metal sleeve coaxially attached to the line can be used to choke (if not completely eliminate) currents by electri-
Figure 9.2: SAR distribution in the middle slice of the anatomical rat model: a) reference rat (no water system), b) rat drinking from the sipper tube of a standard bottle of water, c) rat drinking from the sipper tube of a standard automatic water system.

...cally obtaining a very large input impedance at the open end of the choke [75]. Efforts were focused on adapting this theory to design a water system applicable to the planned NIEHS experiments in reverberation chambers.

Figure 9.4 depicts two different quarter wavelength choke models. The first is a coaxial quarter wavelength choke attached to the sipper tube in the style of [70], leaving the tip of the sipper uncovered. The diameter of the choke was 16 mm for both rat and mouse models with a distance to the sipper tube of 2 mm. This kind of choke, labeled as standard choke (Figure 9.4a), allows the tip of the sipper to be introduced into the cage, leaving the choke outside, thereby preventing contact between the choke and the animal. Figure 9.5a shows a mouse drinking from the automatic water system valve with an standard choke.

The use of this standard choke did not provide a solution for the desired application in either of the two considered water systems: sin-
Figure 9.3: SAR distribution in the middle slice of the anatomical mouse model: a) reference mouse (no water system), b) mouse drinking from the sipper tube of a standard bottle of water, c) mouse drinking from the sipper tube of a standard automatic water system.

ingle water bottles and automatic system. For instance, results of the automatic water system with this choke showed a deviation to the reference case of whole-body peak SAR as large as 13 dB for the rat and 4 dB for the mouse. The tongue was overexposed by 10 dB with respect to the reference case for both the rat and mouse models. These results led to the proposition of a new choke design.

The quarter wavelength choke was then shifted to completely cover the sipper tube tip, and its diameter was enlarged up to 34 mm for the rat and 30 mm for the mouse. These dimensions allow the animal to reach the lixit by comfortably introducing its head into the choke. Additionally, the open end of the choke was equipped with a flange (disc shaped) as shown in Figure 9.4b. The flange has a dual purpose: firstly, it shifts the field maximum registered at the open extreme of the choke further away from the animal whilst drinking, and secondly it reduces the intensity of this field due to the increased periphery. The largest diameter of this flange was 50 mm for both rat and mouse models. Figure 9.5b depicts a mouse drinking from an automatic water system with this choke. Using this kind of choke, the sipper tube
Figure 9.4: Design of two different quarter wavelength choke models: a) standard choke (16 mm inner diameter), b) choke with larger diameter (34 mm inner diameter for the rat and 30 mm for the mouse) and flange-end (8 mm flange width for the rat and 10 mm for the mouse).

is not introduced into the cage and the animal needs to lean out of the cage through a hole in the cage wall to reach the lixit. This is common practice in automatic water systems and prevents the cage from filling with water in the event of a leak.

SAR deviations of the animals drinking from the standard water system provided with flange-ended chokes with respect to the reference animals are presented in Table 9.2 including: whole-body average, whole-body peak spatial and tongue, brain, eyes and embryo average. All assessed values indicated underexposure with respect to the reference case.

<table>
<thead>
<tr>
<th>Standard system</th>
<th>Animal model</th>
<th>$\text{SAR}^{\text{WB}}$</th>
<th>$\text{SAR}^{\text{ps}}_{\text{WB}}$</th>
<th>$\text{SAR}^{\text{ps}}_{\text{long}}$</th>
<th>$\text{SAR}^{\text{ps}}_{\text{eye}}$</th>
<th>$\text{SAR}^{\text{ps}}_{\text{emb}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single bottle</td>
<td>Rat</td>
<td>-1.1</td>
<td>-0.8</td>
<td>-1.8</td>
<td>-1.5</td>
<td>-0.9</td>
</tr>
<tr>
<td></td>
<td>Mouse</td>
<td>-0.8</td>
<td>-1.6</td>
<td>-1.8</td>
<td>-1.5</td>
<td>-0.5</td>
</tr>
<tr>
<td>Autom. system</td>
<td>Rat</td>
<td>-0.2</td>
<td>-0.4</td>
<td>-1.8</td>
<td>-1.5</td>
<td>-3.4</td>
</tr>
<tr>
<td></td>
<td>Mouse</td>
<td>-1.2</td>
<td>-1.9</td>
<td>-3.2</td>
<td>-2.8</td>
<td>-3.9</td>
</tr>
</tbody>
</table>

Table 9.2: Deviation (in dB) of the assessed SAR values in an animal drinking from the standard water systems with a flange-ended choke with respect to the reference animal.
The results from attaching the flange-ended choke to the system with bottles of water showed that the whole-body average SAR is about -1 dB compared to the reference rat and mouse. The whole-body peak SAR is also smaller, -0.8 dB for the rat and -1.6 dB for the mouse. Analogously, brain exposure also decreases, -4.0 dB for the rat and -2.2 dB for the mouse. The organ which presents lowest SAR with respect to the reference case is the tongue, with -8 dB for the rat and -4.4 dB for the mouse.

Following the same tendency, the deviations for an automatic water system with the flange-ended choke attached, given in Table 9.2, show SAR values lower than the reference case. For instance, the whole-body SAR is slightly lower than the reference case for the rat, -0.2 dB, and lower for the mouse, -1.2 dB. The tongue average SAR is substantially lower than the reference, down to -1.8 dB for the rat and -4.2 dB for the mouse, and the whole-body peak spatial SAR values dropped slightly down for the rat, -0.4 dB, and a bit more for the mouse, -1.9 dB. Brain presents an underexposure of -1.5 dB in rats and -2.8 dB in mice.

Figure 9.6 illustrates the SAR distribution in the middle slice of a rat model exposed at 900 MHz drinking from both water systems (single bottles of water and automatic) with flanged chokes. Analogously, Figure 9.7 shows the SAR patterns of a mouse model exposed at 1900 MHz in the same two situations as the rat. SAR distributions revealed that the usage of the flange-terminated choke does not sig-
significantly alter the SAR pattern, avoiding any high local absorption at the animal’s mouth.

![Figure 9.6: SAR distribution in the middle slice of the anatomical rat model: a) rat drinking from the sipper tube of a bottle of water modified with a flange-ended quarter wavelength choke, b) rat drinking from the sipper tube of an automatic water system modified with a flange-ended quarter wavelength choke.](image-url)

The encouraging outcomes from the use of these flange-ended chokes are only valid if the animal is prevented from touching the choke tube or flange. The effect of animal contact to the choke, where surface currents are present, produced high local absorption at the contact region of more than 8 dB in comparison with the reference animals, for both the rat and mouse. The results also showed that if the animal is kept just 1 mm apart from the choke, the SAR pattern remains very similar to the reference case and the large SAR peak disappears. Good isolation between the animal and choke must therefore be ensured.

Traditional water systems use metallic grommets to cover the wall aperture of the cages to prevent animals from gnawing, but these grommets are not desirable in an EMF environment. As an alternative to the traditional metallic grommets, ceramic grommets are
proposed, which in turn meet the NTP requirements. Additionally, to completely guarantee isolation between the animal and the choke, a plastic insert might also be used, inserted between the inner choke wall and the sipper tube, isolating the rodents from the choke (see Figure 9.8). The distance minimum between the animal and the choke using this kind of isolating bodies is 9 mm from the cage interior (thickness of the cage wall + grommet) and 1 mm inside the choke (thickness of the insert).

9.5.3 SAR Variations, Uncertainty Assessment and Limitations of the Numerical Model

The values of interest to be assessed in the context of the water system are only the deviations of animal exposure between the drinking and non-drinking situations while being in the same posture, and not the absolute exposure uncertainty. Therefore, many of the uncertainty parameters can be regarded as identical in both cases, such as (1)
the approximation of using a reduced finite number of plane waves (assessed in Chapter 7), (2) the grid resolution, (3) animal size and weight, (4) the animal anatomy, (5) the model discretization and (6) the tissue/organ dielectric parameters.

The evaluation of the SAR variations (whole-body averaged and peak spatial SAR) was performed considering the proximity of the animal to the water system. Homogeneous animal models were used and positioned at different distances from the water system and sipper tube: 1 mm, 9 mm and 100 mm. SAR variations were calculated according to [44]. Table 9.3 presents the standard variations for the reference animals in the presence of the automatic water system with a flange-ended choke among all considered distances.

<table>
<thead>
<tr>
<th>Model</th>
<th>Std. var. SAR_{avg}^{WB} (dB)</th>
<th>Std. var. SAR_{Peak Sp.}^{WB} (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat @ 900 MHz</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Mouse @ 1900 MHz</td>
<td>0.5</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Table 9.3: Standard variation of the mouse and rat models dependent on proximity to the water system (k=1).

The numerical analysis of the performance of this novel design of
water system regarding SAR in the animals provided decisive information for the design and construction of the first prototype (Figure 9.9). However, any numerical model has some limitations; for instance, it is usually a simplified representation of the experimental model, with less unknowns (losses, reflections), ideal conditions (free space, PEC), limitations related to the discretization of the models. Therefore, the numerical model has to be experimentally validated.

Figure 9.9: CAD model of the automatic water system for a mouse rack (prototype).

Preliminary measurements with the prototype of this water system were performed in the reverberation chamber at IT’IS Foundation [62] using homogeneous broadband gel phantoms (see Figure 9.10) to represent the rat and mouse in two different scenarios: drinking and non-drinking; in the latter scenario the animal is separated a distance of 100 mm from the lixit. Temperature rate in different points at the phantom head in the proximity of the lixit and in the center of its body were measured with temperature probes including flexible tips inserted in the gel. The obtained data showed values in good agreement with the simulations, i.e., the probe at the body center registered a maximum of the SAR in the center of the body in both scenarios,
and the probes inserted at the mouth/nose region indicated an underexposure whilst drinking with respect to the non-drinking case.

![Numerical rat and mouse homogeneous phantoms](image)

Figure 9.10: Numerical rat and mouse homogeneous phantoms (bottom) and proposed phantom models for experimental investigations (top).

Despite the encouraging results obtained in this preliminary analysis, the experimental validation of the numerical model has to be performed in detail. Since the project involving this novel water system is still ongoing, its validation has been scheduled for the end of 2007. The following section intends to be a guideline to perform such a validation.

### 9.5.4 Requirement for the Experimental Validation of the Numerical Model

The method suggested to validate the numerical model of the water system has been described in Chapter 3.

To perform the experimental part, the reverberation chamber should be loaded with the water system and the homogeneous animal phantoms, which represent the animals in both the drinking and non-drinking scenarios in terms of size and absorption. Solid gel phantoms as in Figure 9.10 are recommended since they are easy to model.
9.6. DISCUSSION AND CONCLUSIONS

and change their posture. The method to perform measurements has to be chosen according to the limitations presented by the reverberation chamber. For instance, the utilization of a system like DASY to scan SAR in a volume is not viable. The technique suggested here is based on measuring temperature rate in single points in the phantoms when they are exposed to RF-EMF radiation [76], [77]. Therefore, the employment of temperature probes with flexible tips inserted in the phantom is one possibility [78], although there are alternative techniques to assess temperature change in the phantoms [79]. When using single temperature probes, the position of the probe tip in the phantom must be known in order to compare later the measurements with the simulation results. This is also applicable to any other method. Then, the simulations have to be performed under equivalent conditions.

The SAR uncertainties of both experimental and numerical models should be determined considering the parameters due to the exposure setup and the animal phantoms. These uncertainties are necessary for the validation when one is comparing the data obtained by both experimental and numerical means. According to Chapter 3, a list of the potential uncertainty sources needed for validation of the water system model might include: (1) sensor calibration and sensitivities, (2) electronic readout, (3) position of the phantom in the chamber, (4) other dielectric materials in the chamber (cages, racks, etc); and those which require additional numerical assessment such as: (5) dielectric parameters of the phantom gel, (6) phantom size, (7) probe positioning based on SAR gradient data, and (8) water system model (dimensions, shape). Finally, the already seen condition 3.1 should be fulfilled to confirm the validation.

9.6 Discussion and Conclusions

The preliminary feasibility study of the novel designed water system described in this chapter confirmed the assumption that standard water systems would be non-feasible, leading to local overexposure of the animal while drinking and causing too large power losses in the water. Different solutions were investigated, discovering that the water can be enclosed in metallic tubes or shielded bottles without causing
significant SAR variations in the animals.

The solution found on the quarter wavelength flange-ended choke design became a very suitable solution. The animals can be forced to lean out of the cage while drinking and this allows to reduce the length of the sipper tubes, increases the separation between the system and the animals and stops animals from touching the choke.

However, these conclusions are based on numerical investigation and preliminary experimental analysis. Final experimental validation is still ongoing.
Chapter 10

Comparison of Three \textit{In Vivo} Exposure Setups
10.1 Description of the Setups

The aim of this chapter was to compare three different exposure setups designed for large-scale in vivo animal studies in terms of exposure efficiency, SAR variations in the animals, space requirements and cost. Each of the setups generates a different kind of incident exposure, namely (1) quasi-open plane wave, (2) resonant waveguide and statistically homogeneous and (3) isotropic exposure.

The first setup, described in Adey et al. (2000) [80], consists of a horn antenna providing simultaneous EMF exposure at 836 MHz to nine unrestrained rats. The animals are hosted in cages disposed in a 3x3 matrix in front of the antenna, parallel to the aperture plane of the horn. The distance between the antenna and the cages was sufficient to obtain plane wave exposure. The horn antenna was excited in circular polarization to reduce possible orientation-dependent coupling to the animals. During the 2 hours of daily exposure, the animals did not have access to either food or water.

The second setup, presented in Kainz et al. (2006) [38], consists of a circular cascade of 17 sectorial waveguides excited by a loop antenna placed in the center. This setup was optimized in terms of efficiency and uniformity to simultaneously expose seventeen restrained rats at 902 MHz and H-polarization. The daily exposure with such a setup was time constrained to avoid stress in the animals, e.g., limited to 2 hours.

The third exposure setup is the reverberation chamber evaluated as part of this thesis. Rats and mice were exposed unrestrained at 900 and 1900 MHz respectively, in a statistically homogeneous and isotropic field environment.

10.2 Results of the Comparison

The main outcomes of the comparison of these three exposure setups are given in Table 10.1. Since Adey et al. do not provide all the values required for this comparison, it was necessary to determine them. The highest whole-body averaged SAR in animals exposed in the Adey et al. setup was assessed using the power data available in [80] and the SAR values...
10.2. RESULTS OF THE COMPARISON

Table 10.1: Comparison of three radio-frequency electromagnetic exposure setups for \textit{in vivo} studies. SAR variations were assessed with a confidence interval of 95%, i.e., $k=2$.

<table>
<thead>
<tr>
<th>Setup</th>
<th>Freq. (MHz)</th>
<th>Animals/ source</th>
<th>Restr. animals</th>
<th>Effic. (%)</th>
<th>SAR instant var. (dB)</th>
<th>SAR lifespan var. (dB)</th>
<th>Highest SAR (W/Kg)</th>
<th>Vol./ animal (dm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adey</td>
<td>836</td>
<td>9 rats</td>
<td>no</td>
<td>4.8</td>
<td>3.8</td>
<td>n.a.</td>
<td>0.8</td>
<td>4000</td>
</tr>
<tr>
<td>Kainz</td>
<td>902</td>
<td>17 rats</td>
<td>yes</td>
<td>75-85</td>
<td>2.6</td>
<td>1.2</td>
<td>0.8</td>
<td>130</td>
</tr>
<tr>
<td>Reverb. chamber</td>
<td>900</td>
<td>~100 rats</td>
<td>no</td>
<td>74</td>
<td>2.4</td>
<td>0.8</td>
<td>6</td>
<td>400</td>
</tr>
<tr>
<td></td>
<td>1900</td>
<td>~200 mice</td>
<td>no</td>
<td>50</td>
<td>2.1</td>
<td>0.6</td>
<td>6</td>
<td>200</td>
</tr>
</tbody>
</table>

of plane wave exposure obtained in Chapter 4. It was assumed that animals remained on the horizontal plane during exposure and that their position in this plane was random. Therefore, the SAR in the animals could be assessed as a weighted addition of the normalized SAR caused by plane waves with different polarization in the following manner:

$$SAR_{\text{total}} = \frac{SAR_{E-pol}}{4} + \frac{SAR_{H-pol}}{4} + \frac{SAR_{k-pol}}{2} \quad (10.1)$$

The variation analysis performed of the Adey et al. setup is described in Table 10.2. This analysis focussed in SAR instant variations (within one exposure session) and considered the following parameters: (1) sensor linearity$^1$, (2) power density uniformity across the cage area, (3) weight variations within the exposed group, (4) animal body orientation with respect to the incident field, (5) proximity of the animals in the array and (6) relative animal orientation.

The SAR variation analysis of the Kainz et al. setup can be found in [47]. This variation analysis (as the analysis presented in Chapter 5) is the most detailed of the three exposure setups here presented.

A preliminary analysis of the SAR variations of the mouse and rat exposed in the reverberation chamber was given in Chapter 7. The limitations of that analysis were related to the use of homogenous phantoms for the assessment of array effect, proximity, posture, and relative orientation. The SAR variation values presented in Table 10.1

$^1$the given value is an estimation since this data is not provided in [80]
Table 10.2: SAR variation analysis of the setup described in Adey et al.

include the newest performed evaluations of field uniformity, posture of the animals and rat exposure by sex.

10.3 Discussion and Conclusions

As shown in Table 10.1, the reverberation chamber provides very good efficiency, especially for rats at 900 MHz (74%), comparable to the efficiency of the setup in Kainz et al. (75-85%), while the horn antenna has a very poor efficiency (4-8%).

The largest animal exposure variation was found for the Adey et al. setup. If animals were restrained in this setup, the coupling efficiency might be increased and SAR variations would be reduced. This could be achieved in the Kainz et al. exposure setup, where exposure was optimized by restraining the animals, and therefore providing smaller variations; the effect of neighbors was eliminated using independent waveguides, which also reduced the SAR variations. The exposure in the reverberation chamber presented the lowest SAR variations of the three exposure setups (close to the Kainz et al. setup) mainly due to the fact that it provides statistically homogeneous and isotropic exposure. To minimize SAR variations among the animals due to their position in the setup, it is recommended to make them rotate between exposure sessions. In a reverberation chamber, the body orientation is not as critical as in the other setups, because of its stirred field environment.

The power required by the setups for a specific target SAR, is related to the setup efficiencies. The reverberation chamber showed a
required power per animal slightly lower than the setup in Kainz et al., and substantially lower than in Adey et al.

Regarding space requirements, the volume needed per exposed animal is much lower in the reverberation chamber than in the setup described in Adey et al. (a factor of 10), despite the fact that animals can freely move in both setups. The reason lays on the large number of animals that can be simultaneously exposed in the reverberation chamber. In comparison with the restrained-animal setup presented in Kainz et al., the space requirements per animal in the reverberation chamber are of the same order of magnitude.

To summarize, a comparison of three different RF-EMF in vivo exposure setups was carried out. Preliminary numerical dosimetric analysis of the reverberation chamber showed high exposure efficiency, moderate SAR variations within the animal phantoms as well as reasonable power and space requirements. However, the use of a reverberation chamber such as the described in this thesis might require significant changes within most facilities and standard animal rooms due to the dimensions of the chamber.

The use of reverberation chambers for in vivo experiments exhibits a number of limitations namely the need of statistic data analysis, the repeatability of the measurements (time consuming), the assessment of SAR distributions within the animal phantoms, the temperature measurement within the phantoms and the continuous temperature monitoring within the animals during power-on periods. Final experimental and numerical dosimetry of the reverberation chamber is still ongoing and is expected to provide more conclusive information about the performance of the reverberation chamber.
Chapter 11

Epilogue
In summary, a universally applicable method has been developed to obtain comprehensive and detailed dosimetric information for \textit{in vivo} experiments testing EMF potential hazards. The application of this methodology in future research should contribute to bring light to the controversial results obtained from experiments performed in the past under \textit{apparently} same conditions, since it (1) enhances the quality of the dosimetry, (2) increases the credibility and relevance of the results and (3) provides sufficient information about the exposure for interpretation and potential replication studies.

In the study performed with animals exposed under planewave conditions, the SAR dependency on frequency and polarization has been quantified. Comparable SAR distributions in the animal bodies were found in rats and mice exposed at frequencies close to their body resonance frequency. In future RF-EMF \textit{in vivo} studies and in order to compare effects and results in different species, the SAR distribution might be considered more relevant than the carrier frequency. Moreover, the identified uncertainty due to the discretization of the anatomical models might be solved with the upcoming full 3D CAD models which in turn overcome effects by stair-casing and holes in closed structures. Other future improvements in numerical dosimetry have been identified: (a) a poser to effectively change the posture of the anatomical models and (b) automated post-processing evaluation to reduce the manual work of the data evaluations.

The dosimetry of the 1747 MHz DCS rat exposure setup performed within the framework of this thesis is one of the most complete dosimetric studies ever performed for a large-scale, long-term \textit{in vivo} experiment with animals. Part of my work, although not included in this thesis, was the dosimetric analysis of the 902 MHz GSM and 1747 MHz DCS mouse exposure setups also developed for the PERFORMA project. The 2-year bio-assay experiments, with rats and mice, included in this project have already concluded, and the first publications are completing the submission process.

The last stage of this thesis faced the investigation of the feasibility of a reverberation chamber as exposure setup for large-scale long-term \textit{in vivo} animal studies. A method to numerically represent the exposure of bodies in these chambers has been developed. The preliminary numerical dosimetry delivered very encouraging results and valuable information to improve the exposure efficiency, optimize
space requirements and reduce cost. The results obtained within this thesis contributed to the final decision of the NIEHS to use reverberation chambers in its upcoming lifespan bio-assay experiments planned for the next four years, and where IT’IS Foundation/IIS will play a major role performing the final dosimetry and providing the exposure systems.

A novel system to provide water to animals being exposed in high field reverberation chamber-like environments has been designed and numerically tested within this thesis. The system has been preliminary validated in the reverberation chamber at IT’IS Foundation, but the final experimental validation has been scheduled at the end of this year. This thesis provides the guidelines to perform such a validation.

The still vivid public concern of potential EMF effects on health, and the fact that wireless technology is continuously changing and expanding demand further research on EMF health risk assessment. The contents of this thesis are expected to optimize the exposure concept and dosimetry of upcoming studies, give more relevance to their findings and avoid controversy.
Appendix A

List of Acronyms

ABC: Absorbing Boundary Conditions
ACS: Absorption Cross Section
BMDS: Bio Medic Data Systems
CAD: Computer Aided Design
CDMA: Code Division Multiple Access
CW: Continuous Wave
DASY: Dosimetric Assessment System
DCS: Digital Cellular System
EASY: Exposure Acquisition System
ELF: Extremely Low Frequency
EMC: Electromagnetic Compatibility
EMI: Electromagnetic Interference
EMF: Electromagnetic Field
EUT: Equipment Under Test
FDTD: Finite-Difference Time-Domain
FPGA: Field Programmable Gate Array
GLP: Good Laboratory Practice
GSM: Global System for Mobile Communications
ICNIRP: International Commission on Non-ionizing Radiation Protection
IT’IS: Foundation for Research on Information Technology in Society
MTE: Mobile Telecommunication Equipment
MoM: Method of Moments
NCRP: National Council on Radiation Protection and Measurements
NIEHS: National Institute of Environmental Health Sciences
NIST: National Institute of Standards in Technology
NTP: National Toxicology Program
OATS: Open-Area Test-Site
PML: Perfectly Matched Layer
RF: Radio-Frequency
RFR: Radio-Frequency Radiation
RMS: Root Mean Squared
RTL: Radial Transmission Line
SAR: Specific Absorption Rate
SD: Sprague-Dawley
SEMCAD: Simulation Platform for Electromagnetic Compatibility Antenna Design and Dosimetry
SPEAG: Schmid & Partner Engineering AG
TLM: Transmission Line Matrix
WHO: World Health Organization
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</tr>
<tr>
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</tr>
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</tr>
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</tr>
<tr>
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