Mutation Research 810 (2016) 6–12

Contents lists available at ScienceDirect

Mutation Research/Genetic Toxicology and Environmental Mutagenesis

journal homepage: www.elsevier.com/locate/gentox
Community address: www.elsevier.com/locate/mutres

Short communication

Biological and health effects of radiofrequency fields: Good study design and quality publications

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ARTICLE INFO

Article history:
Received 1 August 2016
Received in revised form 8 September 2016
Accepted 8 September 2016
Available online 9 September 2016

Keywords:
Radiofrequency fields
Electromagnetic fields
In vitro studies
In vivo studies
Human investigations

ABSTRACT

During recent decades, researchers have used several different parameters to evaluate the biological and health effects of *in vitro* and *in vivo* exposure to non-ionizing radiofrequency fields in animals, humans and their isolated cells. The data reported in many of publications in peer-reviewed scientific journals were reviewed by the international and national expert groups of scientists for human risk assessment of exposure to radiofrequency fields. The criteria used for such assessment depended on the study design, methodology and reporting of the data in the publication. This paper describes the requirements for good study design and quality publications, and provides guidance and a checklist for researchers studying radiofrequency fields and other environmental agents.

1. Introduction

Non-ionizing electromagnetic fields (EMF, 0–300 GHz) are ubiquitous in our environment. A multitude of devices that emit radiofrequency fields (RF, 3 kHz–300 GHz) are currently used in industry, medicine, military and a variety of consumer products. An exponential increase in human exposure to RF occurred with the introduction of wireless communication devices (evolved from 1G to the current 4G utilizing 400–2700 MHz RF, and futuristic 5G using higher than 6 GHz energy) which transmit voice, data and images with ever-increasing performance and good value for the money. International organizations such as the Institute of Electrical and Electronics Engineers (IEEE) and the International Commission on Nonionizing Radiation Protection (ICNIRP) have developed safety standards and guidelines to protect occupationally exposed as well as general public from potential adverse health effects due to exposures to EMF. In the case of RF, at the frequencies relevant for mobile communications, the absorption of energy is measured or estimated as specific absorption rate (SAR) which is defined as the energy absorbed by the tissue mass contained in a volume of a given density and expressed as W/kg. SAR has been the basic restriction in exposure limits from 100 kHz to 3 (IEEE) or 10 GHz (ICNIRP). Based on the thermal effects leading to an increase in body temperature at 4 W/kg whole body average SAR, the recommendations are 0.4 W/kg and 0.08 W/kg for occupational and general public (10x and 50x lower) respectively. A 2.0 W/kg averaged over 10 g tissue for localized exposures limit for the general public was derived from effects on cataract formation in rabbits [1–3]. Recently, the International Agency for Research on Cancer has reviewed peer-reviewed scientific literature on the carcinogenic potential of RF exposure *in vitro* as well as *in vivo* in animals and humans [4]. Based on the limited evidence of an association between mobile phone use and cancer in both human and animal investigations, RF exposure is classified as a possible human carcinogen (class 2B) [5]. National and international expert groups of scientists have recommended a precautionary approach as well as further research [6,7].

Thousands of papers on biological effects (including genetic toxicology endpoints, such as evaluation of primary DNA damage in the form single and double strand breaks, chromosomal aberrations, micronuclei, mutations, *etc.*) and health effects of exposure to radiofrequency fields have been published in peer-reviewed scientific journals. Some papers are not easy to interpret, due particularly to faulty experimental design and inadequate dosimetry. Scientists who are new to this area and initiating research on biological and health effects of RF need to be aware of the 'rules of engagement' in designing the study, collection of data, statistical analyses as well as the essential details to be presented in a high-quality publication. This is important since national and international expert groups of scientists are using inclusion and exclusion criteria for considera-

Abbreviations: RF, radiofrequency fields; IARC, International Agency for Research on Cancer; SCENIHR, Scientific Committee on Emerging and Newly Identified Health Risks; SSM, Swedish Radiation Safety Authority.

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http://dx.doi.org/10.1016/j.mrgentox.2016.09.007
1383-5718/

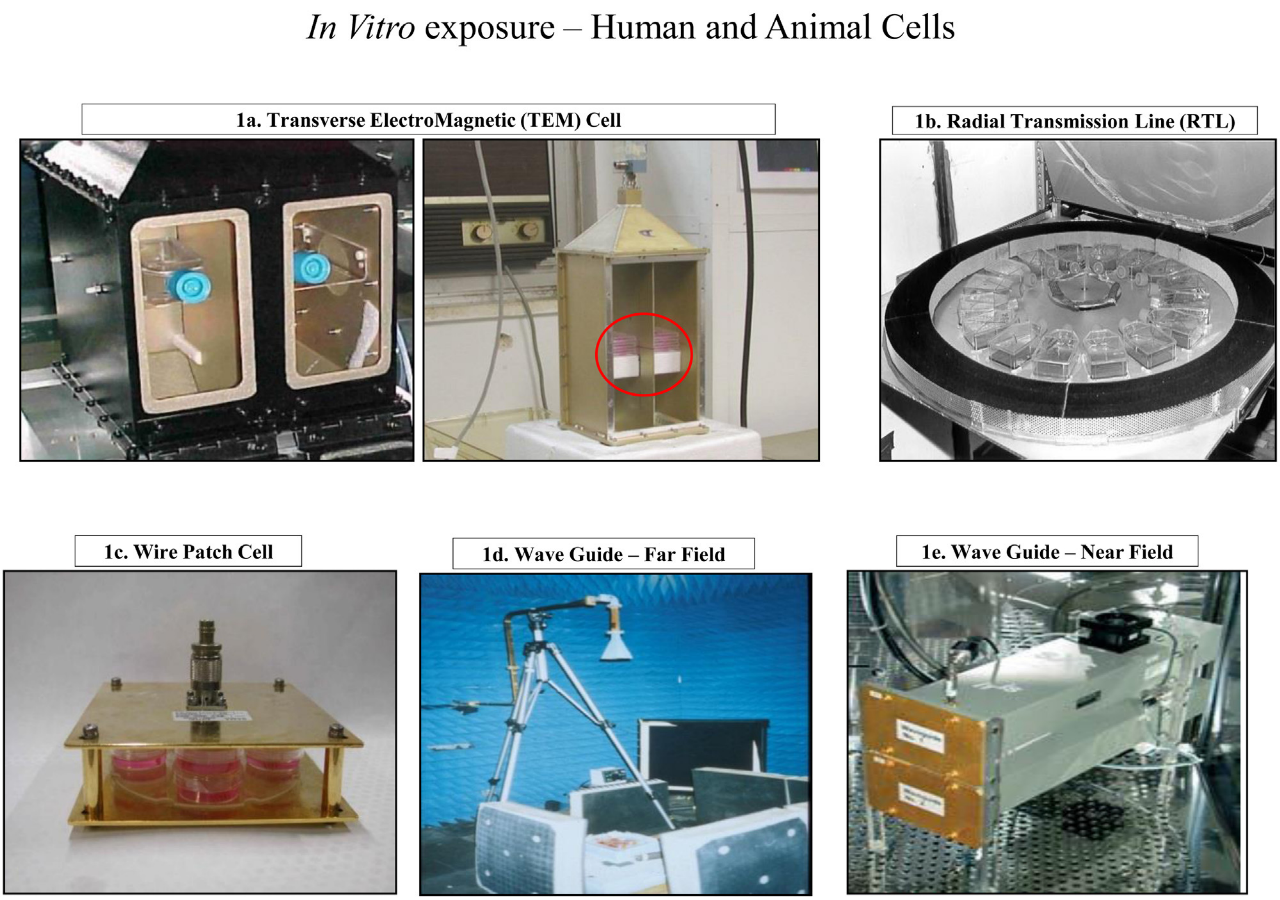

Fig. 1. Exposure equipment used in *in vitro* investigations. Transverse electromagnetic (TEM) cell for cells in Petri dishes or culture flasks (1a); Radial transmission line (RTL) for several culture flasks (1b); Wire patch cell for several petri dishes (1c); Wave guide is kept in far field (1d); Wave guide kept in near field (1e).

tion of publications while assessing the potential adverse effects of RF exposure [5,8,9]. In addition, funding authorities need guidance on good RF study design to assist in the evaluation of research proposals. Much of the text in this paper refers to the criteria for good RF exposure study design and reporting of the data in a scientific publication. The information provides guidance and checklist for researchers who are new to biological and health effects research in radiofrequency fields. However, the same criteria also apply to investigations on exposure to other environmental agents.

2. Study design

Generally, researchers seek answers to questions formulated as hypotheses to be tested with carefully designed experiments. Good quality biological and health effects of RF investigations require: (i) collaboration between biologists and engineers to define well-characterized exposure conditions, (ii) appropriate study design and execution, (iii) sufficient sample size for 'blind' data collection and for statistical power analyses, (iv) proper interpretation and conclusions. Replication and confirmation studies in researchers' laboratory and by independent investigators in other laboratories provides (when they are also conducted in good and repeatable exposure conditions) reliability and acceptability of the data. Three main approaches have been used to examine the effects of RF: (i) *in vitro* exposure using freshly collected and/or continuously growing animal and human cells, (ii) partial and whole body *in vivo* exposure in animals and (iii) provocation (volunteers are exposed to RF under controlled laboratory conditions to provoke and study the response) and epidemiological studies in humans. Some *in vitro* and *in vivo* studies also examined RF exposure combined with other environmental agents reflecting real-life situations. The RF frequency, power intensity, SAR and duration of exposure were used as an index for 'RF dose' [5,8,9].

2.1. Dosimetry

Well-characterized and precise RF dosimetry is critical for replication and confirmation of the observations in investigations. This is crucial and analogous to ionizing radiation source, dose and dose rate or concentration of the test chemical or any other environmental agent used in similar investigations. Different types of RF exposure equipment are available for *in vitro*, *in vivo* and human investigations and are presented in Figs. 1–3 . Depending on the design of the investigation, all of them have been successfully used for *in vitro* exposure of cells (Fig. 11a–1e), *in vivo* exposure of animals (Fig. 22a–2f) and for various human exposure studies (Fig. 33a–3f). The *in vitro* set-up has: (i) a source to generate the required RF frequency, amplitude, modulation scheme, (ii) an amplifier or attenuator, coupler, splitter and a power meter to adjust the signal according to pre-defined requirements, (iii) an antenna or waveguide to propagate RF field into the test sample and (iv) a computer for monitoring and recording.

Heating is the most widely accepted mechanism of RF interaction with biological systems. Hence, precise temperature control and maintenance during RF exposure is of paramount importance for replication and confirmation [10]. In *in vitro* experiments, the cells are spread in petri dishes or culture flasks during RF exposure. The volume of the culture medium, the area occupied by the cells as well as the polarization of the applied field influences the uniformity of RF dose distribution for the entire cell populations