



Intermediate Report Final Report

Please delete as applicable.

Project reference: **B2014-04**

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Project title: „Identification and grouping of relevant experimental parameters to evaluate the effects of radiofrequency magnetic fields in in-vitro studies (GROUPER)“.

1. State of Research.

1.1 Research activities performed, milestones and deliverables accomplished

Please list against the background of the research proposal.

The scientific literature contains numerous experimental studies about biological effects after exposure to radiofrequency electromagnetic fields (RF-EMF), reporting various biological effects (see e.g. Progress report from WHO International EMF project or the comprehensive overviews in the opinions of SCENIHR 2007, 2009). The outcome of the studies is very diverse and the relevance of the results is unclear. Based on the literature, a correlation to any kind of disease development is relatively vague. Usually review studies are not able to compare the available data, due to the large complexity of the applied exposure conditions and biological systems. Therefore the main focus is to detect if any statistical association exists between RF-EMF and cellular responses *in vitro*, considering cell proliferation and apoptosis endpoints separately and also grouped into a unique “cellular life” endpoint.

1.2 Findings

Comment on achieved scientific insights.

The PubMed literature database was searched for the period 1995-2014 for publications regarding cell proliferation and apoptosis endpoints *in vitro*. All available published data were collected, including cellular and molecular investigations, without applying any exclusion criteria. The most relevant parameters in RF-EMF *in vitro* studies (cell culture type, frequency, exposure duration and SAR) were considered. Both endpoints were analyzed separately, and also as a unique “cellular life” group, improving the statistical power of the analysis. Extracted experiments were pooled into specific groups and intervals (cell type, RF-frequency, exposure duration, and SAR value) in order to see if there is any statistical association of positive findings with one or more of these categories. For our purposes, positive findings were experiments in which an effect was detected independently of the direction of the outcome. In addition, five exposure-related quality criteria were defined (temperature control, dosimetry, sham, positive control, and blinded experimental condition) and subsequently used for data analysis. An association study was performed of these parameters with the experimental outcome in term of specific biological endpoints.

We identified 104 articles from which 483 different experiments were extracted and analyzed. Positive findings after exposure to RF-EMF were detected (105 of “cellular life” including 44 cases of apoptosis and 61 of cell proliferation), significantly associated to cell lines rather than to primary cells.

The positive findings were not associated to any other parameter, except for exposure conditions quality, where a highly significant association between negative responses and study quality was detected. Interestingly, the lower the quality of the exposure condition, the more positive results was detected. This was true even when the three specific RF-related exposure criteria were considered, such as temperature, sham exposure and dosimetry. In particular, when moving from one quality criteria (Q1) to five (Q5) we observed an increasing negative association of positive results and number of satisfied criteria, with a significant drop in positive effects for Q5. When all quality criteria were satisfied, only 2 experiments of 109 showed positive results, against an average positive finding of about 27 %.

These findings further highlight the importance to perform experiments under strictly controlled exposure conditions in order to clarify the conflicting results reported in the literature. As a matter of fact, only 109 experiments out of 483 (< 25%) in the period of 1995-2014 satisfied the highest quality denominator Q5.

Here we have observed that, when comparing the literature from the last five years with the preceding period, the average quality has significantly increased from 3 to 3.5 (figure 1) with 105 Q5 records in the most recent decade, but it is still very far from an optimal control of experimental procedures (they correspond to less than 30 % of the total record of the decade).

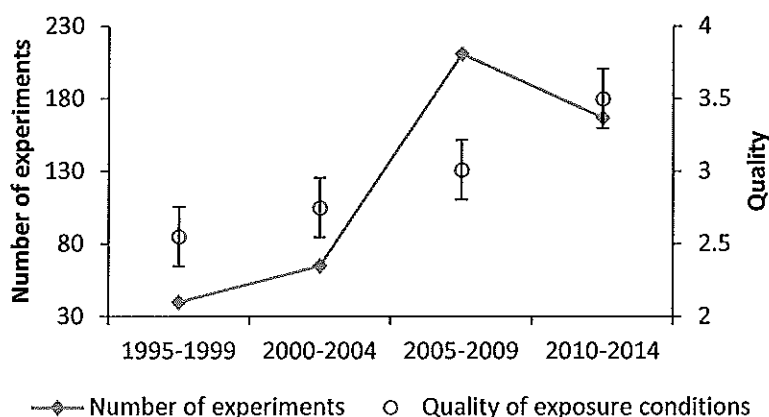


Figure 1 The number of experiments over the years from 1995 to 2014 and the average exposure quality score of the studies.

1.3 Problems

Expand on research, financial or schedule problems, if any. For the intermediate report: please include problems that might occur in the upcoming period.

Not applicable.

2. Annex

2.1 Publications

Please enclose the scientific publications produced in the context of the project.

Not applicable.

2.2 Documents

*In case publications are not yet available or cover only part of the funded research, please include:
- submitted papers (confidentiality is secured),*

The manuscript "Quality matters: Systematic analysis of "cell living" characteristics in in vitro data of radiofrequency electromagnetic field exposure" by Myrtill Simkó, Daniel Remondini, Olga Zeni, Maria Rosaria Scarfi, has been submitted for publication.

Date and Signature

29.02.2016

