



# Pre-Exposure to Radiofrequency Electromagnetic Fields and Induction of Radioadaptive Response in Rats Irradiated with High Doses of X-Rays

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## ABSTRACT

**Background:** Some evidence shows that a pre-exposure to RF can mitigate the effects of subsequent exposures to high doses of ionizing radiation.

**Objective:** We aimed to assess the effect of a pre-exposure to non-ionizing RF radiation on survival, weight changes, food consumption, and water intake of lethally irradiated rats.

**Material and Methods:** In this case-control study, we used a commercial mobile phone (GSM, 900/1800 MHz) as well as a 2.4 GHz Wi-Fi router as the sources of pre-exposure to RF radiation. Forty-eight rats were randomly divided into six groups of control, “8 Gy X-rays”, mobile phone, “mobile phone+8 Gy”, Wi-Fi, and “Wi-Fi+8 Gy”. Then, the survival fraction, weight loss, water, and food consumption changes were compared in different groups.

**Results:** The survival analysis indicated that the survival rates in all of the exposed animals (“8 Gy X-rays”, “mobile phone+8 Gy”, “Wi-Fi+8 Gy”) were significantly lower than the control, “Wi-Fi”, and “mobile phone” groups. The changes in survival rates of “mobile+8 Gy”, “Wi-Fi+8 Gy”, and 8 Gy alone were not statistically significant. However, food and water intake were significantly affected by exposure to both RF pre-exposures and exposure to high dose ionizing radiation.

**Conclusion:** To the best of our knowledge, the existence of a dose window for the induction of AR can be the cause of the lack of AR in our experiment. Our findings confirm that in a similar pattern with the adaptive responses induced by pre-exposure to ionizing radiation, the induction of adaptive response by RF-pre-exposures requires a minimum level of damage to trigger adaptive phenomena.

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## Keyword

Radiofrequency Radiation (RF); Radioadaptive Response; Cell Phone; Electromagnetic Radiation; Survival Analysis

## Introduction

The exposures of human to radiofrequency (RF) radiations of mobile phone and Wi-Fi devices have been increasing during recent years that evoked health concerns in the scientific community [1]. Short-term exposure to non-ionizing radiations could lead to health disorders, including, sleep, heart rate, and blood pressure disorders while long-term exposure to this type of radiation could be a car-

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cinogenic mediator [2]. Hence, an increasing number of reports about the health concerns of RF radiations could approve the importance of this field. Conversely, there are some reports about the beneficial effects of radiofrequency electromagnetic fields (RF-EMFs) in particular dose window and specific conditions [3, 4]. However, there are some limitations in the design of studies in this critical field.

One of the most important limitations in the study of RF-EMF effects on the human population is the variation in levels of RF-EMF exposure, resulting in to bias in the results [5], and non-reproducibility of the results. Moreover, the exposure of human to both non-ionizing and ionizing radiation will arise ethical issues [6] so that the use of animal models is a substitution. Nevertheless, calculations and measurements of RF-EMF dose and uniform delivery of radiations to the subjects could be crucial and achieved by some vehicles introduced by Vijayalaxmi [7]. This, precise dose measurement and uniformity of exposures are fundamental, especially in the studies dealing with the adaptive response (AR) of RF-EMFs.

In AR phenomenon, pre-exposure to a stimulant such as low dose radiation could induce a beneficial adaption to a subsequent challenging dose of ionizing radiation [8, 9]. Most of the current evidence reported the AR after receiving ionizing radiation with the conditioning dose; however, recently, some researchers have reported the AR induced by pre-exposure to RF could be a hopeful window to use this response in radiotherapy and astronaut industry [3, 4, 10]. In addition, there are opposing observations [11], rejecting AR at least some endpoints and there are a specific dose window, dose rates, and time interval of conditioning dose, limiting AR occurrence in subsequent challenging dose [12]. The existence of a dose window for the induction of AR by RF-pre-exposures has been previously addressed by Mortazavi et al, [13]. The exact mechanism of AR has been under study. Furthermore, the RF-induced AR in different doses and other

physical, biologic, and chemical conditions should be evaluated in detail. Nevertheless, in this study, we have assessed the pre-exposure effect of non-ionizing RF radiation and ionizing X-rays on survival, weight changes, food consumption and water intake before and after receiving RF-EMF and a lethal dose of X-ray in the rat.

## Material and Methods

### Design, ethical approval, and irradiation

This case-control study was approved by the ethical committee of Babol University of Medical Sciences, Babol, Iran. 48 rat were randomly divided into six groups, including control, 8Gy, mobile phone, “mobile phone+8 Gy”, Wi-Fi, and “Wi- Fi+8 Gy”. The standard rat polycarbonate cage type 2 was used ( $20 \times 25 \times 15 \text{ cm}^3$ )

The X-ray exposure was done using 6 MV Elekta compact accelerator on 15<sup>th</sup> day. The dose rate was 200 cGy/min, and SSD and depth were 115 cm and 3.5 cm, respectively and MU=983. Field size was  $40 \times 40 \text{ cm}^2$ , and total dose was 8 Gy.

The survival fraction, weight loss, water, and food consumption were compared during 30 days after receiving 8 Gy lethal dose.

### GSM, 900/1800 MHz, and 2.4 GHz RF-EMFs

We used a Nokia 1280 mobile phone device (Nokia, India) for GSM, 900/1800 MHz calculations. The Specific Absorption Rate (SAR) EU of this device reported 1.15 W/kg by the manufacturer for the human head.

The commercial Wi-Fi router was used in this study (D-Link DSL-2740U ADSL2 Plus Wireless N300 Modem Router, China) and the antennas of modem were located at the center of the rat cages. Both mobile phone and Wi-Fi radiations were applied for 14 days at 12 hours a day as the sources of pre-exposure to RF radiation.

The measurement of RF-EMF parameters was done by calibrated EMF meter (TES-593, Taiwan). We have evaluated three parameters, including intensity of electric and magnetic fields and power density ( $\mu\text{V/m}$  or  $\text{mV/m}$ ,  $\mu\text{A/m}$  or  $\text{mA/m}$ , and  $\mu\text{W/m}^2$  or  $\mu\text{W/cm}^2$ , respectively).

### Statistical Analysis

The Kaplan-Meier test was used to analyze the survival fraction of different groups. Food, water consumption, and animal weight during study period were compared by one-way repeated measurement analysis. The *P*-values lower than 0.05 was considered significant.

## Results

### The Specific Absorption Rates

The electric field (V/m), Magnetic field (mA/m), and Power flux-density ( $\text{W/m}^2$ ) of Wi-Fi router and mobile phone were showed in Table 1.

Then, the Specific Absorption Rate (SAR) in (W/kg) could be estimated from the following formula [14, 15]:

$$SAR = \sigma E^2 / \rho$$

Where,  $\sigma$  is tissue conductivity (S/m); *E* is induced electric field strength (V/m), and  $\rho$  is physical density ( $\text{kg/m}^3$ ).

Based on mean  $\sigma$  and  $\rho$  of whole rat body, which were reported 1.34 S/m and  $1040 \text{ kg/m}^3$ , respectively [15] and *E* reported in Table 1, the estimated SAR for mobile phone and Wi-Fi router in our study were 5.57 and  $91.99 \text{ mW/kg}$ , respectively.

### Survival fraction and clinical signs

After receiving RF-EMF for 14 days, and 8 Gy of the X-ray on 15<sup>th</sup> day, 30 days survival fractions were plotted and analyzed in Figure 1. Moreover, the consumption of water and food was monitored carefully during the study, as seen in Figure 2. The repeated measurement analysis revealed a statistically different water intake. Multiple comparisons of groups showed that 8 Gy, “Wi-Fi+8 Gy” had lower uptake than control and Wi-Fi groups. Furthermore, both mobile and “mobile+8 Gy” groups had a lower water intake than control.

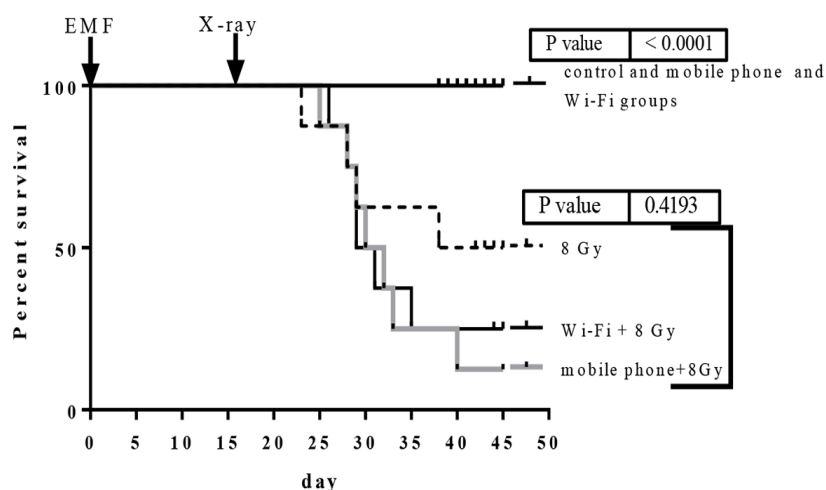
Food consumption in “mobile phone+8 Gy” group was significantly lower than control, 8 Gy, and “mobile phone” groups. In contrast, the multiple comparisons of food intake among Wi-Fi, “Wi-Fi+8 Gy”, 8 Gy, and control revealed no significant difference. The changes in the weight of rats during the last 10 days of their lives were shown in Figure 3.

## Discussion

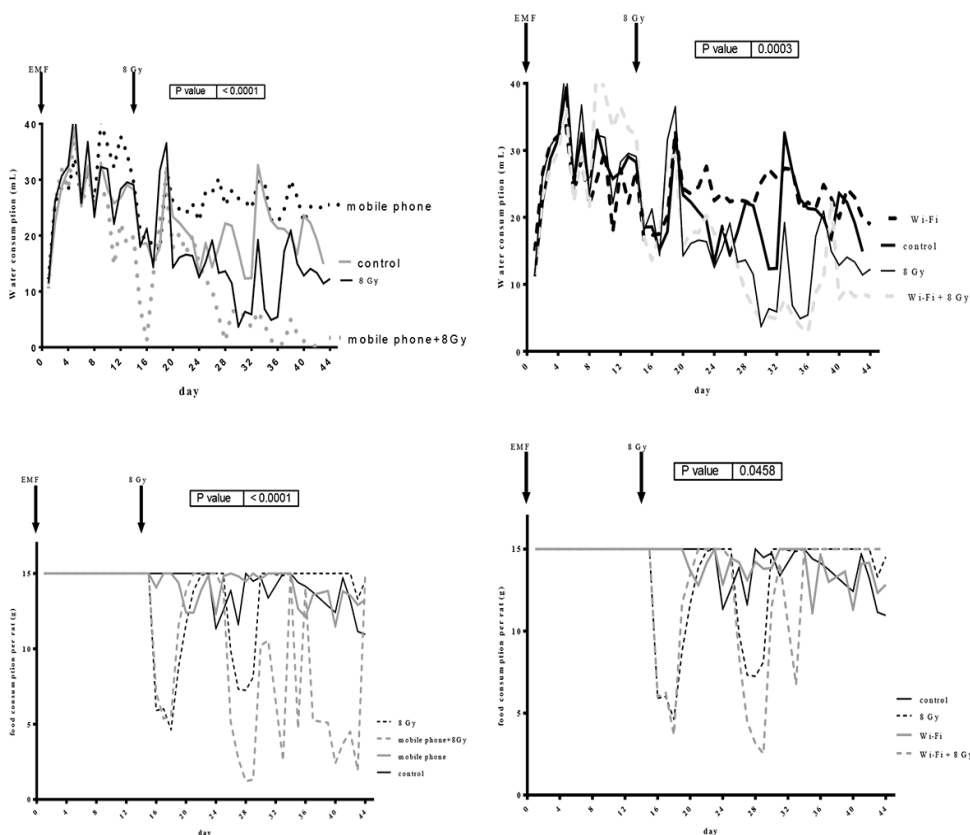
We have evaluated the adaptation to mobile phones and Wi-Fi radiation in a rodent model. The mobile phone and Wi-Fi routers employ RF-EMF, which are the packages of energy at wavelengths higher than visible light [16]. The main effects of RF-EMF on biological systems could be divided into thermal and non-thermal effects [16, 17]. At higher doses, the importance of thermal effects are dominant [16], but at lower doses, which thermal effects could not be measurable, the non-thermal effects depend on several biological and physical parameters such as frequency, time, electromagnetic field,

**Table 1:** The electric field (V/m), Magnetic field (mA/m), and Power flux-density ( $\text{W/m}^2$ ) of Wi-Fi router and mobile phone

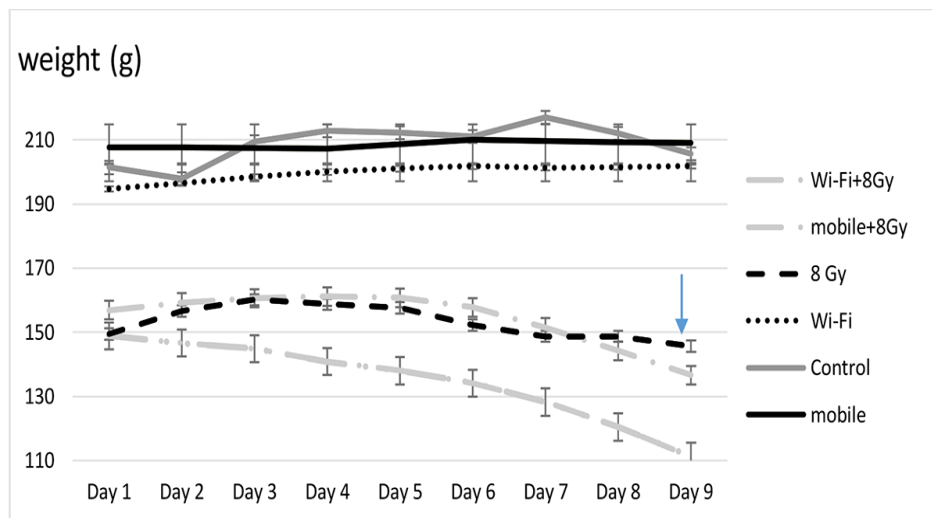
Detector Position	Electric field (V/m)	Magnetic field (mA/m)	Power flux-density ( $\text{W/m}^2$ )
Wi-Fi router	$8.45 \pm 2.93$	$21.68 \pm 5.89$	$163.16 \pm 86.24$
Mobile Phone	$2.08 \pm 1.27$	$5.48 \pm 3.64$	$18.97 \pm 23.20$



**Figure 1:** The survival fraction after exposure to the mobile phone, Wi-Fi, X-ray, and their combinations.



**Figure 2:** Water intake per rat/day during 45 days follow up (0-15 radiofrequency electromagnetic field (RF-EMF) exposure and on day 15 exposure to 8 Gy X-ray) in mobile (upper-left) and Wi-Fi (upper-right) groups. Food consumption per rat/day in the same period in mobile (Lower-left) and Wi-Fi (Lower-right) groups. The repeated measurement analysis p-values were shown on each graph.



**Figure 3:** The weight changes during the last days of rat lives per day.

genotype, and physiological factors [17].

One of the most important factors affecting the thermal and non-thermal effects of RF-EMF is SAR [18]. Hoque et al. have studied SAR of non-ionizing radiation from wireless/telecommunication in Bangladesh [14]. They have reported that the temperature change due to non-ionizing radiation is proportional to SAR and time and inversely proportional to the specific heat capacity of tissue [14]. Then, two factors, including SAR and time, could be set up by researchers in biomedical studies. However, specific heat capacity is a specification of the tissue and biologic system. Then, we could control the received heat by each point of the body by this information. Belpomme et al. believed that at lower doses, non-ionizing radiation does not cause measurable heating in the body [16]. At lower doses, which we have been using for a AR, the molecular changes could be involved in the adaptation process.

Our results showed that after 8 Gy X-ray exposure, 50 percent lethality occurred within 30 days follow up, which is in agreement with previous studies which used this dose as the LD50/30 for the rats. Havelek et al. reported that the LD50/60 of Wistar rat is 7.37 (4.68-8.05) Gy [19], which could confirm the 8 Gy

dose appropriateness.

Pre-exposure to both Wi-Fi and mobile phone before 8 Gy irradiation did not change the survival fraction significantly. Moreover, we had seen a non-significant synergistic effect of pre-exposure on RF-EMFs compared to 8 Gy group. These result would not confirm the AR which could be due to different SAR, dose rate and the time interval between the conditioning and challenging dose of our study in comparison with previous studies [8]. Some researchers reported the existence of AR induced by RF-EMF. Increased radio-resistance to lethal doses of gamma rays after a pre-exposure to microwave radiation is previously reported [20]. Bingcheng Jiang et al. reported that pre-exposure to EMF could induce AR in DNA damage [21]. They assessed the molecular changes while the endpoint of our study was survival fraction. Olga Zeni et al. suggested that the induction of AR depends on the type of EMF, SAR, and frequency [22]. Cao et al. reported that 120  $\mu\text{W}/\text{cm}^2$  could induce AR better 12 and 1200  $\mu\text{W}/\text{cm}^2$  [23]. However, they did not mention their statistical test. There are controversies in the AR induction but what we should notice is that the physical, biological, chemical parameter



is extensive and various aspects of this issue should be exactly clarified. The presence of AR was rejected by some studies, and Cao et al. reported that the 900 MHz EMF exposure has a synergistic effect on the SHG44 cells [11]. Our findings are generally in line with this theory that in a similar pattern with the adaptive responses induced by pre-exposure to ionizing radiation, the induction of adaptive response by RF-pre-exposures requires a minimum level of damage to trigger adaptive phenomena [13].

Our results revealed some alterations in the water, food intake, and also in the weight changes. As the timetable of changes (Figure 2) shows, there is a decrease in the water and food intake at the prodromal stage and also in the manifestation stages of ARS. Our results are in agreement with the Plett study, which established a model for hematopoietic syndrome [24].

## Conclusion

Pre-exposure to two different RF frequencies could not induce adaptive response (AR) in lethally exposed rats. To the best of our knowledge, the existence of a dose window for the induction of AR can be the cause of the lack of AR in our experiment. Our findings confirm this theory that in a similar pattern with adaptive responses induced by pre-exposure to ionizing radiation, the induction of adaptive response by RF-pre-exposures requires a minimum level of damage to trigger adaptive phenomena. It seems that further studies with different levels of RF-pre-exposures, different exposure timing, and other biological endpoints are needed to determine the optimum conditions required to induce AR by RF. The observed changes in food consumption, water intake, and weight could be associated with acute radiation syndrome (ARS) timeframe.

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## Authors' Contribution

A. Shabestani Monfared and SMJ. Mortazavi conceived the idea and E. Zabihi and M. Pouramir contributed in the design of the work. S. Borzoueisileh, F. Niksirat, M. Shafiee contributed in the acquisition of data. S. Borzoueisileh, A. Shabestani Monfared, SMJ. Mortazavi and N. Seyfizadeh analyzed or interpreted the data. All of authors contributed in drafting or revising and final approval the work.

## Ethical Approval

The Ethics Committee of Babol University of Medical Sciences approved the protocol of the study (Ethic cod: MUBABOL.REC.1396.36).

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## Conflict of Interest

None

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