European Review for Medical and Pharmacological Sciences 2014; 18: 992-1000

The effects of mobile phones on apoptosis in cerebral tissue: an experimental study on rats

A. YILMAZ, N. YILMAZ[1], Y. SERARSLAN[2], M. ARAS[2], M. ALTAS[3], T. ÖZGÜR[4], F. SEFIL[5]

Clinic of Neurosurgery, Bayburt State Hospital, II, Bayburt, Turkey
[1]Department of Neurosurgery, Yildirim Beyazit University, Ankara, Turkey
[2]Department of Neurosurgery, Mustafa Kemal University, Hatay, Turkey
[3]Department of Neurosurgery, Akdeniz University, Antalya, Turkey
[4]Department of Pathology, Mustafa Kemal University, Hatay, Turkey
[5]Department of Histology, Mustafa Kemal University, Hatay, Turkey

Abstract. – INTRODUCTION: The concern about mobile phone effects is increasing as the number of users increasing too. Different studies have different results, so this topic is still open to discussion. Aim of this report was to investigate the effects of the mobile phones on the Bcl-2 gene and p53 proteins in rat brains.

MATERIALS AND METHODS: In the study group of 10 rats; mobile phones that spread EMW at a frequency between 1900-2100 MHz and Specific Absorption Rate range between 0.005 W/kg and 0.288 W/kg (Dialing mode), 0.004 W/kg and 0.029 W/kg (Calling mode) were attached to rat ears for simulating usage in daily life for 7 times a day during 5 minutes (3 seconds dialing mode, 4 minutes and 47 seconds of calling mode) for a four week period. Sham group (n=10) rats were only immobilized without EMW exposure. Another group of rats (n=10) were counted as control without any application. immunohistopathological examination was performed for p53 and Bcl-2 expression.

RESULTS: Immunohistopathological examinations revealed that the samples in the study group had more p53 and Bcl-2 positive stained cells and they were stained denser. In both evaluations, these differences between the study and control group were found statistically significant ($p < 0.003$); In Bcl-2 evaluation statistically significant difference was found between study and sham group to ($p < 0.005$); however, the p53 evaluation between the study and the sham group did not show any statistically significant difference ($p > 0.005$).

CONCLUSIONS: Our results showed that the electro-magnetic waves emitted by the mobile phones may have effect on apoptosis. Besides, obtained data revealed that more realistic application of mobile phones during experiments is more important as expected.

Key Words:
Apoptosis, Bcl-2, Brain, Cellular Phone, Electromagnetic Waves, GSM, Histopathology, Mobile Phone, P53, Rat.

Introduction

Communicating with other beings, especially with the other members of the same species, in the nature is a vital necessity. This necessity describes the rapid increase of mobile phone usage in the recent years which is now considered to be the highest level of communication. Every day new systems that emit electro-magnetic waves (EMW) are introduced into our lives. According to International Telecommunication Association, by the end of 2014, there will be approximately 6.8 billion mobile phone users in the world[1]. Therefore, the interest about the effects of the EMW emitted by the mobile phones on the brain increases every day.

These EMW emitted by the mobile phones do not have the power to ionize an atom; however, they have thermal and non-thermal effects depending on the power of the energy emitted. A limitation has been brought in by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) in order to reducing the thermal effects that could harm the organisms[2]. According to this regulation; for regions other than the extremity, the upper limit is; 10 W/kg if the person is aware of the effect of the wave he/she is exposed to and is exposed due to professional reasons; 2 W/kg if the person is not aware of the wave and exposed by the devices used in daily life or the waves are present in the environment. Studies have shown that values above this limits impair the thermoregulation in tissues and cause an increase in temperature more than 1 centigrade degrees (°C). This increase causes various behavioral and physical effects in organisms[3,4]. On the other hand, the devices that emit non-thermal and non-ionizing EMW under this upper limit, in other words mobile phones, really harmless?

Corresponding Author: Atilla Yilmaz, MD; e-mail: admin@atemya.com

Actually, some studies have shown that non-thermal and non-ionizing EMW causes oxidative damage in the organism due to increased levels of nitric oxid, malondialdehyde, xanthine oxidase and adenosine deaminase[5]; and this oxidative damage can harm some proteins that play role in cell cycle and apoptotic path[6].

Apoptosis

Apoptosis is a process of controlled cell death whereby the activation of specific signaling death pathways[7]. Apoptosis occurs normally during development, aging as a homeostatic mechanism to maintain cell populations in tissues[8-10]. A dysregulation of apoptosis can be seen in different pathologies such as neurodegenerative diseases or cancer[10-12].

There are three apoptotic pathways: the extrinsic pathway, intrinsic pathway and perforin-granzyme pathway[7,8,13]. Various factors can stimulate or inhibit the intrinsic pathway. The most typical modifiers of these pathways are Bcl-2 and p53 gene families[8,14].

Bcl-2 gene was first identified in the B-Cell follicular lymphoma[10,13,15] and in this type of lymphoma, Bcl-2 was found to cause more longevity[8]. Bcl-2 members regulate apoptosis by controlling the mitochondrial membrane potential and preventing the release of cytochrome-c into cytoplasm from mitochondria. This situation is thought to increase the possibility of precipitation for malignity by increasing longevity in the cell[10,16-18].

P53 gene arrests the cell cycle at late G1 phase in case of DNA damage and spares time for DNA repair. Meanwhile, if DNA is repaired p53 diminishes and then the cycle will be completed. If the repair attempt is unsuccessful, p53 leads the cell to apoptosis[8,14,19]. Therefore, if p53 gene is damaged, the risk of tumorogenesis will increase due to the increased amount of damaged DNA[8,14]. For this reason p53 is called "The guardian of the genome"[20-23].

The purpose of our study is to investigate the effects of EMW exposure emitted by mobile phones with a more life-like practical method on genes play important roles preventing oncologic pathologies.

Materials and Methods

In our study, thirty 12 weeks-old male Wistar albino rats weighted between 250-350 g were used.

Preparing the Rats and Groups

In order to obtain handling conditions, rats were taken to the laboratory cages one week before the experiment. Rats were kept in groups of five in 30 × 20 × 15 cm Plexiglas cages at temperature of 21°C, 12/12 hour light and dark schedule with unlimited food, and water supply obtained. No medication was given before the experiment.

The rats were divided into three groups of 10 animals, the "study group", "sham group" and "control group". Special care was taken not to make any difference between the average weights of the animals within three groups.

The rats in the study group were exposed to EMW emitted by mobile phones 7 times a day, each application lasted 5 minutes and a total of 920 minutes in four weeks. This length off period was based on a statistical analyses from USA about the average time off calls among middle aged women dated March 2010[24].

The rats in the sham group were kept immobilized for the same duration of period and with the same method as the study group, however, these rats were not exposed to any EMW. 2 of these rats were taken out of the study because they developed an abscess in the chin area.

The rats in the control group were not exposed to any kind of immobilization or any EMW application.

As the purpose of the study was to investigate the apoptotic effects on the rat cerebral tissue, in order to acquire the most realistic results, the study group rats were exposed to EMW in the most realistic way possible. In order to achieve this, special care was taken to position the mobile phone on rat ears to resemble the way humans use the phone; with a new rat immobilization method (AD-ID method).

Rat Immobilization Method (AD-ID Method)

Firstly, the rat was placed face to face to the investigator; then, placed into a small size one fingertip cut off glove with head leading position (Figure 1); then, placed into another small size glove with tail leading. Meanwhile investigator made sure that the tail pointed outwards from the top of rat's head. The head was taken out of the cut off fingertip of the first glove up to the back of the ears (Figure 2).

By this method, the rats were immobilized without using any chemical agents or immobi-

Figure 1. First stage of the immobilization.

Figure 2. Last stage of the immobilization.

lization devices. Furthermore, they were exposed to EMW in the most realistic way possible.

Applying EMW via Mobile Phones

In our study we used the third generation mobile phones emit 1900-2100 MHz frequency EMW and can also be used for the wireless technological communication methods other than ordinary call protocols such as Global Positioning System (GPS), Wireless Local Area Network (WLAN) and Bluetooth.

After the rats were immobilized with the "ADID method", the phone that were going to be placed on the rat ears called another phone then the caller phone was placed on to the rat ears as soon as "dial" button was hit, and kept for 3 seconds (Dialing mode). After the 3 seconds, the phone that was being called was answered, the caller phone was kept in same position for 4 minutes and 57 seconds (Calling mode) (Figure 2).

After the total duration of 5 minutes (dialing + calling mode) was completed, the rats were taken out of the gloves and placed back in to their cages without any more application.

Measuring the EMW Emitted During the Application

The electrical field values formed by the EMW that were emitted to the rats during the application were measured by an electromagnetic radiation measuring device that conforms to the international standards (Narda EMR-300 for isotropic measurements of electromagnetic fields, Wandel & Goltermann GmbH & Co., Eningen, Germany). The measured results showed that the mobile phones emitted different amount of EMW during the dialing and calling modes even in various moments within these modes (Tables I, II).

Calculating the Specific Absorption Rate Value

While calculating the Specific Absorption Rate (SAR) value in accordance with the measured data, the rat brains' dielectric constant was calculated[5] as (σ 0, 62 s/m^2, and mass density was calculated[26-28] as (ρ) 1040 kg/m^3. When these values together with electrical field obtained by the measurement device are applied to SAR calculation formula:

$$SAR = \frac{\sigma * (E^2)}{\rho}$$

The SAR value that affected the rat brains was calculated to vary between 0.005 W/kg and 0.288 W/kg during dialing mode and between 0.003 W/kg and 0.029 W/kg during calling mode. The rate between the highest and lowest measured value (highest during dialing mode/lowest during calling mode) was found 72 (Table III).

Another significant data we obtained was that; the SAR value significantly decreases by 10 cm distance, and diminishes to a level almost equal to the value caused by the EMW pollution in the environment at 20 cm distance (Table IV).

Table I. Values measured during dialing mode.

	Moment of dialing	1 second later	2 seconds later	4 seconds later	5 seconds later
Average	6.2 V/m	17.5 V/m	6.7 V/m	2.9 V/m	2.9 V/m

Table II. Values measured during call mode.

	Moment of answering	1 second later	2 seconds later	4 seconds later	5 seconds later
Average	2.7 V/m	3.05 V/m	3.3 V/m	2.55 V/m	2.55 V/m

Table III. Values measured during call mode.

Highest during dialing	Lowest during dialing	Rate
0.288 W/kg	0.005 W/kg	57.5
Highest during calling	**Lowest during calling**	
0.029 W/kg	0.004 W/kg	7.5

Table IV. SAR values measured by distance (As seen in the table, SAR value created by a mobile phone is reduced by a rate of 1012 at a 30 cm distance).

Attached to the ear during dialing	30 cm distance during dialing	Rate
0.238461538 W/kg	0.00059615 W/kg	400.003
Attached to the ear during calling	**30 cm distance during calling**	
0.029211538 W/kg	0.00002885 W/kg	1012.53

Preparing Samples

Immediately after the applications on the last day, the rats were undergone micro craniotomy under general anesthesia induced with mixture of 10 mg/kg ketamine HCL and 90 mg/kg xylazine HCl intraperitoneal injection.

The rat brain tissues were taken out of their craniums with special care not to cause any damage and were placed in to containers filled with 10% of formalin. These tissues placed in the container were then transported to the Department of Pathology for immuno histopathological (IHP) examination.

Immunohistopathological Examination

IHP examinations were carried out by a pathology specialist at Mustafa Kemal University School of Medicine Pathology Department. The pathologist was unaware of the samples whether they were study, sham or control.

10 separate fields taken randomly out of the substances made out of the samples from the glial tissues of the rats in all groups were examined in terms of p53 and Bcl-2 staining.

The samples were applied with a mouse monoclonal antibody against human Bcl-2 (1:100, clone 124; Dako, Carpinteria, CA, USA) for Bcl-2 staining and with a mouse monoclonal antibody against human p53 (1:100, clone 124; Dako, Carpinteria, CA, USA) for p53 staining. The percentages of the stained cells within the detected magnification area (×100) were determined. The intensity of stained cells and the distribution was also evaluated. Data obtained at the end of the inspection was scored by the semi-quantitative scoring system[29,30]. In this scoring system, the scoring was made as per the intensity of the cells staining by the antibody and the distribution percentage of the positive stained cells. In the assessment per stain intensity; cells that were not stained at all were given "0" point, cells that were slightly stained were given "1" point, cells that were moderately stained were given "2" points and cells that were intensely stained were given "3" points.

In the assessment per stained cell distribution; no stained cells in the environment was given "0" points, a rate of 1-25% cells was given "1" point, 26-50% "2" points, 51-75% "3" points and 76-100% rate was given "4" points.

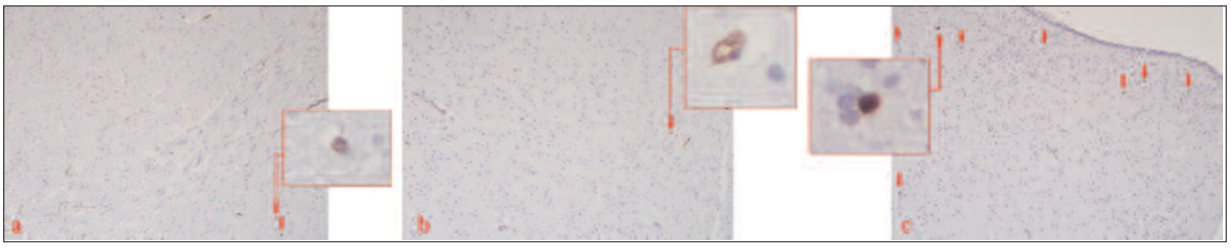

Figure 3. ***a,*** p53 control group. ***b,*** p53 sham group. ***c,*** p53 study group.

The sum of intensity and distribution scores (a value between 0-7) was assessed as the final score of staining. The final score of 0-1 was counted as a negative result value "-", 2-3 as a weak result value "+", 4-5 as an average result value "++", and 6-7 as a strong result value "+++". Final score was also defined numerically as 0, 1, 2, 3.

Statistical Analysis

Final scores were evaluated with the statistics software "SPSS® for Windows" (SPSS Inc., Chicago, IL, USA) and Chi square test was used to detect statistical significance; the level of significance was set at $p < 0.05$.

Results

p53 Findings

As a result of the IHP assessment, the cells in the study group were observed to have been stained in greater numbers and more intensively compared than other groups (Figure 3).

After final scores of each sample calculated, intergroup comparisons were evaluated (Table V).

In the P53 examination, the differences between the study and control group; and between sham and control group were determined to be statistically significant ($p < 0.003$). However, the difference between the study and sham group did not show any statistically significance.

Bcl-2 Findings

As a result of the IHP assessment, the Bcl-2 stained cells in the study group were observed to be in larger quantity and stained more intensely compared to the other groups (Figure 4).

After final scores of each sample calculated, intergroup comparisons were evaluated (Table VI).

The difference between the study and control group was determined to be statistically significant ($p < 0.003$). Also the difference between the study and sham group was determined to be statistically significant too ($p < 0.003$).

Discussion

Because of the capabilities such as internet access, mobile phone usage time in daily life is rapidly increasing. This increase raises the con-

Table V. p53 final scores.

p53		Final score		
Control group	Number of rats	8	2	0
	% in group	80.0%	20.0%	0.0%
	% in result	100.0%	14.3%	0.0%
Sham group	Number of rats	0	6	2
	% in group	0.0%	75.0%	25.0%
	% in result	0.0%	42.9%	33.3%
Study group	Number of rats	0	6	4
	% in group	0.0%	60.0%	40.0%
	% in result	0.0%	42.9%	66.7%
Total	Number of rats	8	14	6
	% in group	28.6%	50.0%	21.4%
	% in result	100.0%	100.0%	100.0%

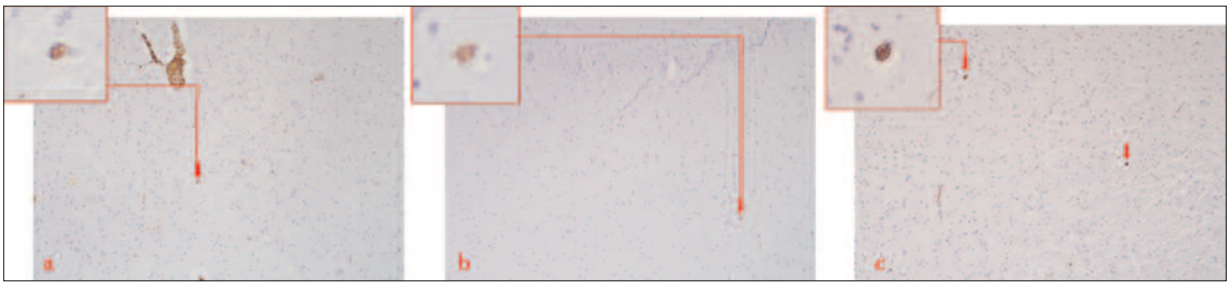

Figure 4. ***a,*** Bcl-2 control group. ***b,*** Bcl-2 sham group. ***c,*** Bcl-2 study group.

cerns about mobile phone effects on health. However, unfortunately experimental studies obtain different kind of results.

Our study was planned to contribute to this current discussions. We obtained greater amount of damaged cells in study group specimens by means of p53 and Bcl2 IHP evaluation.

In our study, the highest result score of "2" was at a rate of 66.7% in the study group for p53 assessment, this rate reaches up to 75% in the Bcl-2 assessment. This situation leads us to think that EMW impact is present; in other words, mobile phones cause p53 and Bcl-2 expression in cerebral tissue and affect apoptosis.

The study performed by Yilmaz et al[31] on rats, achieved the result; contrary to our study; the application of 900 MHz frequency and 0.29-0.87 W/kg SAR range EMW exposed from a real mobile phone for 20 minutes a day for 4 weeks did not cause a significant difference in Bcl-2 expression levels[31]. In this study, the mobile phone was placed under the plexiglas cage and rats were freely roaming inside the cage and the application was only carried out during the calling mode. In this study the distance between the rat in the cage and the mobile phone was not set to be standard. Moreover, considering the thickness of the plexiglas cage and the position of the rat's head in the cage, the distance was probably around 10-20 cm. It should be considered that these factors may have played a role in obtaining a non-activity result as opposed to our study.

In the study performed by Liu et al[32] on the cortical neuron cell cultures, the application of 1800 MHz EMW emitted from a real mobile phone during 24 hours caused a significant increase in Bax levels in cortical neurons, and a significant decrease in Bcl-2 expressions[32]. Another study by Liu et al[33] on rat astrocyte cell cultures, 1950 MHz frequency and 5,36 W/kg SAR EMW produced by a radiofrequency (RF) generator was applied for 12, 24, and 48 hours. Significant mitochondrial damage, distinctive apoptosis in astrocytes, increase in Bax levels and considerable decrease in Bcl-2 expressions was only seen in the 48 hour application group[33]. Both studies achieved similar results as our study.

Table VI. Bcl-2 final scores.

Bcl-2		Final score		
Control group	Number of rats	7	3	0
	% in group	70.0%	30.0%	0.0%
	% in result	87.5%	18.8%	0.0%
Sham group	Number of rats	1	6	1
	% in group	12.5%	75.0%	12.5%
	% in result	12.5%	37.5%	25.0%
Study group	Number of rats	0	7	3
	% in group	0.0%	70.0%	30.0%
	% in result	0.0%	43.8%	75.0%
Total	Number of rats	8	16	4
	% in group	28.6%	57.1%	14.3%
	% in result	100.0%	100.0%	100.0%

In the study performed by Zhao et al[34] on neuron and astrocyte cell cultures, it was pointed out that application of 1900 MHz frequency EMW generated with a real mobile phone for 2 hours caused a significant increase in Bax levels[34]. The result of this study is also parallel to ours and the daily application duration is also closer to ours than other studies.

In the study performed by Buttiglione et al[35] on SH-SY5Y neuroblastoma cell cultures, showed that the application of 900 MHz frequency and 1 W/kg SAR EMW emitted by RF generator for 24 hours via Wired Patch Cell (WPC) caused a significant decrease in Bcl-2 and mRNA amounts in the cells[35]. The result of this study is also parallel to ours and it is quite remarkable that the application duration was set to be a long period of time just like the other studies that used RF generators.

As for the studies that were carried out to investigate the effect of mobile phones on the p53 protein, a study similar to ours performed on rats Dasdag et al[30] indicated that application of 900 MHz frequency and 0.25,1,2, and 4 W/kg SAR value EMW produced by RF generator for a period of 2 hours a day, for 10 months did not cause a significant change in the p53 protein levels of cerebral tissues[30]. EMW applied to the fixated rats in plexiglas cages was obtained by RF generators and this wave was applied via a monopole antenna placed in the middle of the rats. No activity was detected at the end of the study, we believe that might have been because the EMW applied was produced by an RF generator which has different featured to that of mobile phones, also because there was a distance of approximately 10 cm between the aerial and the rat's ear as well as a barrier made out of plastic.

In the study performed by Bourthoumieu et al[22] on human amniotic cell cultures, it was shown that the application of 900 MHz frequency and 0.25, 1, 2 and 4 W/kg SAR EMW via WPC for 24 hours did not cause a significant change in the activation of the p53 protein[22].

In the study carried out by Hirose et al[36] on human glioblastoma A172 cell cultures, showed that application of 2,1425 Ghz frequency and 0.17-0.58 W/kg SAR value EMD for 28 hours via Horne aerial did not cause a significant change in phosphorylated p53 or total p53 levels[36]. Lee et al[6] performed out a study on human MCF7 carcinoma cell cultures and this study showed that application of 857 Mhz or combined 857 and 1950 Mhz. frequency, 4 W/kg SAR value EMD for 1 hour via Horne aerial did not cause a significant change in p53, p21 and cyclin kinase values[6]. In these last four separate p53 studies, we believe not using mobile phones is an important detail. We also believe, it is important to consider the fact that; mobile phones expose different amount of EMW having wide range of SAR values during different activity modes and at different distances. The results of the experiments would be affected by the use of an RF generator that emits standard EMW.

Conclusions

Our study is an investigation of the effects of EMW on brain cells where Bcl-2 and p53 protein expressions are evaluated together as differ from to the studies where they were evaluated separately.

Our results showed that EMW emitted by mobile phone have an effect on apoptotic and anti-apoptotic proteins. Apoptosis is a mechanism that diminishes the damaged cells and prevents the potential malignancy; our results would support the hypothesis that this type of EMW could be one of the triggering etiological factors that play a role in cerebral carcinogenesis.

We cannot imagine not using mobile phones because of their harmful effects as they make our lives so much easier and provide communication as well as quick Access to information; however, if there was at least a compromise on its harmful effects, some legal obligations could be brought in where producers have to design systems that would decrease the harmful effects.

Statement of Interests

This study was funded in full by "Mustafa Kemal University Scientific Research Projects Coordination Unit", grant number 401.

Ethical approval

This study was funded in full by "Mustafa Kemal University Scientific Research Projects Coordination Unit", grant number 401.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

1) Measuring Information Society. Vol 2013. Switzerland: International Telecommunication Union, 2013.
2) Protection ICON-IR. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (Up To 300 Ghz), 1998.
3) Hyland GJ. Physics and biology of mobile telephony. Lancet 2000; 356: 1833-1836.
4) Yurekli AI, Ozkan M, Kalkan T, Saybasili H, Tuncel H, Atukeren P, Gumustas K, Seker S. GSM base station electromagnetic radiation and oxidative stress in rats. Electromagn Biol Med 2006; 25: 177-188.
5) Ilhan A, Gurel A, Armutcu F, Kamisli S, Iraz M, Akyol O, Ozen S. Ginkgo biloba prevents mobile phone-induced oxidative stress in rat brain. Clin Chim Acta 2004; 340: 153-162.
6) Lee KY, Kim BC, Han NK, Lee YS, Kim T, Yun JH, Kim N, Pack JK, Lee JS. Effects of combined radiofrequency radiation exposure on the cell cycle and its regulatory proteins. Bioelectromagnetics 2011; 32: 169-178.
7) Kerr JF, Wyllie AH, Currie AR. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. Br J Cancer 1972; 26: 239-257.
8) Elmore S. Apoptosis: a review of programmed cell death. Toxicol Pathol 2007; 35: 495-516.
9) Hawkins CJ, Vaux DL. The role of the Bcl-2 family of apoptosis regulatory proteins in the immune system. Semin Immunol 1997; 9: 25-33.
10) Tsujimoto Y. Role of Bcl-2 family proteins in apoptosis: apoptosomes or mitochondria? Genes Cells 1998; 3: 697-707.
11) Kayihan E, Özyardimci N. Akciger Kanserleri Tani ve Tedavide Temel Ikeler ve Uygulamalar Avrupa Tip Kitapçilik Ltd. Sti, 2001.
12) Joubert V, Leveque P, Cueille M, Bourthoumieu S, Yardin C. No apoptosis is induced in rat cortical neurons exposed to GSM phone fields. Bioelectromagnetics 2007; 28: 115-121.
13) Chen Q, Ray S, Hussein MA, Srkalovic G, Almasan A. Role of Apo2L/TRAIL and Bcl-2-family proteins in apoptosis of multiple myeloma. Leuk Lymphoma 2003; 44: 1209-1214.
14) Kumar V, Abbas AK, Fausto N, Robbins SL, Cotran RS. Robbins and Cotran pathologic basis of disease. Elsevier Saunders, 2005.
15) Brambilla E, Negoescu A, Gazzeri S, Lantuejoul S, Moro D, Brambilla C, Coll JL. Apoptosis-related factors p53, Bcl2, and Bax in neuroendocrine lung tumors. Am J Pathol 1996; 149: 1941-1952.
16) Yang J, Liu X, Bhalla K, Kim CN, Ibrado AM, Cai J, Peng TI, Jones DP, Wang X. Prevention of apoptosis by Bcl-2: release of cytochrome c from mitochondria blocked. Science 1997; 275: 1129-1132.
17) Santini MT, Ferrante A, Rainaldi G, Indovina P, Indovina PL. Extremely low frequency (ELF) magnetic fields and apoptosis: a review. Int J Radiat Biol 2005; 81: 1-11.
18) Kluck RM, Bossy-Wetzel E, Green DR, Newmeyer DD. The release of cytochrome c from mitochondria: a primary site for Bcl-2 regulation of apoptosis. Science 1997; 275: 1132-1136.
19) Siganaki M, Koutsopoulos AV, Neofytou E, Vlachaki E, Psarrou M, Soulitzis N, Pentilas N, Schiza S, Siafakas NM, Tzortzaki EG. Deregulation of apoptosis mediators' p53 and bcl2 in lung tissue of COPD patients. Respir Res 2010; 11: 46.
20) Amaral JD, Castro RE, Steer CJ, Rodrigues CMP. p53 and the regulation of hepatocyte apoptosis: implications for disease pathogenesis. Trends Mol Med 2009; 15: 531-541.
21) Djebaïli M, De Bock F, Baille V, Bockaert J, Rondouin G. Implication of p53 and caspase-3 in kainic acid but not in N-methyl-d-aspartic acid-induced apoptosis in organotypic hippocampal mouse cultures. Neurosci Lett 2002; 327: 1-4.
22) Bourthoumieu S, Magnaudeix A, Terro F, Leveque P, Collin A, Yardin C. Study of p53 expression and post-transcriptional modifications after GSM-900 radiofrequency exposure of human amniotic cells. Bioelectromagnetics 2012; 34: 52-60.
23) Gotz C, Montenarh M. P53 and its implication in apoptosis (review). Int J Oncol 1995; 6: 1129-1135.
24) African-Americans, Women and Southerners Talk and Text The Most in the U.S. In: Company TN, editor: The Nielsen Company, 2011.
25) Sekino M, Ohsaki H, Yamaguchi-Sekino S, Iriguchi N, Ueno S. Low-frequency conductivity tensor of rat brain tissues inferred from diffusion MRI. Bioelectromagnetics 2009; 30: 489-499.
26) Chou CK, Chan KW, McDougall JA, Guy AW. Development of a rat head exposure system for simulating human exposure to RF fields from handheld wireless telephones. Bioelectromagnetics 1999; Suppl 4: 75-92.
27) Del Bigio MR, Slobodian I, Schellenberg AE, Buist RJ, Kemp-Buors TL. Magnetic resonance imaging indicators of blood-brain barrier and brain water changes in young rats with kaolin-induced hydrocephalus. Fluids Barriers CNS 2011; 8: 22.
28) Brands DW, Bovendeerd PH, Wismans JS. On the potential importance of non-linear viscoelastic material modelling for numerical prediction of brain tissue response: test and application. Stapp Car Crash J 2002; 46: 103-121.
29) Endo K, Terada T. Protein expression of CD44 (standard and variant isoforms) in hepatocellular carcinoma: relationships with tumor grade, clinicopathologic parameters, p53 expression, and patient survival. J Hepatol 2000; 32: 78-84.
30) Dasdag S, Akdag MZ, Ulukaya E, Uzunlar AK, Ocak AR. Effect of mobile phone exposure on apoptotic glial cells and status of oxidative stress in rat brain. Electromagn Biol Med 2009; 28: 342-354.

31) Yilmaz F, Dasdag S, Akdag MZ, Kilinc N. Whole-body exposure of radiation emitted from 900 MHz mobile phones does not seem to affect the levels of anti-apoptotic bcl-2 protein. Electromagn Biol Med 2008; 27: 65-72.

32) Liu ML, Wen JQ, Fan YB. Potential Protection of Green Tea Polyphenols Against 1800 MHz Electromagnetic Radiation-Induced Injury on Rat Cortical Neurons. Neurotox Res 2011; 20: 270-276.

33) Liu YX, Tai JL, Li GQ, Zhang ZW, Xue JH, Liu HS, Zhu H, Cheng JD, Liu YL, Li AM, Zhang Y. Exposure to 1950-MHz TD-SCDMA Electromagnetic Fields Affects the Apoptosis of Astrocytes via Caspase-3-Dependent Pathway. PLoS One 2012; 7: e42332.

34) Zhao TY, Zou SP, Knapp PE. Exposure to cell phone radiation up-regulates apoptosis genes in primary cultures of neurons and astrocytes. Neurosci Lett 2007; 412: 34-38.

35) Buttiglione M, Roca L, Montemurno E, Vitiello F, Capozzi V, Cibelli G. Radiofrequency radiation (900 MHz) induces Egr-1 gene expression and affects cell-cycle control in human neuroblastoma cells. J Cell Physiol 2007; 213: 759-767.

36) Hirose H, Sakuma N, Kaji N, Suhara T, Sekijima M, Nojima T, Miyakoshi J. Phosphorylation and gene expression of p53 are not affected in human cells exposed to 2.1425 GHz band CW or W-CDMA modulated radiation allocated to mobile radio base stations. Bioelectromagnetics 2006; 27: 494-504.