



Original Article:

Oncogenic Potential of Radiofrequency Emissions for Mobile Phones

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Abstract:

With the advent of the rising telecom industry there is growth in the usage of the mobile phones by manifold and when we are in country like India, in order to cover one billion population, several transmission towers have been installed to create a jungle of such masts rising atop many buildings in the densely populated parts of India. The erection of these towers has lead to speculations that there may be increased incidence of cancer after exposure to the RF emissions from mobile telephone base stations. There are no high-quality epidemiologic studies that can be used to evaluate health risks from RF exposure. Laboratory studies in this area have been somewhat confusing. Some animal studies suggest that RF fields accelerate the development of sarcoma colonies in the lung, mammary tumors, skin tumors, hepatomas, and sarcomas. In contrast, other studies conducted on large scale on the cell lineage and people working in areas with high RF emissions have not found carcinogenic effects. These conflicting results indicate the need for more well-conducted studies. This paper provides a review of the laboratory studies and indicates what conclusions about RF-induced cancer can be drawn.

Key Words: Radiofrequency fields, Cancer, Health effects, Laboratory studies, Mobile phones

Introduction:

There has been tremendous growth in the number of mobile phone users in the world during the last five years. The reasons point to easy access, affordability, fairly good reliability and better geographical coverage by the service providers. Of course, the need to communicate has always been there ever since the evolution of mankind. Though other forms of communication do help to serve the purpose but nothing beats the excitement and the emotions involved in being able to contact and converse with someone at the click of a few keys on the mobile phone.

Technically, the growth in this sector has been much faster and wider in India than in any other country. It would be probably correct to say that at any given moment, India would be having the largest numbers of active mobile phone users in the world. Quite naturally, to cover a population of almost a billion, several transmission towers have been installed to create a jungle of such masts rising atop many buildings in the densely populated parts of India. Each year, many such towers

are being added in order to ensure negligible loss in transmission and hence the retention of existing and multiplying clients list. A fierce competition, even in this age of recession, continues to exist between multiple phone companies all of whom seem to adopt aggressive marketing for their products while working at ensuring commitment to the punch lines like "wherever you go we will follow you". No doubt, a large part of the social and economic development in the country in various sectors and efficiency in the work places is due to the excellent communication. However, from time to time, this industry and its users have faced extremely scary reports on harmful effects of electromagnetic radiations (EMR) on human health. There are many conflicting reports in the literature citing definite damage as many as those reports which attempt to convince the scientific community of no such effects with the intensity of the EMR by either the mobile phone sets or the transmission towers located in residential areas. There are several petitions, where the residents, scared by the existing ambiguity, have requested the removal of such towers from the thickly populated areas. Of the greatest concern to the scared population is the fear of contracting cancers in any part of the body due to the harmful effects of EMR used in and for mobile phones receiving and transmission. There have been several reports endorsing the finding that the incidence of brain cancers is much higher in individuals using mobile phones for a much longer period and more frequently in the course of the day. There are several other health hazards quoted in the literature regarding the effect of EMR on melatonin secretion, sleep alteration, stress induction, sensory neural deafness and changes due to thermal effects. However there are almost equal numbers of studies which vehemently insist that such changes with the EMR frequency, power and SAR as used in different mobile phone sets or those emitted by the roof top masts are incapable of producing such effects. True or not, the mobile user who considers it as a necessary evil is still confused. Amidst all controversy, the ghost of cancer still looms large in a common man's mind.

Interestingly, several multinational companies are spending millions in terms of bringing new products with fascinating features which compel the user to use the equipment for entertainment at almost all hours. The mobile phone has turned into a gadget of indulgence and obsession. It is this development in technology and addition of features, which is partly respons-

ible for enormous sale of the hand sets and penetration even to the remotest part of the country. No mobile phone company, including the one owned by the government has spent even a fraction of the marketing budget in either educating the community about possible harmful effects, if there are any, or ensuring the public that the equipment and the service provided by them is completely hazard free. Except for one instance where Motorola participated in a research, literature is silent on involvement of any mobile phone company to initiate or support the research on effects of EMR on various groups of human population some of whom may not be using the phone but may be living in the vicinity of the transmission tower installation

Perception of Radiofrequency Raditions and Cancer Risks:

In the mobile technology there are 2 systems of working, the Global System for Mobile Communication (GSM) and Code Division Multiple Access (CDMA) standard. These services operate within the frequency ranges 872–960 MHz(Megahertz) and 1710–1875 MHz respectively and radiate an average power of 0.2- 0.6 W, 40 per cent of which is absorbed in the hand and the head.[1] Over recent years the third generation of mobile phones, 3G or universal mobile telecommunication system (UMTS), using 1,900 MHz RF(Radiofrequency) fields has been introduced worldwide The FCC (Federal Communications Commission, USA) limits peak exposure to 1.6 W/kg of tissue averaged over any single gram of tissue (or 1.6 mW/g) though the European limits are less restrictive, specifying 1.6 W/kg averaged over 10 grams

RF radiation cannot ionise atoms or molecules like far-ultraviolet radiation and X-rays. These non-ionising electromagnetic radiations, however, is believed to be harmless at very low intensities, although it can be damaging at high intensities. This external electromagnetic field interacts with an internal biological process through the action of free radicals. Research has shown that magnetic fields increase the average concentration of free radicals, lengthen their lifetime, and enhance the probability of radical reactions with cellular components[2,3] biologic mechanism that could explain any possible carcinogenic effect from radiofrequency radiation has not been identified. It is generally agreed that the heating of tissue by radiofrequency radiation from mobile phone use is negligible and that any carcinogenic effect would have to be mediated through a non thermal mechanism. No studies to date have had an exposure time long enough to properly address the potential adverse late health effects of mobile phone use. So, this increasing use of wireless telephone communication has raised concerns about health risks, primarily increased risk for brain tumours, owing to the proximity of the brain to the radiation antenna, with the potential for absorbing a comparatively large amount of electromagnetic energy the emission at the head surface is typically 10,000 times stronger than that reaching the head of a user standing within 30m of the base of a mobile phone relay transponder mounted on a tower 30m above ground

A large proportion of research on incidence of cancer in mobile phone users has taken place in Europe, followed by North America, while Asian studies, mainly from Japan, are relatively few. Studies have attempted to study a wide variety of neoplastic phenomena affecting different body systems. The most frequently studied malignancies include the intracranial tumors, such as astrocytomas, gliomas and acoustic neuromas. The studies have mostly been case-control studies using patient-reported usage information to correlate duration and intensity of usage to the association with cancer.

Several studies have found a greater association of long-term mobile phone usage with intracranial malignancies. It was seen that there is a significant association between analog phone use and brain tumors, with the greatest risk being for

grade III-IV astrocytoma after a latency period of >10 years after first use. The association with tumors after a >10 year latency was significant for analog, digital as well as cordless phones.[4] Another study found the prevalence of various cancers amongst regular mobile phone users had a significant association between acoustic neuromas and astrocytomas in users of analog, digital and cordless phones. The same study did not find significant associations for other tumors, such as salivary gland tumors, non-Hodgkin lymphoma (NHL) or testicular cancer.[5] Association of various cancers on exposure of >2000 hours of cumulative usage of mobile phones has also been quantified.[6] The same study also found that the risk for developing high-grade astrocytoma was higher with usage >10 years with analog phones and digital phones, but not with cordless phones. Two recent meta-analyses showed that long-term (>10 years) usage of mobile phones was associated with a greater risk of intracranial tumors,[7] with the greatest risk being for ipsilateral gliomas and ipsilateral acoustic neuromas.[8] Significant association between the occurrence of benign or malignant parotid neoplasms and the use of mobile phones was studied and it was found that individuals with high exposure and non-hands-free users were an at-risk group for developing these tumors on the side of predominant usage.[9]

It is now widely accepted that cancer is initiated by alterations in the genetic material (DNA) in the cell (genotoxic effects), although some non-genotoxic chemicals and epigenetic carcinogens have been recognised. After initiation, the cell may progress to full malignancy without any further external stimulus but more often further events are required. An agent which will cause this further progression towards malignancy is often termed a promoting agent.

Role of Melatonin

When it comes to cancer promotion there are various agents, but none such as melatonin. Melatonin is a hormone secreted by the pineal gland, which controls our diurnal rhythm (Day-night cycle). Peak levels are produced in people during the night (in the dark period). It affects the mammalian reproductive system, as well as other physiological and biochemical functions.[10] It is an efficient scavenger of free radicals, which can damage cells, and there is evidence that melatonin has a protective effect against cancer. Thus, changes in melatonin secretion could conceivably alter tumour initiation and promotion.[11,12] There have been various studies on melatonin levels getting affected by the exposure to radiofrequency radiations. There are reports that extremely low frequency (ELF) electromagnetic fields may affect pineal function, although the data are inconsistent. This has led to the “melatonin hypothesis”, suggesting a link between ELF fields and cancer.[13] This raises the question whether exposure to RF fields might also have an effect on the pineal gland. Radiofrequency photon energies are much higher than those at ELF, lying between the ELF and visible parts of the electromagnetic spectrum. In contrast to visible radiation, neither ELF fields nor RF fields directly affect photopigments in photoreceptors in the eye, and they are therefore very unlikely to affect pineal function by the same anatomical pathway as does visible radiation. It is conceivable that RF fields might influence the synthesis or secretion of melatonin by the pineal gland through a direct influence on either the suprachiasmatic nucleus or the pineal gland itself, although there is no obvious theoretical reason to expect such influences. Only a few studies testing effects of RF exposure on melatonin synthesis have been conducted.

Effect of continuous and intermittent radiations on dairy cattle herds located in the vicinity of a short-wave (3–30 MHz) radio antenna when studied showed no chronic effect on salivary melatonin levels, although a short-term rise in melatonin was

noted when the antenna was energised after being turned off for three days.[14] Similar studies on specifically the pineal gland functions of rats and hamsters exposed to very low level 900 MHz fields for up to six hours, showed no effects on nocturnal melatonin production [15], since majority of these studies were conducted on animals so the relevance to the use of mobile phones could, in any case, be assessed only through laboratory studies of people because of species differences in the pattern of circadian rhythms. It must also be emphasised that the hypothalamus and pineal gland are much further from the surface of the head in people than in animals. Therefore, even if there were an effect on melatonin production in animals resulting from a direct interaction of fields within the brain, it would be much less likely to occur in people. Since the function of melatonin is cancer protective, its altered levels are linked with cancer incidence.

Role of Ornithine Deoxycarboxylase (ODC)

High ODC activity is characteristic of the unregulated growth of tumor cells, Pulse-modulated RF fields from mobile phones may cause a slight increase in ODC levels and activity, at non-thermal levels and ODC activity has been shown to be sensitive to both extremely low frequency magnetic fields and to radiofrequency fields.[16,17] However, it is very unlikely that these small changes could, on their own, have a tumour-promoting effect. It is also unlikely that such effects act synergistically with other environmental hazards and contribute to tumour promotion.

DNA Damage

An increase in the number of single-strand and double-strand DNA breaks was reported in the brain cells of rats exposed for two hours to pulsed or continuous-wave 2.45 GHz radiation. [18,19] Moreover, this effect was blocked by treatment, before or after exposure, with melatonin or another free-radical scavenger.[20] Chromosomal aberrations are generally thought to be due to damage to DNA or unusual interactions between DNA and protein molecules. Their accumulation is evidence of genotoxicity and is usually associated with cancer, but can also result in developmental abnormalities or miscarriage, if present in the tissue that generates eggs or sperm, or in the developing embryo or fetus. It was also described that there were increased chromosomal aberration in human lymphocytes after exposure to 167 MHz RF fields at 55 W/m² for up to 72 h. [21] Also chromosomal aberration in the lymphocytes of people who had experienced occupational exposure to 30–300 GHz at 10–50 W/m² were noticed.[22]

Effect of Genotoxic Agents

There are several published studies that suggest that RF radiation can have an epigenetic effect in vivo, working to exaggerate the genotoxic influences of ionizing radiation or cancer-inducing substances, or to potentiate other epigenetic factors. However, the evidence for an epigenetic effect of RF exposure is equivocal, with several failures to replicate positive results. Latent transformation of a cultured cell line was also reported on exposure to 2.45 GHz radiation.[23,24] This RF radiation potentiated the tumour-transforming effect of X-rays or the carcinogenic substance benzo[a]pyrene, but only in the presence of TPA, a known epigenetic agent. Reports on the amplification of the genotoxic effects of the mitogenic substance mitomycin-C, as judged by the presence of micronuclei in cultured bovine lymphocytes in presence of RF radiations were reported.[25] A small but statistically significant enhancement of the effects of mitomycin-C on human lymphocytes after exposure to 935.2 MHz radiation for two hours has been described.[26]

Since from the above discussion it is not very confounding whether the radiofrequency causes cancerous changes we will like to review some studies which show the safety of these radiations

Evidence of Safety of Radiofrequency Radiations:

Current scientific evidence indicates that exposure to RF fields, such as those emitted by mobile phones and their base stations, is unlikely to induce or promote cancers. Several studies of animals exposed to RF fields similar to those emitted by mobile phones found no evidence that RF causes or promotes brain cancer. The United Kingdom NRPB Advisory Group on Non-ionising Radiation concluded that there is no firm quantitative evidence of a carcinogenic hazard from electromagnetic field exposures for the general public and workers in the electrical, electronics, and telecommunications industries.

A study showed that there was no increased glioma risk with regular mobile phone use, even when analog or digital phones were analyzed separately. However, ipsilateral tumor risk was borderline for usage ≥ 10 years, while risk for contralateral usage was not significant.[27] In-vitro studies of human glioma cells (MO54), measuring phosphorylation of various heat-shock proteins, showed no increased tumorigenic effects of mobile phone radiation.[28] Several studies, however, have not shown any association between intracranial malignancies and mobile telephone usage. Some of these studies have included exposures of >10 years, exposure from cordless phone base-units, or even predominant unilateral use.[29-33] Two time-trend analyses have been published highlighting the change in incidence of various tumors since the introduction of mobile phone technology. Both showed no significant rise in the incidence of intracranial malignancies despite the exponential growth of the mobile telephone industries.[34,35] Studies on other cancers[36] found no association between mobile phone usage and testicular cancers (seminoma and non-seminoma tumors). On study of lifetime exposures to mobile phone radiation as <10 hours, 10-100 hours and >100 hours and found no associations, for any of the groups, with incidence of NHL.[37] A study of malignant parotid tumors by[38] showed no association with mobile phone exposure, even when exposures exceeded 10 years.

A large-scale in vitro study was conducted focusing on low-level radiofrequency (RF) fields from mobile radio base stations employing the International Mobile Telecommunication 2000 (IMT-2000) cellular system to test the hypothesis that modulated RF fields induce apoptosis or other cellular stress response that activate p53 or the p53-signaling pathway.[39] Human glioblastoma A172 cells were exposed to W-CDMA radiation at SARs of 80, 250, and 800 mW/kg, and CW radiation at 80 mW/kg for 24 or 48 h. Under the RF field exposure conditions described above, no significant differences in the percentage of apoptotic cells were observed between the test groups exposed to RF signals and the sham-exposed negative controls, as evaluated by the Annexin V affinity assay. No significant differences in expression levels of phosphorylated p53 at serine 15 or total p53 were observed between the test groups and the negative controls by the bead-based multiplex assay. Moreover, microarray hybridization and real-time RT-PCR analysis showed no noticeable differences in gene expression of the subsequent downstream targets of p53 signaling involved in apoptosis between the test groups and the negative controls. This results confirm that exposure to low-level RF signals up to 800 mW/kg does not induce p53-dependent apoptosis, DNA damage, or other stress response in human cells.

Another study was conducted to demonstrate the effect of the RF on the molecular level that is DNA structural configuration. In this exposed human glioblastoma A172 cells and normal human IMR-90 fibroblasts from fetal lungs to mobile communication frequency radiation to investigate whether such exposure produced DNA strand breaks in cell culture. Under the same RF field exposure conditions, no significant differences in the DNA strand breaks were observed between the test groups exposed to W-CDMA or CW radiation and the

sham exposed negative controls, as evaluated immediately after the exposure periods by alkaline comet assays.[40] There have been earlier studies to investigate cytogenetic damage in human blood lymphocytes after exposure to 2450 MHz RF radiation conducted[41], immediately after the RF-radiation exposure; the lymphocytes were cultured to determine the incidence of chromosomal aberrations and micronuclei. The incidences of chromosomal damage, exchange aberrations and acentric fragments in the lymphocytes exposed to RF radiation (continuous or intermittent) were not significantly different from those in sham-exposed cells. Comparison of micronuclei in the lymphocytes exposed to RF radiation was not significantly different from that in the sham-exposed cells. When the continuous and intermittent exposures were compared, there were no significant differences in any of the cytogenetic parameters investigated. Another study conducted[42] found no chromosomal aberrations in antenna maintenance workers who had been exposed to various RF fields at least one hour each day for more than a year. Studies on bacteria, plant and animal cells exposed in vitro, where thermal effects can be directly observed and/or controlled, have failed to reveal direct evidence of DNA damage or repair, even at power densities up to 100 W/m² and SARs up to 20 W/kg.[43-49] Same results were obtained[50] that there was no cell transformation in similar experiments involving 836.55 MHz radiation. Even in the presence of cancer promoting agents, it was found that no epigenetic influence of RF radiation on the production of chromosomal aberrations by mitomycin-C or another mitogen, adriamycin.[51,52] A number of other studies have failed to demonstrate enhancement of the mutagenic action of chemical carcinogens.[53-55] It was reported that the chronic exposure to 2.45 GHz RF radiation had no effect on the incidence or size of colon cancers induced in mice by dimethylhydrazine.[56] No effect of exposure at the Japanese cellular phone frequency of 1.439 GHz for six weeks using the standard medium-term rat liver tumour promotion model, in which neoplastic foci are induced in the liver by diethylnitrosamine and partial hepatectomy were found.[57] Similar results for 929.2 MHz radiation had been reported previously.[58]

Case control study carried out in US[59], involving 782 cases of intracranial tumours of the nervous system identified between 1994 and 1998, and 799 hospital based controls. Use of mobile phones was by self report of type of mobile phone, start and end of time of use, duration of "regular" use, frequency of use, and hand used to hold the phone. Results when adjusted for socioeconomic variables and history of medical exposure to ionizing radiation showed no association between ever use or regular use of a cell phone and risk of any of the types of brain tumour (OR = 1.0 overall; 0.7 for high exposed group); nor was a higher risk identified for those with longer use, increasing duration or frequency or total cumulative use of cellular phones. No association was seen between laterality of tumor and laterality of phone use. A study of nearly 200,000 Motorola employees representing 2.7 million person-years of possible exposure between 1976 and 1996 was done. The investigators concluded that their findings "do not support an association between occupational RF exposure and brain cancers or lymphoma/leukemia. Also there are reviews conducted by number of authorities of the potential health risks associated with exposure to RF fields.[60]

The advice of the U.S. Health Physics Society (a professional society of specialists in radiation safety) is that there is no reason to believe that cellular base station towers could constitute a potential health hazard to nearby residents or students. [61]

Several groups in Great Britain have evaluated potential health effects of RF. The Advisory Group on Non-Ionizing Radiation (2003) updated the year 2000 report of the Independent Expert Group on Mobile Phones (2000) and concluded that "expos-

ures due to living near to base stations are extremely low, and the overall evidence indicates that they are unlikely to pose a risk to health.[62]

Even in mice exposed to 800 MHz RF radiation for 2 h/day, 5 days/week, for 35 weeks. When checked for end points included erythrocyte and leukocyte count, hemoglobin level, hematocrit, activity level, body weight and life span. No significant differences between the RF-radiation-exposed and sham-exposed groups were seen for any of these measures. [63] The mean life span of the exposed group (664 days) was slightly but not significantly longer than that of the sham-exposed group (645 days)

Conclusions:

The epidemiological evidence currently available does not suggest that RF exposure causes cancer. This conclusion is compatible with the balance of biological evidence, which suggests that RF fields below guidelines do not cause mutation, or initiate or promote tumour formation. However, mobile phones have not been in use for long enough to allow comprehensive epidemiological assessment of their impact on health, and we cannot, at this stage, exclude the possibility of some association between mobile phone technology and cancer. In view of widespread concern about this issue, continued research is essential. There is a pressing need for case-control studies to examine whether leukaemia and cancers of the brain, acoustic nerve and salivary gland are caused by mobile phone use.

We propose that large case-control studies of brain cancer, acoustic neuroma, salivary gland cancer, and leukaemia should be funded. We further recommend that this programme be financed by the mobile phone companies and the public sector (industry departments, health departments and the research councils)

The baffling evidence swaying in either direction of the prevailing controversy regarding relationship between EMR and mobile phone users is quite remarkable. With increasing number of users of this facility which is expected to increase 1.5 times in the next couple of years, the urgency to solve the puzzle should take a priority. It has been observed that the major fear lies with the populations residing in close proximity to the transmission base stations or EM towers which emit EMR continuously to power levels from a few watts to 100 watts depending on the "cell size" or area of coverage. If there are any risks, these are maximum for those living in the vicinity of larger cell size base stations.

The need to reconsider international guidelines developed by International Commission on Non-Ionizing Radiation Protection (ICNIRP) or by International Agency for Research on Cancer (IARC) becomes relevant on the basis of phenomenal increase in the number of service providers, mobile phone users, installations of new base stations near dense populations as also the fact that the population at risk has increased due to ever escalating population in almost every country.

In India and other countries where this facility is accessed by significantly higher population, there is a need to raise the level of understanding about this technology and EMR, to reduce any real or perceived threats. More research is required at the cellular and molecular level to critically and accurately assess the effects of different levels and duration of exposure of EMR. Based on such data and with an effective coordination between scientists, health authorities, industry and the public, revised public health information on this subject needs to be evolved. The time to clear the mist over this cancer controversy couldn't be any better than now when some of the service providers may be willing to join hands with the scientific community to observe safety measures or to reassure the user. The curiosity over the controversy may generate enough stress. It may not be the EMR but the stress related to the mys-

tery that may eventually kill. After all, don't they say, curiosity kills the cat!

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