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NON-IONIZING RADIATION, PART 2: RADIOFREQUENCY ELECTROMAGNETIC FIELDS

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IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

International Agency for Research on Cancer

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GENERAL REMARKS

This one-hundred-and-second volume of the *IARC Monographs* contains evaluations of the carcinogenic hazard to humans of radiofrequency electromagnetic fields. This is the second volume on non-ionizing radiation, after Volume 80 (Static and Extremely Low-Frequency (ELF) Electric and Magnetic Fields; IARC, 2002), and the fourth and last in a series on physical agents, after Volume 75 (Ionizing Radiation, Part 1: X- and Gamma-radiation, and Neutrons; IARC, 2000) and Volume 78 (Ionizing Radiation, Part 2: Some Internally Deposited Radionuclides; IARC, 2001). Solar radiation and ultraviolet radiation were evaluated in Volume 55 (IARC, 1992). The types of radiation evaluated as human carcinogens (Group 1) were revisited in Volume 100D (IARC, 2012). A summary of the findings in the present volume has appeared in *The Lancet Oncology* (Baan *et al.*, 2011)

The topic of this *Monograph* is the evaluation of the carcinogenicity of radiation in the radiofrequency (RF) range (30 kHz to 300 GHz) of the electromagnetic spectrum. This type of radiation is emitted by devices used in wireless telecommunication, including mobile phones, and by many other sources in occupational and general environmental settings. Exposures are ubiquitous in more developed countries and rapidly increasing in developing countries, in particular with respect to the use of mobile phones. There is rising concern as to whether exposure to RF radiation emitted by a mobile phone affects human health and, specifically, whether mobile-phone use increases the risk of cancer of the brain. The general public, manufacturers, regulatory authorities and public health agencies are seeking evidence on the safety of mobile-phone use. Consequently, there has been intense interest in the development and outcome of this *IARC Monograph*. This interest reflects the high prevalence of exposure (which increasingly extends to children), the vast scope of the telecommunications industry, the findings of some epidemiological studies that suggest an increased risk of cancer, and a high level of media coverage of the topic of mobile phones and cancer.

Although the preparation of this *Monograph* had been scheduled so as to include the results of the large international case–control study INTERPHONE on mobile-phone use (conducted in 2000–2004; published in 2010), it should be emphasized that the evaluations in this volume address the general question of whether RF radiation causes cancer in humans or in experimental animals: it does not specifically or exclusively consider mobile phones, but rather the type of radiation emitted by mobile phones and various other sources. Furthermore, this *Monograph* is focused on the potential for an increased risk of cancer among those exposed to RF radiation, but does not provide a quantitative assessment of any cancer risk, nor does it discuss or evaluate any other potential health effects of RF radiation.

The Working Group recognized that mobile-phone technology has transformed the world, making wireless communication rapidly available, especially in less developed countries, with important

benefits to society. With this, an increasingly large population will be exposed, and for longer and longer periods of time. Undoubtedly, questions will continue to arise about the health risks of mobile-phone use and possibly other emerging sources of exposure to RF radiation. This *Monograph* is a comprehensive review of the currently published evidence that also identifies gaps in the available information. These gaps should be resolved with further research if ongoing concerns about the health risks of mobile-phone use are to be addressed with greater certainty.

The Working Group agreed to consider three categories of human exposure to RF radiation: (a) environmental sources such as mobile-phone base stations, broadcast antennae, smart meters, and medical applications; (b) occupational sources such as high-frequency dielectric and induction heaters, and high-power pulsed radars; and (c) the use of personal devices such as mobile phones, cordless phones, Bluetooth devices, and amateur radios.

The general population receives the highest exposure from transmitters close to the body, including hand-held devices such as mobile phones, which deposit most of the RF energy in the brain. Holding a mobile phone to the ear to make a voice call can result in high specific rates of absorption (SAR) of RF energy in the brain, depending on the design and position of the phone and its antenna in relation to the head, the anatomy of the head, and the quality of the connection with the base-station antenna: the better the connection, which is ensured by a dense network of base stations, the lower the energy output from the phone. In children using mobile phones, the average deposition of RF energy may be two times higher in the brain and up to ten times higher in the bone marrow of the skull than in adult users. The use of hands-free kits lowers exposure of the brain to less than 10% of the exposure from use at the ear, but it may increase exposure to other parts of the body.

Typical environmental exposures to the brain from mobile-phone base stations on rooftops and from television and radio stations are several orders of magnitude lower than those from GSM (Global System for Mobile communications) handsets. The average exposure from DECT (Digital Enhanced Cordless Telecommunications) phones is around five times lower than that measured for GSM phones, and third-generation (3G) phones emit, on average, about 100 times less RF energy than second-generation GSM phones, when signals are strong. Similarly, the average output power of Bluetooth wireless hands-free kits is estimated to be around 100 times lower than that of mobile phones. In occupational settings, exposure to high-power sources may involve higher cumulative deposition of RF energy in the body than with exposure to mobile phones, but the energy deposited locally in the brain is generally less.

Epidemiological evidence of an association between RF radiation and cancer comes from time-trend, cohort, and case–control studies. The populations in these studies were exposed to RF radiation in occupational settings, from sources in the general environment, and from use of wireless (mobile and cordless) phones. Two sets of data from case–control studies were considered by the Working Group as the principal and most informative basis for their evaluation of the human evidence, i.e. the INTERPHONE study and the Swedish case–control studies; both sets of data focused on brain tumours among mobile-phone users.

The Working Group recognized not only the rapid increase worldwide in the use of wireless communication systems – both in number of users and in duration of use – but also the considerable technological developments in this area, with the introduction of third- and fourth-generation (3G and 4G) devices during the past decade. It is of interest to note that the key epidemiological studies mentioned above were conducted in the late 1990s and the early 2000s. In the INTERPHONE study, all participating countries in Europe had GSM networks. It is worth mentioning that the 3G and 4G

mobile phones commercially available today – equipped with adaptive power control – emit considerably less RF energy than the GSM phones used more than a decade ago.

Experimental evidence from cancer bioassays was evaluated by the Working Group after reviewing more than 40 studies that assessed the incidence of tumours in rodents exposed to RF radiation at various frequencies, some of which simulated emissions from mobile phones. In the evaluation of studies of cancer in experimental animals, exposure assessment deserves critical consideration. In this regard, the conduct of cancer bioassays with RF radiation presents challenges that are not ordinarily encountered in studies with chemical or other physical agents. For example, the radiation frequency is an important determinant of the specific absorption rate (SAR). The whole-body SAR provides little information about spatial or organ-specific energy deposition, as it strongly depends on field polarization and animal posture. Furthermore, long-term exposure to RF radiation at a fixed frequency and power density will result in substantial changes in SAR over time as an animal gains body weight. Even if the power is adjusted for body weight changes, the spatial distribution can vary. Full dosimetric analyses of all these variables are only available in a few studies. Furthermore, SARs to which animals can be exposed without the induction of systemic toxicity are generally limited by the induction of thermal effects; increases in body temperature may induce biological responses that are not seen at the (generally much lower) levels of RF radiation to which humans may be exposed. In a substantial number of studies, exposure was at SAR values below the maximum tolerated dose (MTD); nonetheless, these studies were considered to provide useful data, and were included in the evaluation.

Several cancer bioassays with RF radiation were conducted with exposure systems in which animals were restrained (usually in tubes) or non-restrained (in cages) during exposure. In this *Monograph*, study designs involving animal restraint were identified as such. Exposures involving animal restraint are generally limited to periods of no more than 4 hours per day. They have the advantage of optimal exposure uniformity and maximal local delivery of RF-radiation energy to the head or other selected body parts. Exposure of animals in cages – whole-body exposure – can be for up to 24 hours per day. The design of some bioassays with restrained animals included both sham-exposed and cage-control animals; because of the possibly confounding effects of restraint stress, the Working Group compared tumour responses in the exposed groups only to the responses in sham-exposed controls. Lack of a sham-exposed control group was considered a serious flaw in the study design.

The Working Group reviewed a large number of studies with end-points relevant to mechanisms of carcinogenesis, including genotoxicity, effects on immune function, gene and protein expression, cell signalling, oxidative stress, and apoptosis. Studies on the possible effects of RF radiation on the blood–brain barrier, and on a variety of effects in the brain itself were also considered. The Working Group found several studies inadequately controlled for the thermal effects of RF radiation, but also noted well conducted studies showing aneuploidy, spindle disturbances, altered microtubule structures or induction of DNA damage. While RF radiation has insufficient energy to directly produce genetic damage, other changes such as induction of oxidative stress and production of reactive oxygen species may explain these results. Indeed, several studies *in vitro* evaluated the possible role of RF radiation in altering levels of intracellular oxidants or activities of antioxidant enzymes. While the overall evidence was inconclusive, the Working Group expressed concern about the results from several of these studies.

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