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دور الإشعاعات الكهرومغناطيسية في تطور السرطان: مراجعة علمية

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المستخلص:

أدى التزايد المستمر في التعرض للإشعاعات الكهرومغناطيسية (Electromagnetic Radiation, EMR) في حياتنا اليومية إلى إثارة نقاشات علمية وصحية واسعة حول دورها المحتمل في التسرطن البشري. تقدم هذه المراجعة العلمية عرضًا شاملًا للأدلة المتاحة في الأدبيات العلمية الحالية بشأن تأثير الإشعاعات الكهرومغناطيسية في بدء السرطان وتطوره عبر مختلف أطياف الإشعاع. تُصنف الإشعاعات المؤينة والأشعة فوق البنفسجية (Ultraviolet Radiation, UV) بشكل قاطع على أنها مواد مسرطنة للإنسان، مع وجود علاقات واضحة بين الجرعة والاستجابة، إضافةً إلى آليات مباشرة لإحداث الضرر الجيني. وعلى النقيض من ذلك، فقد صنفت الوكالة الدولية لأبحاث السرطان (International Agency for Research on Cancer, IARC) حقول الترددات الراديوية (Radiofrequency Fields, RF) ضمن المجموعة (B٢)، أي «قد تكون مسرطنة للإنسان»، إلا أن هذا التصنيف لا يزال محل جدل علمي، كما يستمر النقاش حول التأثيرات الصحية للإشعاعات غير المؤينة، بما في ذلك الحقول الكهرومغناطيسية ذات التردد المنخفض جدًا (Extremely

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(Low–Frequency Electromagnetic Fields, ELF–EMFs). وتستعرض هذه المراجعة الأدلة الوبائية المستمدة من الدراسات الجماعية (Cohort Studies) ودراسات الحالات والشواهد (Case–Control Studies)، بالإضافة إلى الآليات البيولوجية المحتملة التي تشمل الإجهاد التأكسدي، والتغيرات اللاجينية (Epigenetic Changes)، والتأثيرات العصبية (Neurotropic Effects). كما تناقش الأطر التنظيمية الحالية التي تستند في معظمها إلى التأثيرات الحرارية للإشعاعات الكهرومغناطيسية. كما تُبرز تقييمات جودة الدراسات عددًا من أوجه القصور المنهجية الأساسية، بما في ذلك تضارب المصالح المحتمل، وعدم دقة أساليب تقييم التعرض، مما يحد من إمكانية تقدير المخاطر بصورة موثوقة. وتخلص المراجعة إلى أن التوسع العالمي المتزايد في التعرض لتقنيات الاتصالات من الجيل الخامس (G٥) والبنية التحتية المتوقعة للجيل السادس (G٦) يمثل أولوية ملحة في مجال الصحة العامة العالمية، ويؤكد الحاجة إلى تطوير سياسات تنظيمية قائمة على الأدلة العلمية لإدارة المخاطر السرطانية المحتملة بما يتماشى مع التطور التقني.

الكلمات المفتاحية: الإجهاد التأكسدي، الإشعاع المؤين، حقول الترددات الراديوية، التسرطن، الإشعاع الكهرومغناطيسي.

The Role of Electromagnetic Radiations in Cancer Development: A Review

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Abstract

The increase in electromagnetic radiation (EMR) in our daily lives has led to scientific and public health debate about EMR-related human carcinogenesis. This review provides a vigorous overview of current literature evidence on the impact of electromagnetic radiation in cancer initiation and development throughout the entire radiation spectrum. Ionizing

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and UV (ultraviolet) radiation are unequivocally classified as human carcinogens with well-defined dose-response relationships and direct genotoxic mechanisms. By contrast, radiofrequency fields have been classified as possibly carcinogenic to humans (Group 2B) by the International Agency for Research on Cancer (IARC), and this classification is still controversial; non-ionizing radiation includes even extremely low-frequency electromagnetic fields till now. This review summarizes epidemiological evidence from cohort and case-control studies, biologic mechanisms involving oxidative stress, epigenetic changes, and neurotropic effects, and scans current regulatory frameworks that appear largely to be based on thermal effects. Quality ratings have shed light on fundamental methodological flaws, including supposed conflicts of interest and deficient exposure assessment procedures that prevent risk estimation. The review also identifies the expanding global population exposure to fifth-generation (5G) and projected sixth-generation infrastructure as an urgent global public health avoidance priority, which also signifies a platform for addressing evidence-based policy reform towards potential carcinogenic risk management consonant with technology advancement.

Keywords: Oxidative stress, Ionizing radiation, Radiofrequency fields, Carcinogenesis, Electromagnetic radiation.

Introduction

Nowadays, daily exposure to presence of electromagnetic radiation (EMR) in contemporary environments has become a growing concern with respect to carcinogenicity. Electromagnetic radiation includes an extremely wide range of energy, from ionizing forms, such as X-rays and gamma rays)—established carcinogens that directly damage DNA—to non-ionizing forms such as electromagnetic fields (EMF) in the extremely low-frequency (ELF) range emitted by power lines or radiofrequency (RF). EMF is emitted by telecommunication infrastructure or wireless communication devices (IARC, 2013). The International Agency for Research on Cancer classifies electromagnetic radiation (EMR) by carcinogenic risk. Examples of ionizing radiation (e.g., X-rays, gamma rays) are listed as Group 1 (carcinogenic to humans), with evidence strongly supporting an association with cancers.

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Radiofrequency electromagnetic fields (Category 2B: possibly carcinogenic for humans; evidence in humans is limited). Depending on available data, other exposures may be Group 2A (probably carcinogenic) or Group 3, which are not classifiable (IARC, 2013).

Wireless technology has diffused globally and fundamentally changed how humans are exposed to RF electromagnetic fields. Given the fact that there are around five billion mobile phone subscriptions worldwide and an increasing global rollout of fifth-generation (5G) networks, the general public is exposed to higher levels of chronic, low-level radiofrequency (WHO 2020). Meanwhile, ELF magnetic fields from living near high-voltage power lines and electrical installations remain a public health issue, in particular for childhood leukemia. The IARC classifies ELF magnetic fields as Group 2B carcinogens based on epidemiological evidence of a consistent, albeit weak, association with childhood leukemia risk (IARC, 2002). These classifications highlight an essential difficulty of radiation toxicology: separating real biological effects from artifacts due to methodological limitations, confounding factors, and the inherent complexity of measuring long-term multi-factorial exposures (IARC, 2013; WHO, 2020).

Recently, the WHO commissioned systematic reviews designed to summarize the vast literature investigating potential cancer risks associated with exposure to RF radiation (Karipidis et al., 2024). They determined that there exists "moderate certainty evidence" that mobile phone use may not increase the risk of glioma, meningioma, acoustic neuroma, pituitary tumors, salivary gland tumors, or pediatric brain tumors. However, independent scientific organizations such as the International Commission on the Biological Effects of Electromagnetic Fields (ICBE-EMF) have strongly challenged these conclusions due to severe methodological problems, biased inclusion criteria, and possible conflicts of interest that render the review's claims unsustainable (Frank et al., 2024). Hardell and Nilsson (2025) also showed that the WHO-commissioned review had systematically omitted studies showing increased risk at the highest levels of exposure, or with the longest latencies, which may disguise real exposure-response relationships.

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Such academic dissonance demonstrates the extent of the challenges in producing credible epidemiology on this topic and highlights lack of specificity in exposure assessments (Hardell, 2024; Hodge, 2022) together with the decades-long wind-up effect are also called into question for their role in researcher financial malfeasance during these times through non-disclosure agreements (NDAs) between proponents and researchers (Parker et al., 2019; Schoemaker et al., 1998).

At least at the biological plausibility level (for which the mechanistic basis considers data that go beyond purely epidemiological), there is compelling evidence in favor of non-ionizing radiation carcinogenesis. Experimental studies are accumulating evidence to consider RF radiation as a non-thermal biological effect that includes oxidative stress, DNA strand breaks, and changes in gene expression profiles (ICBE—EMF 2022). It remains to be clarified whether these molecular perturbations are mediated via the generation of reactive oxygen species influencing cellular signaling pathways in such a manner as to render a cell 'permissive' for malignant transformation, underlying the danger of any such non-ionizing injury. In addition, RF radiation neurotropism—demonstrated by differentiation to neurons in experimental models of blood–brain barrier permeability and neuronal injury—provides a mechanism that could explain associations between mobile phone exposures and central nervous system malignancies (ICBE-EMF, 2022).

Conducting a thorough and unbiased assessment of the cancer-causing potential of EMR is not merely an academic concern; it also holds pressing consequences for public health policy. The current exposure guidelines developed by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) are mainly based on thermal effects, while dismissing the overwhelming evidence of biological effects at intensities that are far below these thresholds (ICBE-EMF 2022). As technological innovation is always faster than HIA, the introduction of new wireless technologies such as 5G networks operating at higher frequencies and possible deployment of 6G requires a precautionary approach based on a full and open scientific assessment. The objective of this review is to provide a critical synthesis of

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the present evidence on electromagnetic radiation as a carcinogen, highlighting epidemiological, experimental, and mechanistic data needed to understand gains made in the knowledge base, what uncertainties remain, and how they may be offset through science-based recommendations for public health protection in an increasingly electrified environment (Hardell&Nilsson, 2025; ICBE-EMF, 2022).

Carcinogenic Risk Profiles of Electromagnetic Radiation

The electromagnetic spectrum is a continuous range of types of radiation arranged by wavelength, frequency, and photon energy; the carcinogenic potential across this spectrum can thus change quite dramatically (Table 1). Low energy ionizing radiation such as X-rays, gamma rays, and particulate radiation has enough energy to displace orbital electrons from atoms, creating reactive ions directly capable of DNA damage, strand breaks, and chromosomal aberrations (Hall&Giaccia, 2019). This direct genotoxic mechanism explains the well-established carcinogenicity of ionizing radiation, which is classified as Group 1 (carcinogenic to humans) by the International Agency for Research on Cancer (IARC) in all exposure scenarios evaluated to date (IARC 2012). The carcinogenic risk is dose-dependent, where acute expiratory, high-dose exposure induces deterministic effects and chronic low-dose exposure generally increases stochastic cancer risks in a probabilistic fashion, which is currently modeled using the linear no-threshold hypothesis (National Research Council, 2006).

Ultraviolet (UV) radiation is a type of non-ionizing radiation located between visible light and X-rays in the electromagnetic spectrum, which is the most important environmental carcinogen associated with almost all types of skin cancer. Traditionally, UV radiation has been divided into UVA (315–400 nm), UVB (280–315 nm), and UVC (100–280 nm) wavelengths, with UVB being the most carcinogenic part of this spectrum, showing high efficiency in the induction of cyclobutane pyrimidine dimers and 6-4 photoproducts after absorption by DNA molecules (Ravanat et al., 2001). The International Agency for Research on Cancer (IARC) have 2

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categorized UV-emitting tanning devices as Group 1 carcinogens 3 and solar radiation also as Group I; epidemiological data show strong dose-response relationships for both melanoma and non-melanoma skin cancers (IARC, 2012). El Ghissassi et al. (2009) reported that the global burden of all UV-induced carcinomas remains on the rise, especially amongst light-skinned populations and those with increasing patterns of recreational sun exposure.

Extremely low-frequency electromagnetic fields (ELF-EMF), which are produced by electrical power transmission and distribution systems, household appliances, and industrial equipment, have frequencies that lie below 300 Hz. The carcinogenicity of ELF magnetic fields is still controversial despite decades of epidemiological research. In 2002, the IARC determined that ELF magnetic fields should be classified as Group 2B (possibly carcinogenic to humans) according to the infrequent correlations in epidemiological studies associating increased risk of childhood leukemia with residential exposure to magnetic fields above an intensity threshold of 0.3–0.4 microtesla (IARC, 2002). Kheifets et al. (2010) have characterized these exposures at 1–2 μg/m3; pooled analyses by Mergency et al (2010) show a pooled odds ratio of approximately 2.0 for childhood leukemia; yet lack of strong biological evidence and uncertainty in exposure assessment prevent more definitive classification. However, ELF electric fields have not been accused similarly, indicating that perhaps only the magnetic field components are biologically active, either via magnetite biomineralization or radical pair reactions (Henshaw 2002).

Due to the extensive implementation of wireless telecommunications technologies, radiofrequency electromagnetic fields (RF-EMF), covering frequency bands from 3 kHz up to and including 300 GHz, currently represent the most rapidly growing type of human exposure. The odds of glioma were statistically significantly elevated by 40% in the highest decile of cumulative call time according to the Interphone study; nevertheless, this association was obscured by methodological limitations including differential participation and recall biases (Interphone Study Group, 2010). Recent systematic reviews by Karipidis et al. (2024) imply that cell phone usage may be a cause of brain tumors; however, the (nonprofit and

independent) researchers criticized these results, noting that positive association studies were omitted from the analysis (Hardell&Nilsson, 2025).

The biological interactions of microwave radiation applied at the higher end of the radiofrequency (RF) spectrum (300 MHz to 300 GHz) and biological systems are similar to those of lower frequency RF fields, with the primary mechanism at high intensities being tissue heating. Extrapolations from the much larger body of RF-EMF literature are heavily relied upon for assessments of the potential of microwave exposure to be carcinogenic, as epidemiological data of effects of microwave is still relatively limited (Repacholi, 2012). The millimeter-wave spectral region (30–300 GHz), which is the foundation of imminent 5G networks and expected future 6G telecommunications infrastructure, remains a domain with high scientific unknowns. Established exposure guidelines for this frequency band are primarily based on thermal effects, as the depth of penetration of the tissue is small (Simkó&Mattsson, 2019).

For static electric and magnetic fields—for instance, those produced by magnetic resonance imaging (MRI) devices and direct current (DC) transmission lines—there is insufficient evidence for classification, according to the International Agency for Research on Cancer (IARC). Static magnetic fields were therefore grouped in Group 3 (agents not classifiable as to their carcinogenicity) on the basis that both clinical evidence is limited and conflicting results have been obtained in the few experimental studies (IARC, 2002). Static fields do not result in tissue heating (and thus thermal effects) nor do they directly ionize molecular structures; however, mechanisms with biological plausibility for carcinogenic effects have been hypothesized, for example, by the radical pair mechanism and magnetoreception (Hore&Mouritsen, 2016).

Given the heterogeneity of carcinogenic risk across the electromagnetic spectrum, radiation-specific approaches are needed for both exposure assessment and risk mitigation. In the case of ionizing radiation, risk is expressed as a function of absorbed dose (in gray) as well as equivalent dose (in sievert), etc., and there are dose limits for both occupational and general public exposure. In contrast, non-ionizing fractions of the International

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Commission on Non-Ionizing Radiation Protection (ICNIRP) guidelines are based primarily on specific absorption rate (SAR) thresholds designed to avoid measurable thermal warming of biological tissue and do not consider possible non-thermal biological endpoints that influence carcinogenic mechanisms. The two-tiered approach to regulation is representative of the basic difference in the mechanisms of underlying biological interactions; however, it may fall short in addressing the growing body of evidence supporting low-intensity, non-thermal effects, especially in situations of chronic and widespread RF-EMF exposure as is common in today's environment (ICNIRP, 2020).

Table 1. Classification of Electromagnetic Radiation Types, Physical Characteristics, and Carcinogenic Risk Profiles (El Ghissassi et al., 2009)

Principal Exposure Sources	Key Cancer Associations	IARC Carcinogen Classification	Primary Interaction Mechanism	Wavelength Range	Radiation Type
Medical imaging, radiotherapy, nuclear fallout, radon decay products	Leukemia, thyroid cancer, breast cancer, lung cancer, solid tumors	Group 1 (Carcinogenic to humans)	Direct DNA ionization, double-strand breaks, chromosomal aberrations	<1 nm	Ionizing radiation (X-rays, gamma rays)
Solar radiation, artificial tanning devices, welding arcs	Cutaneous melanoma, basal cell carcinoma, squamous cell carcinoma	Group 1 (Solar radiation); Group 1 (UV-emitting tanning devices)	DNA absorption, pyrimidine dimer formation, oxidative damage	10–400 nm	Ultraviolet (UV) radiation
High-voltage power lines, electrical transformers, household wiring	Childhood leukemia (limited evidence)	Group 2B (Possibly carcinogenic to humans)—magnetic fields only \	No ionization; hypothesized radical pair mechanisms, magnetite interactions	>1 Mm	Extremely low-frequency electromagnetic fields (ELF-EMF)
Mobile phones, base stations, Wi-Fi, broadcast transmitters	Glioma, acoustic neuroma (limited evidence in heavy users)	Group 2B (Possibly carcinogenic to humans)	Tissue heating (thermal effects); non-thermal effects under investigation	1 mm–100 km	Radiofrequency electromagnetic fields (RF-EMF)

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Radar systems, microwave ovens, telecommunications	Brain tumors (inferred from RF-EMF literature)	Group 2B (as subset of RF-EMF)	Dielectric heating, rotational molecular excitation	1 mm–1 m	Microwave radiation

Epidemiology of radiation-induced carcinoma

Radiation-associated carcinomas are the best-studied poison exposures in environmental oncology, both from ionizing and non-ionizing electromagnetic radiation. No question, ionizing radiation, such as medical diagnostic exposures, occupational exposures, and environmental sources, especially radon, behaves like a m/human carcinogen with strong dose–response relationships, consistently observed across large cohort studies (Brenner et al., 2003). The Life Span Study of Hiroshima and Nagasaki atomic bomb survivors is the foundational study for radiation epidemiology, showing that leukemia, breast cancer, thyroid cancer, and lung cancer risks increase with radiation dose (excess relative risks persisting up to decades after exposure) (Ozasa et al., 2012). The data presented have been pivotal in the establishment of the linear no-threshold model which grounds present-day radiation protection standards, although the appropriateness of this model for low-dose exposure continues to be debated (Tubiana et al., 2009). Medical radiation is an important and increasing source of population exposure. We can see measurable increases in cancer incidence, especially among pediatrics, for computed tomography (CT) scans, which have effective doses that are orders of magnitude greater than those from conventional radiography. Children exposed to cumulative CT doses of 50 mGy are at threefold increased risk for leukemia and 2.5 fold increased risk for brain tumors (Pearce, et al., 2012) Similarly, Mathews et al. (2013) conducted a meta-analysis from a large Australian cohort study including 680000 young adults indicated that CT exposure resulted in an overall increase by 24% for all types of cancer with a dose-response gradient consistent with causation. These data have led to efforts by international bodies to improve radiological protocols and reduce unnecessary imaging, reflecting the principle of as low as reasonably achievable (ALARA) in clinical practice (Hricak et al., 2011).

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Presented here are important lessons on the carcinogenic potential of occupational radiation from chronically exposed worker cohorts. This 15-country pooled analysis of monitored nuclear industry workers, more than 400 000 in total, showed a strong association between protracted low-dose photon exposure and all cause cancer mortality with an excess relative risk consistent with the high-dose atomic bomb survivor data (Cardis et al., 2005). Rates of lung cancer among uranium miners exposed to radon and its decay products show well-described increases, with pooled analyses of European cohorts (Darby et al., 1995) and North American cohorts, both consistently establishing a linear exposure-response relationship, without indication of a threshold. Such occupational studies, especially those that include careful internal comparisons and detailed dosimetric reconstruction, are unique strengths as they help minimize the healthy worker effect (Lubin et al., 1995).

The epidemiology of carcinomas secondary to non-ionizing radiation is bedeviled by significantly greater methodological problems and misunderstanding in interpretation. In 2011, the International Agency for Research on Cancer (IARC) classified RF-EMF as Group 2B (possibly carcinogenic to humans) based primarily on epidemiological evidence from Interphone and pooled analyses by Hardell&Carlberg (2015) suggesting elevated risks of glioma and acoustic neuroma in heavy mobile phone users IARC (2013). Although several earlier studies had shown increasing risk of glioma with high levels of use, one well-known study using a multinational case-control design reported 40% excess odds of glioma in the highest decile group for cumulative call time (Interphone Study Group, 2010), but this finding was coupled with uncertain methods, including potential selection and recall biases. Subsequent updates from the CERENAT study in France corroborated these associations, demonstrating a two- to threefold increased risk of glioma and meningioma among heavy mobile phone users, particularly those with ipsilateral exposure (Coureau et al., 2014).

Epidemiological studies regularly demonstrate a twofold increased risk for childhood leukemia associated with exposure to extremely low-frequency magnetic fields (ELF-MF) above the residential level of ~0.3–0.4

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microtesla, as consistently reported in pooled analyses (Kheifets et al., 2010). The landmark study of Greenland et al. (2000) reported that the association of SSRIs and perinatal outcome is statistically significant (albeit modest), unlikely to entirely reflect confounding or selection bias. Nevertheless, a clear biological mechanism has yet to be identified in supportive studies, and there is inconsistency between different animal models that would allow for a definitive classification of ELF-MF as a carcinogen, which is why the IARC retains its categorization as Group 2B (IARC, 2002).

Examples of more recent epidemiological advances include the Million Women Study in the UK and investigated mobile phone use and cancer occurrence among 800,000 women. Benson et al. The lack of an overall increased risk for brain tumours related to mobile phone use (later, 2013) only revealed when considering data with a relatively short follow-up; meaning this study subsequently lacked enough time to properly assess the risks associated with long-latency malignancies such as some tumours. In contrast, National Toxicology Program (NTP) toxicology and carcinogenesis studies of rodents exposed to RF radiation show weaker but somewhat supportive evidence of carcinogenic potential, presenting statistically significant increases in schwannomas of the heart and glioma tumors in high-dose male rats, although external validity for human exposure scenarios is controversial (Wyde et al. 2018).

Novel exposure modalities (including the physical spatial/temporal footprint of fifth-generation telecommunications infrastructure and millimeter-wave technologies) further complicate the epidemiological landscape of radiation-induced carcinomas. Because of the recent implementation of 5G networks, there is currently no epidemiological data focused on health impacts due to 5G exposure, which warrants prospective cohort designs with detailed assessment of the levels at which individuals are exposed in order to assess causal links to carcinogenic risk. At a basic level, the intrinsic limitations of observational epidemiology, such as exposure misclassification (especially in case–control studies), latency issues, and contemporary reliance on wireless devices that use available non-ionizing radiation, constrain firm conclusions

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about whether non-ionizing radiation from wireless devices leads to cancer (Simkó&Mattsson 2019).

Biological Mechanisms of Carcinogenesis induced by radiation

Electromagnetic radiation has a multitude of biological effects, with its carcinogenic potential mediated by mechanisms that reflect the interacting influences of inherent energy, exposure characteristics, and susceptibility in target tissue. Carcinogenesis induced by ionizing radiation occurs primarily via direct and indirect genotoxic pathways, while non-ionizing radiation acts through mechanisms, such as oxidative stress, signal transduction disruption, and epigenetic modification of genes that create conditions conducive to malignant transformation. A mechanistic understanding of the pathways is necessary to build biologically plausible connections between radiation exposure and cancer risk, particularly for non-ionizing forms in which epidemiologic associations remain controversial (Hall&Giaccia 2019).

Ionizing radiation delivers energy to tissues as a result of excitation and ionization events, creating reactive oxygen species (ROS) through radiolysis of water molecules—the most abundant molecule in biological systems. This group also includes ROS, including hydroxyl radicals, superoxide anions, and hydrogen peroxide, which can cause DNA base lesions as well as sugar-phosphate backbone lesions, resulting in single-strand breaks, double-strand breaks, or complex clustered lesions fundamental resistant to known cellular repair machinery (Cadet et al., 2017). In general, DNA lesions are divided into two major types: indirect or direct damage. Unfortunately, DSBs are perhaps the most cytotoxic and mutagenic type of lesion since misrepair or incomplete repair leads to chromosomal aberrations, translocations, and gene fusions that may produce oncogene activation or tumour suppressor gene inactivation. Retinoblastoma (RB) exemplifies the paradigm of radiation-induced carcinogenesis, as ionizing radiation exposure increases the risk of developing second primary cancers through inactivation of the RB1 tumor suppressor gene, and thyroid cancer following childhood irradiation is characterized by chromosomal rearrangements leading to RET/PTC fusions, which are signature molecular events (Nikiforov 2006).

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The type and extent of DNA damage induced is governed by the linear energy transfer (LET) of radiation. Some radiation has higher relative biological effectiveness; specifically, the dense ionizing (high-LET) alpha particle tracks produced by radon decay products are known to produce complex clusters of DNA damage that have a lower probability of being correctly repaired compared to sparsely ionizing (low-LET) photon radiation. This mechanistic differentiation is critical as the dose-response relationships derived from low-LET gamma or X-ray exposures may be insufficient to describe risks following high-LET alpha particle exposure in uranium miners and radon-exposed populations (Goodhead, 2006).

Oxidative Stress and Chronic Inflammation

Because non-ionizing radiation such as radiofrequency electromagnetic fields (RF-EMF) and extremely low-frequency electromagnetic fields (ELF-EMF), does not have high enough photon energy to induce direct ionization of biomolecules. As such, carcinogenic mechanisms will need to occur via other routes, with oxidative stress emerging as the unifying hypothesis. Recent experimental works showed that RF-EMF can produce ROS, significantly decrease the activities of antioxidant enzymes (for instance, superoxide dismutase, catalase, and glutathione peroxidase), as well as cause both lipid peroxidation and protein oxidation. This oxidative cellular environment induces DNA base alterations, notably 8-hydroxy-2'-deoxyguanosine (8-OHdG), leading to G:C→T: A transversion errors if not repaired before the DNA replication cycle (Yakymenko et al., 2016).

This feeds into ongoing chronic oxidative stress, which further sustains a pro-inflammatory microenvironment permissive to neoplastic progression. Studies have indicated that RF-EMF exposure can activate pro-inflammatory cytokines including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and vascular endothelial growth factor (VEGF) via upregulation of transcription factors such as nuclear factor-kappa B (NF-κB) and activator protein 1 AP-1. Angiogenesis, remodeling of the extracellular matrix, and immune evasion are hallmark capabilities that enable tumor initiation and progression; these are promoted by several mediators. Accordingly, chronic low-grade inflammation triggered by long-term RF-EMF exposure could be

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an important mechanistic link between environmental exposure and cancer initiation, specific to proliferative tissues or for protracted exposures (Toledano-Macías et al., 2024).

Gene expression and epigenetic modifications

In addition to frank genetic damage, radiation exposure causes heritable epigenetic changes that affect gene expression without altering the DNA sequence. Ionizing radiation is associated with global hypomethylation and gene-specific hypermethylation of DNA, especially at promoter regions of tumor suppressor genes (p16INK4a and MLH1), affecting expression silencing, cell cycle regulation, and deficient DNA mismatch repair. MicroRNA [miRNA] dysregulation induced by radiation alters oncogenic and tumor suppressor pathways at additional levels, with some miRNAs (such as miR-21, miR-155 and miR-34a) exhibiting expression profiles persisting possibly down to the next generation of cells (Koturbash et al., 2016).

Like RF-EMF exposure, it can cause epigenetic changes; however, the mechanistic pathways are less well defined. Data on changes in gene expression patterns, which affect cell proliferation and apoptotic processes due to altered DNA methylation patterns and histone modifications after chronic RF-EMF exposure, have been reported. Together, these epigenetic perturbations may cumulatively compromise genomic integrity and potentiate tumorigenic susceptibility over the life course when exposures occur during developmental windows associated with rapid epigenetic remodeling (Zothansiama et al., 2017).

Neurotropic Impact and Compromise of the Blood-Brain Barrier

The exclusive sensitivity of the CNS to RF-EMF-induced carcinogenesis is thought to be due to neurotropic biological effects leading to impaired integrity of neural tissues. In experimental studies, RF-EMF exposure is shown to increase blood–brain barrier permeability, leading to changes in tight junction protein expression, which may allow neurotoxic agents, inflammatory mediators, and circulating carcinogens into the brain

parenchyma (Salford et al., 2003). Moreover, neuronal damage resulting from RF-EMF exposure that manifests as chromatolysis and edema of the neuron with abnormal neurotransmitter metabolism forms a microenvironment in the tissue, which promotes transformation to glial cells. The differential absorption of RF energy in brain tissues during mobile phone use, the paucity of regenerative capacity of neurons, and long latency periods for glioma development collectively offer a biologically plausible underpinning to the epidemiological links observed between heavy mobile phone use and risk of brain tumor. These neurotropic mechanisms may act in concert with genetic predisposition and/or concomitant environmental exposures to delineate the probability of cancer for an individual (Hardell&Carlberg, 2015).

Conclusion

This review investigates the connection between electromagnetic radiation (EMR) and carcinogenesis throughout the complete spectrum of radiation. Mechanisms directly linked to ionizing radiation (IARC Group 1), such as X-rays and gamma rays, as well as UV radiation, are characterized by direct DNA damage at the molecular level, where cancer risk increases with increasing dose. The same is a far more complex story as pertains to non-ionizing radiation—so-called extremely low frequency (ELF) fields and radiofrequency (RF) fields from phones, wifi, etc. Based on limited evidence linking regular use of mobile phones with brain tumours, RF-EMF is classified in Group 2B (possibly carcinogenic to humans) by the IARC; however, a meta-analysis has suggested an increased risk or dose–response relationship in some studies, and such epidemiological results have been inconsistent and contested. Biological mechanisms for non-ionizing radiation include oxidative stress, DNA damage through reactive oxygen species (ROS), chronic inflammation, epigenetic modification, and blood-brain barrier intervention, but these remain untested. The criticism of current regulations based on thermal effects only is that it does not take into account non-thermal biological effects. The review recognizes the need for available precautionary measures; improved assessment of exposure and independent

research to address uncertainties as 5G extends and new technologies are developed.

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