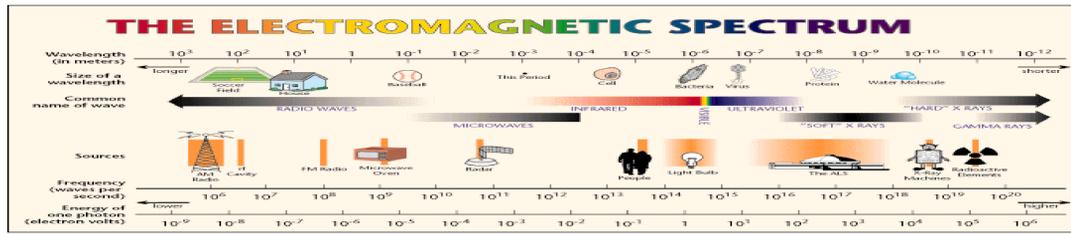


Non-ionizing and Ionizing Radiations : Recent Highlights

Fatiha EL Ghissassi on behalf of the IARC Monograph Programme



Radiofrequency electromagnetic fields (RF-EMF): classified in Group 2B "Possibly carcinogenic to humans"

Background

- Human exposures to RF-EMF: frequency range 30 kHz–300 GHz
- Probably most prevalence human exposure (some 5.5 billion people) and public concern of hazard

Personal devices

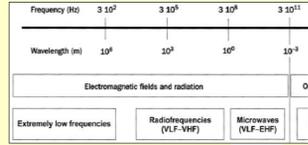
- Mobile telephones, cordless phones
- Bluetooth, amateur radios

Occupational sources

- High frequency dielectric and induction heaters
- High-powered pulsed radars

Environmental sources

- Mobile-phone base stations, broadcast antennas
- A voice call can result in high specific RF energy absorption-rate (SAR) values in the brain.
- Use of hands-free kits lowers GSM phones exposure to the brain to below 10% of the exposure from use at the ear, but it might increase exposure to other parts of the body.



Case-control studies on glioma and use of mobile phones

Studies	Cases/Controls	Mobile and/or Cordless-phone use	OR (95%CI)
INTERPHONE study ¹ (2010)	2708/2438	Ever use vs never use Cumulative call time •Deciles 1-9 •Highest decile > 1640 h of use	0.81 (0.70–0.94) ≤ 1 1.40 (1.03–1.89)
Swedish research group ² (2011)	1148/2972	> 1 year of use > 2000 h of use	1.3 (1.1–1.6) 3.2 (2.0–5.1)

Ipsilateral use of the mobile phones and cordless phones was associated with higher risk

Epidemiological studies

- Multicountry INTERPHONE case-control study¹ on mobile phone and brain tumour including glioma, acoustic neuroma, and meningioma
- Studies from a Swedish Research Group²
- Pooled analysis of two very similar studies on mobile and cordless phone and glioma, acoustic neuroma and meningioma

IARC Working Group Conclusion

Both Studies are susceptible to bias (recall error and selection for participation).

A causal interpretation between mobile phone RF-EMF exposure and glioma is possible.

Similar results obtained for acoustic neuroma but not for meningioma.

Mechanisms of carcinogenesis: "Weak evidence" relevant to RF-EMF-induced cancer in humans
Evidence of an effect of RF-EMF on some of endpoints: genotoxicity, effects on immune function, gene and protein expression, cell signalling, oxidative stress, apoptosis, effects on the blood-brain barrier and on the brain

In view of the "limited evidence" in humans and in experimental animals, the IARC Working Group classified RF-EMF as "possibly carcinogenic to humans" Group 2B

- References**
- INTERPHONE Study Group. Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case-control study. *Int J Epidemiol* 2010; **39**: 675–94.
 - Hardell L, Carlberg M, Hansson Mild K. Pooled analysis of case-control studies on malignant brain tumours and the use of mobile and cordless phones including living and deceased subjects. *Int J Oncol* 2011; **38**: 1465–74.

Radon-222 reaffirmed "carcinogenic to humans" Group 1

Background

- Radon-222 is a radionuclide that emits α -particles
- Densely ionising radiation with low capacity to penetrate tissue (< 0.1 mm)
- Health hazards occur after internal deposition
- Indoor-exposure:** mainly through contaminated indoor air by radon released from soil and building materials
- Occupational exposure:** in uranium and underground haematite-mining

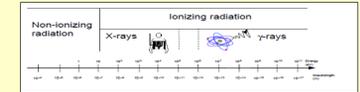
Burden of cancer

"Sufficient evidence" for lung cancer after exposure to indoor-residential exposure

- Cohort studies on uranium and haematite miners confirmed previous assessments of an increased risk of lung cancer.
- Combined analyses of case-control studies on indoor-residential exposure now provided clear evidence of an increased risk of lung cancer⁴.
- Risk of lung cancer attributed to radon in Europe and North America is about 8-15%.
- Radon is one of the main causes of lung cancer after tobacco smoke.

- References**
- Darby S, Hill D, Auvinen A, et al. (2005) Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. *BMJ*; **330**: 223.

X-radiation and γ -radiation reaffirmed "carcinogenic to humans" Group 1



Background

- X and γ -radiations are produced by some α - and β -particle emitters and nuclear reactions including those from the sun and from cosmic radiations
- X-radiations are photons emitted from the electron shell
- γ -Radiations are from the atomic nucleus and particles annihilation
- Highly ionizing forms of energy
- X-radiations: down to a few 10 eV
- γ -radiation: up to a few 10 MeV
- High capacity to penetrate and damage living tissue
- They interact primarily with orbital electrons

Major study populations

- Atomic-bomb survivors
- Medical patients (diagnostic or therapy)
- In-utero* exposure (offspring of pregnant medical patients and atomic-bomb survivors)

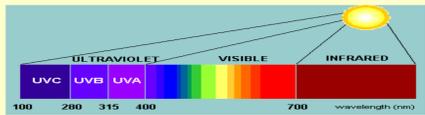
Epidemiological studies

Group-1 agent	Tumour sites on which "sufficient human evidence" is based
X- and γ -radiation	Salivary gland, oesophagus, stomach, colon, lung*, bone, skin (BCC), female breast*, urinary bladder, brain and CNS, leukaemia* (excluding CLL), thyroid*, kidney* (atomic-bomb survivors, medical patients) <i>In-utero</i> exposure (multiple sites, above-mentioned cancers and childhood cancers) ^{7,8}

* New target sites identified since the previous IARC evaluation (2000)⁹

- References**
- Preston DL, Cullings H, Suyama A, et al. (2008) Solid cancer incidence in atomic bomb survivors exposed in utero or as young children. *J Natl Cancer Inst*; **100**: 428–36.
 - Wakeford R, Little MP. (2003) Risk coefficients for childhood cancer after intrauterine irradiation: a review. *Int J Radiat Biol*; **79**: 293–309.
 - IARC (2000). Ionizing radiation, Part 1: X- and gamma radiation and neutrons. *IARC Monogr Eval Carcinog Risks Hum*; **75**: 1–492

UV-emitting tanning devices classified in Group 1 "carcinogenic to humans" Solar radiation reaffirmed "carcinogenic to humans"



Background

- Solar radiation is the main source of human exposure to ultraviolet (UV) radiation
- Artificial sources of UV: Sunbeds and Sunlamp
- Use widespread in many developed countries
- Users are mainly young women

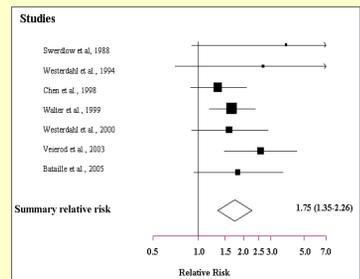
Epidemiological studies

Meta-analysis

- Increase risk of skin melanoma by 75% when use starts before ~30 years of age
- In line with known susceptibility to carcinogenic effects of solar radiation at younger ages

Case-control studies

- Causal association for ocular melanoma particularly choroid and ciliary body



Relative risk for cutaneous melanoma associated with first use of indoor tanning equipment at age < 35 years³

Group-1 agent	Tumour sites with "sufficient evidence" in humans
Solar radiation	Skin: BCC, SCC, melanoma
UV-emitting tanning devices	Skin: melanoma particularly choroid and ciliary body

SCC: Squamous cell carcinoma; BCC: basal cell carcinoma

Ultraviolet radiations (bandwidth 100-400 nm encompassing UVC, UVB and UVA) are classified in Group 1 "carcinogenic to humans" based on mechanistic evidence

- Overlapping profile of DNA adducts (OH-dG and thymine glycol) and pyrimidine dimers (PDs) observed depending on the radiation wavelength and cell type and species.
- PDs produced after exposure to either UVA or UVB in human skin ex-vivo resulting in C→T transitions
- C→T transitions detected in humans and animal cells exposed to UVA, UVB or UVC
- Such transitions are detected in *TP53* gene of human skin SCC and solar keratosis.
- Mutations in *p53* gene of hair-less mice can be induced by UVA, at the same hotspots well-known for UVB induced tumours.
- C→T transitions are not a specific "fingerprint" for UVA, UVB or UVC
- Any of the UV radiation subtypes may be at the origin of the carcinogenesis initiation.
- In the previous IARC Monograph (1992)⁴, UVA, UVB and UVC were classified in Group 2A "probably carcinogenic to humans"

Welding: "sufficient evidence" for increased risk of ocular melanoma based on epidemiological studies

- Welders are also exposed to other harmful agents, therefore this association could not be attributed specifically to UV radiation.
- A full review of the carcinogenic hazards of welding will be undertaken by IARC with high priority.

- References**
- IARC Working Group (2006) The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: a systematic review. *Int J Cancer*; **120**: 1116–22.
 - IARC (1992) IARC Monographs on the evaluation of carcinogenic risks to humans. Solar and ultraviolet radiation. *IARC Monogr Eval Carcinog Risks Hum*; **55**: 1–316.

Radioiodines including Iodine-131 reaffirmed "carcinogenic to humans"

Background

- Radioiodines are radionuclides emitting β -particles.
- Less ionising but more penetrating (up to few millimetres).
- The health hazards occur after internal deposition.

Accidental sources

- Windscale fire (1957, UK) and Three Mile Island (1979, USA)
- Chernobyl (1986, USSR)
- Fukushima (2011, Japan)

Medical exposure

- Treatment of hyperthyroidism and cancer of thyroid

Epidemiological studies

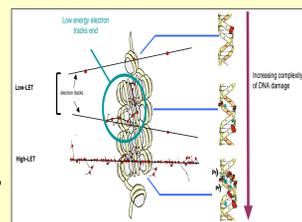
"Sufficient evidence" for cancer of thyroid

- Increased risk of thyroid cancer in childhood and adolescence related to exposure to radioiodines after Chernobyl accident⁵
- In the previous IARC evaluation (2001)⁶ the evidence for cancer of the thyroid was only for children exposure

- References**
- Cardis E, Howe G, Ron E, et al. (2006) Cancer consequences of the Chernobyl accident: 20 years on. *J Radiat Prot*; **26**: 127–40.
 - IARC (2001). Ionizing radiation, Part 2: some internally deposited radionuclides. *IARC Monogr Eval Carcinog Risks Hum*; **78**: 1–559.

All types of ionizing radiation are "carcinogenic to humans" Group 1 based on mechanistic evidence

- All types of ionizing radiations transfer and deposit their energy to biological material through free electrons-mediated mechanism resulting in different molecular lesions



- DNA: clustered damage: SSB, DSB, DNA protein cross-link
- Cells: chromosomal aberrations, mutations, genomic instability and bystander effects
- All these events contribute to the carcinogenesis process

Publications of the outcomes

Summaries of the outcomes of the IARC Monographs meetings on different types of radiations were published 3 weeks (RF-EMF) to 6 weeks (Radiation, Part D) after the meeting in *The Lancet Oncology*.

- El Ghissassi F, Baan R, Straif K et al.; WHO International Agency for Research on Cancer Monograph Working Group (2009). A review of human carcinogens—part D: radiation. *Lancet Oncol*; **10**: 751–752. doi:10.1016/S1470-2045(09)
- Baan R, Grosse Y, Lauby-Secretan B et al. WHO International Agency for Research on Cancer Monograph Working Group (2011). Carcinogenicity of radiofrequency electromagnetic fields. *Lancet Oncol*; **12**: 624–626.
- IARC Monographs (2012) A Review of Human Carcinogens: Radiation, A Review of Human Carcinogens: Radiation. Vol 100D, 1–341
- IARC Monographs (2013) Non-ionizing Radiation, Part 2: Radiofrequency Electromagnetic Fields, Vol 102, 1–460

Dissemination, impact and regulations

RF-EMF

- IARC Monograph meeting announced at the day of Press Conference for interphone
- Outcomes of the IARC RF-EMF and mobile phone evaluation were covered worldwide in all types of media, often on front page



Visits to the IARC website after publication of press releases on IARC Monographs Volumes 102, RF-EMF

- Cross-Section (with ENV) and international collaboration, including after the meeting, commentary on new studies and research gaps: Samet JM, Straif K, Schüz J, Saracci R (2014) Mobile Phones and Cancer, Next Steps after the 2011 IARC Review. *Epidemiology*; **25**: 23-27

UV-Tanning devices

- Outcomes of the UV-tanning device were also diffused by the media in many countries
- Many countries adopted exposure limits to UV-emitting appliances.
- WHO advises against exposure to UV-tanning devices before the age of 18 years.
- France, recently Canada and other countries adopted the age of 18 years as the legal minimum age for indoor tanning
- Brazil (2011) and recently Australia (2013) banned sunbeds

Radon

WHO Recommendations

- Reduction of the population's risk from exposure to the national average radon concentration
- Reduction of risk for individuals exposed to high radon levels
- Building codes should be implemented to reduce radon levels in homes under construction.
- A national reference level of 100 Bq/m³ is recommended**
- However, if this level cannot be reached under the prevailing country-specific conditions, the reference level should not exceed 300 Bq/m³



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