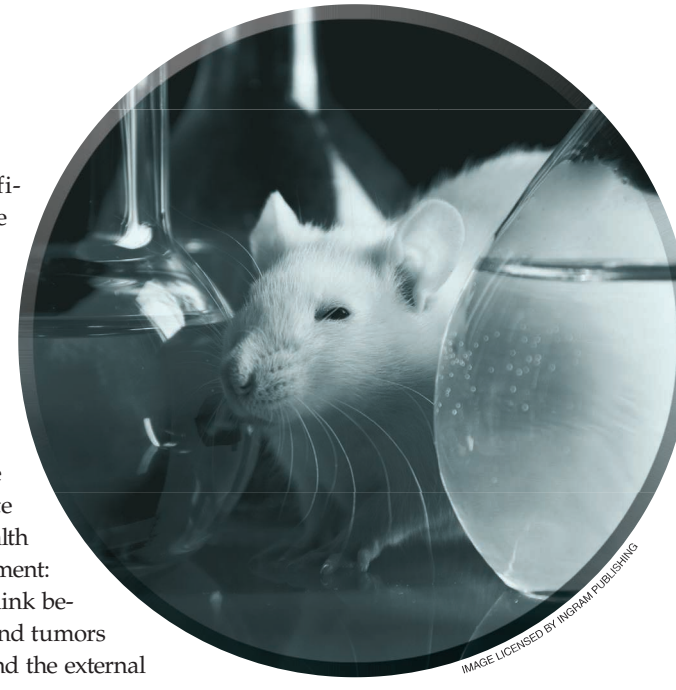


Health Matters

The Significance of Primary Tumors in the NTP Study of Chronic Rat Exposure to Cell Phone Radiation

■ James C. Lin



Most media accounts of the U.S. National Toxicology Program's (NTP's) final report have understandably focused on the statistically significant finding of "clear evidence" that both GSM- and code-division multiple access (CDMA)-modulated 900-MHz wireless RF radiation led to the development of malignant schwannoma, a rare form of tumor, in the hearts of male rats. In addition to this, unusual patterns of cardiomyopathy, i.e., damage to heart tissue, were observed in both RF-exposed male and female Sprague–Dawley rats compared with concurrent control animals, although the findings for female rats were deemed as providing only uncertain or "equivocal" evidence for schwannomas and malignant gliomas, compared to concurrent controls [1], [2].

The results, however, also included pathology findings showing positive indications or "some evidence" of carcinogenic activity in the brains of male rats, specifically glioma. (The designation of "some evidence" for carcinogenicity was based on the NTP's classification of the strength of observed evidence in its report.) It is important to note the National Institute of Environmental Health Sciences/NTP's statement: "We believe that the link between RF radiation and tumors in male rats is real, and the external experts agreed" [3].

The study also concluded that there were positive findings of carcinogenicity in the adrenal gland. The number of pheochromocytomas, i.e., tumors of the adrenal gland, was significantly higher in male rats at 1.5 and 3 W/kg of specific absorption rates (SARs), compared to the concurrent controls. Moreover, the increase in malignant tumor-like hyperplasia in the adrenal glands of female rats was significantly higher at 6 W/kg, relative to the concurrent controls. The myriad carcinogenic observations of the NTP study have prompted questions about total primary cancer occurrences in these chronically exposed animals.

A Closer Look at the NTP Findings

In all fairness, the primary cancer or overall cancer rates detected in any organ or tissue inside the animal body do not appear to have been purposefully overlooked or unnoticed. Indeed, the results for total primary cancer or tumor occurrences in NTP animal studies can be found in the appendices of its final reports [1]. However,

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Digital Object Identifier 10.1109/MMM.2019.2935361
Date of current version: 11 October 2019

although the data may not have been purposefully disregarded or ignored, the NTP excluded them from its publicized report summaries. An independent analysis of the data showed that rats exposed to GSM and CDMA RF radiation had significantly higher overall or total primary tumor rates than did the concurrent control rats [4].

In particular, the highest overall cancer (or malignant tumors) rates were found in male rats exposed to whole-body SARs of 3 W/kg from 900-MHz cell phone RF radiation (42 and 46% for GSM and CDMA, respectively), and the lowest rate was found in the concurrent control group (27%). Thus, the RF-exposed groups had significantly higher overall or total primary cancer rates than did the concurrent control rats. Moreover, the highest overall tumor rates (either a benign or malignant tumor in any organ or tissue) were observed in male rats exposed to SARs of 3-W/kg (87 and 84% for GSM and CDMA, respectively) cell phone RF radiation. As stated previously, the lowest rate was seen in the concurrent control group (63%). The RF-exposed groups had significantly higher overall tumor rates than did the concurrent control rats. Male rats in the lowest RF-exposed groups (whole-body SARs of 1.5 W/kg) had significantly higher rates of benign primary tumors (76 and 73% for GSM and CDMA, respectively) than did concurrent or sham control groups (54%).

Other Studies

Many laboratory rat cancer studies have been conducted and reported during the past quarter century in an attempt to assess the possible health risks of microwave and RF radiation from wireless communication devices and systems [5]. To date, not including the NTP investigation mentioned previously, there are six published studies on the carcinogenic potential of two-year or lifelong exposure of Sprague–Dawley rats to RF and microwave radiation. Some of these investigations involve the use of cocarcinogens to evaluate the potential of cell phone RF radiation, especially with regard to the induction and promotion of neural and mammary tumors. In one study, rats were injected with a known neural carcinogen, ethylnitrosourea, followed by exposure to 860-MHz RF to evaluate any increases in brain tumor induction. In four papers, the promotion of 900-MHz RF radiation was tested using dimethylbenzanthracene-induced mammary tumors in female Sprague–Dawley rats.

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Only one of the six earlier research studies involving Sprague–Dawley rats was designed to examine the health effects of lifelong exposure to pulsed microwave radiation. Beginning at eight weeks of age and continuing daily for 21.5 h/day, male Sprague–Dawley rats (100 each for exposure and sham control) were individually irradiated in circularly polarized waveguide exposure chambers for up to 25 months [6]. Pulsed 2,450-MHz microwave power—modulated at 8 Hz, pulsed at 800 Hz and delivered at 0.144 W to the exposure chamber—produced 0.15 to 0.4 W/kg of whole-body averaged SARs. A statistically significant increase was observed in primary cancers at death, i.e., 18 exposed rats versus five in sham-exposed control, or 18 and 5%, respectively. A near-fourfold increase of primary cancers in the exposed animals is provocative. The biological significance of this difference was questioned at the time; however, these data cannot be considered artifacts because different statistical analyses have led to similar results. The fact remains that the total primary cancer or overall cancer rate is significantly elevated in the RF-exposed group.

The most recent 900-MHz reverberation chamber and the previous 2,450-MHz circular waveguide systems provided near-zone, whole-body exposure conditions. In fact, these are the only two currently available RF and microwave exposure studies employing the Sprague–Dawley strain of rats—without, however, using any cancer-promoting agents (or cocarcinogens). Despite the methodological differences, both investigations showed consistent results in significantly increased total primary cancer or overall tumor rates for exposure to whole-body SARs of 1.5, 3, and 6 W/kg in one case and 0.15 and 0.4 W/kg in the other. What makes these two RF and microwave radiation animal cancer studies so valuable is the good laboratory practice with which the studies were conducted and the remarkable consistency of total primary or overall cancer findings.

Considering SARs

A few words of description are in order to place SARs in their proper perspective. SARs are accepted metrics or measures that correspond to the relative amount of RF and microwave power deposition or energy absorption rate in a part of or the whole body (e.g., any part of a user of a wireless device or cell phone handset or the entire body in the radiation domain of a Wi-Fi antenna or base station). In the United States, the RF and microwave exposure rules established by the U.S. Federal Communications Commission (FCC) are based on SARs and maximum permissible exposure (MPE) limits [7]. The basic restrictions for human exposure are defined by SAR limits. MPE limits are derived from SAR limits in terms of free-space field strength and power density.

For exposures from cell phones, the FCC specifies a quantity of local-tissue SAR of 1.6 W/kg, as found in any 1 g of body tissue. In addition, a value of 0.08 W/kg in any 1 g of body tissue was set for whole-body exposures. The FCC rules impose basic restrictions on SAR limits for general public and occupational exposures to avoid whole-body heat stress and excessive localized tissue heating, specifically

to prevent biological and health effects in response to an induced body temperature rise of 1 °C or more for an average time of 6 min [7], [8]. This level of temperature increase results from the exposure of individuals under moderate environmental conditions to a whole-body SAR of roughly 4 W/kg for approximately 30 min. A whole-body average SAR of 0.4 W/kg was chosen as the restriction to provide protection for occupational exposure. An additional reduction factor of five was introduced for public exposure, giving an average whole-body SAR limit of 0.08 W/kg. This value was purposefully relaxed by a factor of 20 to permit a maximum local-tissue SAR of 1.6 W/kg.

It is noteworthy that the then-recognized protection afforded by the whole-body SAR of 4 W/kg is within the same range of 1.5-, 3-, and 6-W/kg NTP-study SARs. Furthermore, these SARs did not raise the body temperature of exposed rats by more than 1 °C. Similarly, for the earlier 2,450-MHz study at lower whole-body SARs of 0.15 and 0.4 W/kg, a body temperature elevation was not reported in the exposed rats. Nevertheless, both experimental studies revealed consistent results in significantly increased total primary cancer or overall tumor rates.

Another point that should be noted with regard to SARs is that the NTP study report indicated that an RF field uniformity within 10% was achieved throughout the reverberation exposure chamber. This level of field uniformity enabled similar SAR values throughout the rats' bodies. Specifically, the local SARs in the brains and hearts of rats were a mere 1.05 and 2.27 times the whole-body average SAR, respectively. This also means that tissues and organs inside the rats' bodies experienced similar SARs from RF exposures.

IARC Assessment

The International Agency for Research on Cancer (IARC) assessed the then-available scientific literature and concluded that the epidemiological studies on humans that had reported increased risks for malignant gliomas and acoustic neuromas among heavy or long-term users of cell phones were sufficiently strong to support a classification of 2B, i.e., possibly carcinogenic to humans [9]. With its classification of RF radiation as a 2B carcinogen, the IARC suggested that it also believed the available scientific evidence was incomplete and limited, especially with regard to results from animal experiments.

An increase in the rate of gliomas was observed in exposed female rats at the highest field strength (50 V/m), but it was not deemed statistically significant.

The time is right for the IARC to upgrade its previous epidemiology-based classification of RF exposure to higher levels in terms of the carcinogenicity of RF radiation for humans. Recently, two relatively well-conducted RF and microwave exposure studies employing the Sprague–Dawley strain of rats—without, however, using any cancer-promoting agents (or cocarcinogens)—showed consistent results in significantly increased total primary cancer or overall tumor rates in animals exposed to RF radiation.

Postscripts

In August 2018, the Cesare Maltoni Cancer Research Center at the Ramazzini Institute in Bologna, Italy, published the final results from its comprehensive study on carcinogenicity in Sprague–Dawley rats exposed (either lifelong or prenatal until death) to 1,800-MHz GSM RF radiation [10]. The study involved whole-body exposure of 2,448 male and female rats under plane-wave equivalent or far-zone exposure conditions with incident electric-field strengths of 5, 25, and 50 V/m (the frequency-dependent maximum allowable value is approximately 61 V/m [11]). The authors estimated that the whole-body SARs were roughly 0.001, 0.03, and 0.1 W/kg during exposures of 19 h/day for approximately two years. Assuming a differential factor of 20 between the average whole-body SAR and local-tissue SAR, as was done in setting safety guidelines, the corresponding local-tissue SARs could be 0.02, 0.6, and 2.0 W/kg, in this case.

A total primary or overall cancer rate was not reported in this article, due to uncertainty about whether it could be part of the study protocol; however, a statistically significant increase in the rate of schwannomas in the heart of male rats was detected for the highest RF field strength (50 V/m). Furthermore, an increase in the rate of heart Schwann cell hyperplasia was observed in exposed male and female rats at the highest RF field strength (50 V/m), although this was not statistically significant. An increase in the rate of gliomas was observed in exposed female rats at the highest field strength (50 V/m), but it was not deemed statistically significant.

It is important to note that the recent NTP and Ramazzini animal RF exposure studies presented similar findings in heart schwannomas and brain gliomas. The increased schwannomas and abnormal heart tissue development/damage to heart tissue are significant findings in RF-exposed animal research studies. In addition to this, the incidence of benign pheochromocytomas of the adrenal medulla was found to be higher in the exposed group than in the sham controls for the 2,450-MHz circular waveguide experiment [6]. Interestingly, in the recent NTP study, there was "some evidence" of carcinogenicity in the adrenal gland. The number of pheochromocytomas was significantly higher ($p < 0.05$) in male rats at 1.5 and 3 W/kg, compared with the concurrent controls. Moreover, the increase in malignant tumor-like

hyperplasia in the adrenal gland of female rats was significantly higher at 6 W/kg, relative to the concurrent controls ($p < 0.05$).

A particular perspective to keep in mind is that, with the induction of cancer by a carcinogen, an agent is typically considered carcinogenic if it induces a significant response in a specific tissue.

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project C, 5% to project D. Sometimes project E would be added to the mix. The outcome of taking on too much is predictable: everything suffers. Prescribing how to allocate resources in minute detail doesn't help. When resources are limited, dividing them into smaller pieces does not increase the total.

"Shiny New Object" Syndrome

We often have to deal with a related problem. Let's say we've pared down our projects and have all of our resources appropriately allocated. Then something new comes up: the shiny new object. This is neither hypothetical nor rare. Most organizations involved in R&D or product development can expect to have new opportunities and ideas come up. It seems to be a particularly significant issue with start-ups.

Shiny new objects are distracting. They will demand some attention, even if only to determine if they are worth looking at more closely. Making such a determination should be the role of either the engineering manager, the marketing manager, or both. If the decision is to take a closer look, some engineering resources will need to be allocated, and something else will suffer. And if there is a further decision to pursue, some other project will likely need to be sacrificed.

There are different types of shiny new objects. Sometimes it's a variation on something that's underway, a new requirement. The trick here is to not distract the engineering team with multiple simultaneous requirements. If one key requirement for the project significantly changes or if a significant new specification or function is added, a decision needs to be made. Should we delay the project to address the new needs? Should we refocus the effort for the new requirements? If there are too many of these shiny new objects in succession, the project may never be completed. Sometimes, the most important thing is to finish a project, to get a product on the market and so generate revenue and collect valuable feedback.

For a start-up, the challenge can be worse. Most start-ups begin with a specific target: a product and application. And, in most cases, that initial target changes. After all, a start-up is developing something new. This means that the technical approach hasn't been fully demonstrated and productized. It also means that the market for the product hasn't been confirmed. Start-ups need to be nimble and adaptable. If there's a core technology, it can likely be used in multiple ways. It's probable that adjacent ideas and inventions will arise. Start-ups have limited resources, often very limited resources, so they need to focus. The trick is to focus on the right thing. The last thing a start-up can afford is to become paralyzed by too many tasks. This necessarily contributes to the high failure rate of start-ups.

So keep in mind that it's important to be selective, to keep an organization's work aligned with its resources. In these cases, "no" might be the most positive thing a leader can say.