

At this point, without more detailed information on experimental results, it is not possible to say whether the statistically significant effects are real or a chance-finding.

There are numerous misconceptions and misrepresentations of the NTP study and its outcome. However, one thing is certain, this is the best animal study that can be done with the existing technical and financial limitations. Even with the \$25 million funding, scientists cannot do all what they would like and need to do, in order to thoroughly address all issues and answer all questions.

I can't more agree with Christopher Portier, who said:

"This is by far—far and away—the most carefully done cell phone bioassay, a biological assessment. This is a classic study that is done for trying to understand cancers in humans. There will have to be a lot of work after this to assess if it causes problems in humans, but the fact that you can do it in rats will be a big issue. It actually has me concerned, and I'm an expert."

Further on, he continued:

"The NTP does the best animal bioassays in the world. Their reputation is stellar. So if they are telling us this was positive in this study, that's a concern."

... [Christopher Portier is a retired head of the NTP who helped launch the study.]

There have been complaints that (i) the radiation dose was very high and (ii) the whole body was exposed. But we need to remember that this is toxicology research, where animals are intentionally exposed to very high doses of the tested compounds; doses so high that humans will never encounter such exposures in real life. This is the way to determine whether the tested compound causes health problems to animals; if it does, it means that it is possible that also human health might be affected. It does not prove that human health will be affected in the same way, but it shows that the possibility exists and that humans should be careful.

The approach to use very high doses of cell phone radiation in the NTP study followed from the two tests performed before the actual 2-year test began (a 5-day pilot and 28-day pre-chronic toxicology study). These tests looked for the highest possible dose tolerated by the animals. Even the highest of the selected doses were tested to be tolerated by the animals - not increasing the body temperature more than the ICNIRP's recommended 1°C.

The whole body exposure of the animals has been criticized for the reason that humans get predominantly head exposure. Exposing only heads of rats and mice would require, as in some previous studies, a Ferris wheel type set-up. This would involve lots of handling of the animals by the personnel and would limit the time available for exposures. Housing free animals in cages allows longer exposures (up to 9 hours/day) and causes less stress due to the handling of animals (no frequent putting in and removing as when using the Ferris wheel).

Of course, also freely moving rats and mice, normally living in packs, experienced e.g. social stress of living lifetime alone in single-housed cages.

A commonly misunderstood issue is the transfer of knowledge gained with animals to humans. We cannot perform experiments on humans. Information obtained from animal studies is not directly transferable to human situation. However, animal studies have no such purpose - to provide information directly applicable to human health. Animal studies provide information whether the health of a complex living organism is affected by the examined agent. Such information is then used, in combination with epidemiological studies and laboratory in vitro studies, to determine the human health risk. Animal studies used as a supportive evidence.

Therefore, the outcome of the NTP study should be considered in the context of all the evidence from the to-date performed epidemiological, animal and in vitro studies. The combination of all the elements suggests that cell phone radiation possibly (or probably) affects human health because

- three case-control epidemiological studies (Interphone, Hardell's group, CERENAT) have shown increased risk of developing glioma in avid, long-term users of cell phone (30 min/day for 10+ years)

- several animal studies have shown increased health risk in exposed or co-exposed animals (e.g. Chou et al., Tillman et al, Lerchl's group, NTP-study).

Lack of the knowledge of the mechanism does not mean that a certain event doesn't happen. In the context of the recent study by Schmid & Kuster showing that the cell culture experiments were under-exposing cells to radiation, it is probable that the majority of the in vitro studies have shown a weak effect or lack of effects because of this under-exposure. Higher doses, as suggested by Schmid & Kuster, would certainly lead to more robust effects in vitro. Replication of some of the in vitro experiments with higher exposures might bring out some evidence of mechanism(s).

Epidemiological cohort studies, like the Danish Cohort or Million Women study, are of poor quality and cannot be used as a reliable proof of no effect.

We still do not have the definite proof that cell phone radiation causes cancer or increases risk of developing brain cancer. However, combination of the evidence from the case-control and animal studies indicates that the health risk is possible or even probable. The NTP study strengthens the evidence for the "probable health risk".

The conclusion of the "probable health risk" strengthens the call for the implementation of the Precautionary Principle in the use of cell phones. It seems that the human health risk might not only be possible rather probable; in the IARC classification, cell phone radiation could be upgraded from group 2B to group 2A.

My remarks

Based on the results of the NTP study Dariusz Leszczynski rightly demands that mobile phone radiation rather soon be upgraded from "possibly carcinogenic (2B)" to "probably carcinogenic (2A)" within the IARC's classification system. For him, however, a final proof that mobile phone radiation causes brain tumours in humans is still pending. Yet, I am of the opinion that research already provides the highest grade of certainty it is able to for the causality of a link between mobile phone radiation and the development of brain tumours also in humans. Still open to me is only the question of how high the brain tumour risk really is. For the time being the question hangs over us like a sword of Damocles.

Here are my reasons:

- 1) A review article by Phillips et al. [1] and a report from the BioInitiative [2] both show, it was discovered already many years ago that *in vitro* research could prove the genotoxic potential of radiofrequency radiation. Yet, the results did not receive the importance they deserved as they could not always be replicated in follow-up studies – either intended or because of incompetence or for biological reasons – or as in case of the REFLEX study when fabrication was wrongfully claimed in order to get rid of its findings. The REFLEX study showed that GSM-modulated mobile phone radiation causes DNA strand breaks in isolated human fibroblasts and granulosa cells from rats and proved this with the Comet Assay [3]. Similar results were obtained with UMTS-modulated mobile phone radiation, the genotoxicity of which seems to be even higher than that of GSM [4]. Using the same assay, the NTP study has now shown similar DNA damages in the radiation-exposed male and female rats.
- 2) The authors of the NTP study euphemistically describe the observed numbers of tumours in the rats as being very low. However, if we add the percentage of hyperplasia of the cell types from which the detected glioblastoma and schwannoma originated the tumour rate increases to a remarkable 8.5% [5]. The existence of pre-carcinogenic alterations – and these are the hyperplasia – allows the conclusion that tumour incidence would have been higher in case the study had been prolonged by several months. Yet, the NTP researchers decided against a prolongation. Furthermore it is important to know that, based on the selected statistical procedure, the probability to expect a significantly increased tumour rate was rather low from the beginning. The fact that nevertheless this did occur lends additional weight to the study.
- 3) The NTP study is not the only extensive one in which rats showed tumours after exposure to radiofrequency radiation. As Joel Moskowitz reports, the U.S. Air Force carried out a first study

between 1980 and 1982 – probably within the secret Pandora Project of the U.S. Government – in which 18% of the 100 male rats, exposed for two years to radiofrequency radiation of low intensity, showed tumours. While in the sham-exposed group of also 100 rats only 5% developed cancer, the relative cancer risk for the exposed group was 4.46. The course of the study was documented in nine technical reports. Ten years later Chou *et al.* summarized the results and published them in the scientific journal *Bioelectromagnetics* [6]. Even if the sites of the tumours were quite different compared to the NTP study – probably depending on the different types of radiation: here radar, there mobile phone radiation – the carcinogenic potential of radiofrequency radiation is substantiated with this study, too.

- 4) While Dariusz Leszczynski generally mistrusts the reliability of epidemiological studies because of the rather inadequate dosimetry, I am of the opinion that the vague measurement of the radiation intensity must even be seen as a confirmation that a brain tumour risk does exist. There is no doubt, that the members of the study group of long-term and frequent users of mobile phones in which compared to the not or at least less exposed control group the increased brain tumour risk was found are not at all exposed to the same radiation intensity. This Intensity might have differed by a factor of 20 or even more depending on the model of the mobile phone used, the way of how it was used and the location of where it was used. From this it can be assumed that the calculated average brain tumour risk of the study group is exclusively caused by the much higher brain tumour risk of its heavily radiation-exposed members. Based on the fact that in several epidemiological studies an increased brain tumour risk was indeed detected, the often repeated statement ‘*if there is any brain tumour risk, this must be very low*’ is a quite questionable one.
- 5) There is yet another reason to assume a causality of the relation between exposure to mobile phone radiation and brain tumours detected in epidemiological studies; because conspicuous is the fact that the epidemiological studies showed in long-term and frequent users of mobile phones among the many possible tumour types nearly concurring with an increase of malignant glioma and acoustic neurinoma. That the originating cells of these tumour types are identical with the ones from which also the brain and heart tumours of the exposed rats in the NTP study developed might be coincidence. However, regarding the numerous cells in humans and in rats which were exposed to an obviously identical kind of radiation and which did not react like glioma and schwannoma cells, this seems much less likely to me than the hypothesis that there is a specific process leading to the same result for humans and for rats.
- 6) The strongest argument, widely used by the scientific mercenaries of the mobile phone industry in order to on principle exclude a brain tumour risk of mobile phone users, is the claim that despite an increase of up to 6 billion users in the meantime the brain tumour rate to a great extent has remained the same worldwide. However, this claim seems to be based mainly on unreliable national cancer statistics [5]. Regarding glioblastoma, one of the most malignant tumours in humans, the year-by-year increase was 3.1% in the Netherlands between 1990 and 2010, while the total brain tumour rate did not increase. There seems to be a comparable trend in the United States. In addition, it turns out there that glioblastoma developed mainly in the frontal lobes of the brain, which are most intensely exposed to mobile phone radiation. In Sweden the number of people, who died because of a brain tumour of unknown nature between 2008 and 2013, rose by 157% [6]. In Denmark a previous report on an increase of brain tumours in humans now seems to be kept under lock and key [8].

A risk assessment applying scientific criteria has to consider the results of the triad *in vitro*-research, animal studies and epidemiology. If these so clearly point to the same direction as they do with mobile phone radiation, we are confronted with the question what still has to happen until this radiation is acknowledged as carcinogenic to humans and until it is classified in the IARC’s system accordingly. **In the opinion of Karl Friedrich von Weizsäcker (a famous German scientist and philosopher) there is no problem which could not be solved by our common ability to reason, yet our political system, our social situation, and our mental state make it nearly impossible.** To me this lack of a common ability to reason is especially conspicuous when it comes to health and environmental topics, where as a rule industry and its economic interests are generally conceded more reason than organizations that care for the protection of mankind and nature [9].

How the mobile phone industry is dealing with science so far is an example for this misconception. The many scientists secretly or openly tied to the mobile phone industry all over the world together with certain especially cash-hungry media will most probably prevent that the public is truthfully informed about the biological effects of mobile phone radiation and that it is in no way protected against the obvious health risks. When some day the increase in health damages cannot be denied anymore, politics and mobile phone industry will probably fall back on an apparent solution already used in the case of the tobacco industry. By printing a warning on mobile phones such as '*using mobile phones is a hazard to your health*' it would be achieved that the affected ones themselves are made responsible for their illness and that, in addition, the mobile phone industry is released from any product liability. And business could go on blithely ...

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