REPORT from the BioEM2016

The Annual Meeting of BEMS & EBEA held in Ghent, Belgium on June 5-10, 2016

prepared by

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Introductory comments

BioEM2016 conference took place on June 6 -10, 2016 in Ghent, Belgium. Seen here is the view of the conference site, Het Pand, the large building on the left on the Leie River, a former monastery.

This report has been prepared for the **Pandora Foundation, Germany**, and **Competence Initiative, Germany,** which supported travel and participation of the author in BioEM2016. Parts of this report were published during the course of the BioEM2016 as blogs on "BRHP – Between a Rock and a Hard Place" site.

Only several topics presented at the BioEM2016 are presented and discussed in this report. For the full list of topics presented at the BioEM2015, please, consult the freely available program book. However, the book of extended conference abstracts is accessible only for the registered participants of the BioEM2015, and for the members, in good standing, of the BEMS and EBEA.

Hot topic: the NTP study

The most anticipated event of the BioEM2016 was the last moment addition of the presentation of the US NIEHS National Toxicology Program study on effects of cell phone radiation in rats and mice. The 8 am Wednesday plenary session, provocatively titled, "**Hot Topic Plenary: The US NTP Study: A Real Game Changer or Just Another Study?**" presented by Myles Capstick of the IT'IS Foundation and Michael Wyde of the US NIEHS NTP.

Myles Capstick presented briefly the exposure set up for the NTP study. If anyone wishes to do replication using the same exposure equipment may forget it. The equipment was already dismantled and in some way disposed. The exposure chambers do not exist anymore. It was too costly to keep them after the exposure of animals was over. Of course, it is necessary to remember that due to a rapid technological development over the period of the execution of the NTP study the chambers, with all associated electronics, has become obsolete. Furthermore, the chambers were built for the 2G technology exposures vanishing from the consumer market, replaced by the 3G, 4G and soon the 5G.

The results of the NTP study were presented by **Michael Wyde**. In essence, all that Michael presented was already known from the **NTP Study Draft**.

However, there was some additional information, the results of **the comet assay, indicating the possible DNA damage caused by the RF-EMF exposure for rats and mice** (see the table)**.** 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.

MALE						
Rats	CDMA	Frontal cortex	Cerebellum	Hippocampus	Liver	Blood
	GSM	Frontal cortex	Cerebellum	Hippocampus	Liver	Blood
Mice	CDMA	Frontal cortex	Cerebellum	Hippocampus	Liver	Blood
	GSM	Frontal cortex	Cerebellum	Hippocampus	Liver	Blood
FEMALE						
Rats	CDMA	Frontal cortex	Cerebellum	Hippocampus	Liver	Blood
	GSM	Frontal cortex	Cerebellum	Hippocampus	Liver	Blood
Mice	CDMA	Frontal cortex	Cerebellum	Hippocampus	Liver	Blood
	GSM	Frontal cortex	Cerebellum	Hippocampus	Liver	Blood
	statistically significant trend and pairwise SAR-dependent increase					
	statistically significant trend or pairwise increase					
	no significantly different but increase in two or more groups					

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 word. 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^{o}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.

Wireless charging

The conference began on Monday morning with a plenary session on an extremely timely topic of wireless charging, with **Akimasa Hirata** (Japan) and **Mark Douglas** (Switzerland) as speakers. The reasons for the fast technological development of practical applications in this area are technological progress in efficient wireless energy transfer and somewhat "laziness" of humans, wanting it all without cables and right in the spot wherever they happen to be. The biological research, as always, lags badly behind. What is done right now, is modelling of the exposures by using different numerical models of humans of various sizes, shapes and postures (a virtual family developed by **Niels Kuster**'s team at IT'IS). Using these virtual models scientists test whether safety limits for humans are being met by the wirelessly charging appliances. Some important aspects of the wireless charging technology are still unresolved, like (i) leakage of radiation from the chargers, (ii) accidental misuse of the charging devices that might be e.g. in-built into street surface and (iii) effects caused in people with various man-made implants. One of the comments concerned the animal welfare - what happens to a cat or a dog that gets into the space between a charger and charging device, like getting under a bus standing while being charged. How about accidents with small children crawling or sticking their hands or toys there where they should not... Also, using numerical modeling is a good way to get fast estimates of radiation compliance with safety standards. However, is the accuracy of these models sufficient for estimates for real-life and real-persons exposures? These and many other safety issues should be addressed before implementing the technology on a massive scale. Things are happening in a way as **Frank Barnes** commented - technology is developed first and, while already being broadly and profitably in use, people realize that health hazards occur and only then the biomedical research begins. **In our "society blinded by the technology" it seems impossible to change this practice, of only *post factum* reacting to technology-caused health hazard.**

New avenues in epidemiology

The last plenary session of the **BioEM2016** was dedicated to epidemiology with the title inviting to debate "**New avenues of epidemiological research - added value or old challenges, or both?**". The set of invited speakers was also impressive, with **Mireille Toledano** (**COSMOS**), **Elisabeth Cardis** (**GERoNiMO**) and **Martin Röösli** (**HERMES** within **GERoNiMO**). This setting kept people at the meeting until the exceptionally well-attended last session.

Unfortunately, even the debate-inviting title did not do the trick. The debate was sluggish and conventional. But also the presentations did not speak about any really "new avenues" of epidemiological research. The speakers presented and justified designs of the ongoing studies, **COSMOS** and **GERoNiMO**, with a bit of preliminary data. Nothing yet to get excited but the projects are still "young" and gathering data, which is a slow process. **COSMOS** just collected the first five years

of data and we should expect soon the first publications. **GERoNiMO** has been in the works for just for a couple of years, so it is not yet time for published results.

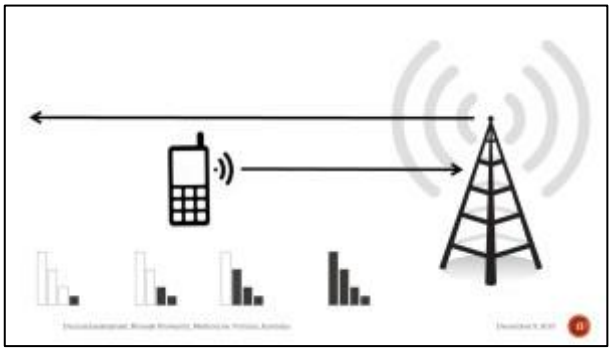
Finally, there was really not much anything new presented as "new avenues in epidemiology". However, one old/new issue got, at least me, excited. It happened in presentation of **Martin Röösli**...

One serious problemin all the presentations was the lack of a good and reliable exposure data for epidemiological studies. Technology is changing very fast. Phones used by study subjects are becoming rapidly obsolete and outdated and are replaced with new units several times during the course of an epidemiological project. What is more, phones are not the sole source of exposure. Yes, phones are the major source of the radiation exposure but other sources, like wi-fi, wlan, DECT, to name just a few, should not be neglected. Furthermore, in the era of smart phones, people keep in pockets phones connected to the internet (should not!). This causes that during data traffic areas of the body close to the location of the pocket are exposed, in some circumstances as much as during a call. This means that some significant exposures are "relocating" from the head to other areas of the body.

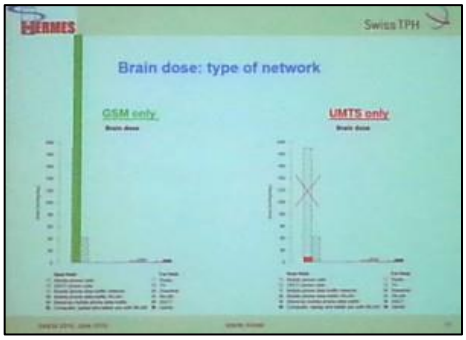
COSMOS study, for example, tediously collects data on numbers of performed calls and send messages, but it has no information at all on real radiation exposures. Also, wi-fi is completely excluded. So, how valuable and reliable will be the exposure data collected by **COSMOS**? I dare to say that it will be of very little real value. Epidemiological studies published with such data will remain unreliable and, most likely, will not show any dose dependency of exposure and health outcome. The reason is "simple" and should be obvious to anyone dealing with dosimetry.

Collecting information on the number of calls and on their length does not provide information on radiation exposure. As in studies done by the **Interphone**, **Hardell's group**, **CERENAT**, **Danish Cohort**, **Million Women** project, and by **Chapman et al**., the **COSMOS** and **GERoNiMO** also collect a surrogate of the radiation exposure. **None of the epidemiological studies executed to-date collected real radiation exposure data**. All of them have collected either bad or very bad surrogates of radiation exposure.

A graph, taken from my recent lecture at the Monash University, explains, in a very simple way, why the calling minutes or years of contract with an operator are nearly worthless surrogate for the real radiation exposure data. The weaker the reception of the phone the more exposed is the user because phone automatically emits more radiation to contact cell tower. This is not accounted at all in all “surrogate” radiation exposures in all epidemiological studies.



Most of the exposure a user receives from the cell phone. The further the cell phone is from the nearest cell tower, the more radiation a cell phone emits to connect. Furthermore, any radiation absorbing obstacles between a cell phone and cell tower, e.g. buildings or natural terrain, will cause a cell phone to emit more radiation. Thus, two persons making a call of the same length may be (will be) exposed to a dramatically different levels of radiation, depending on the person's proximity to the cell tower. This means that placing two persons in the same exposure group, based on the length of calls (or years of subscription with an operator), as done in epidemiological studies, puts together, in the same "exposed" group, highly exposed and little exposed persons. This might be one of the reasons why the epidemiological data do not show, in more robust way than the three case-control studies, that highly exposed persons are at risk of developing brain cancer. This might be also the main reason why the dose dependency has never been seen and that it is likely it will not be seen neither in the **COSMOS** nor **GERoNiMO**. **Epidemiological studies are mixing persons with high and low exposures in the same exposure groups!**



Additional reason for the urgent need to improve the quality of the collected exposure data was a slide presented by **Martin Röösli** (green bar = exposure using GSM network and red bar = UMTS network). It speaks for itself. Exposures of persons using the GSM network are dramatically higher than exposures of persons using the UMTS network. However, which network is used and when? The user does not know this. In modern phones, the switching between networks happens automatically, to keep call of good quality, without the users' knowledge. So, the users, by reporting just minutes of calls in epidemiological studies, provide useless "surrogate" information on radiation exposure.

This **poor radiation dosimetry in all the epidemiological studies to date is the main reason why I, personally, do not agree with the calls to upgrade the carcinogenicity of the RF-EMF to the group 1 of the IARC scale**. We have indications that RF-EMF is *possibly* (group 2B) or even *probably* (group 2A) carcinogenic, likely only to some selected group of more sensitive persons (do not mix with self-diagnosed EHS!), but **we do not have yet solid scientific proof that the RF-EMF is actually carcinogenic in humans**.

This is why I call for the use of the **Precautionary Principle** in matters of RF-EMF for the time being, as long as the health risk question is not resolved scientifically to a better degree of reliability.

The only way to determine the radiation exposure in epidemiological studies with sufficient accuracy is to install on the cell phones (smart phones) of the participants an app that will record all exposures to radiation, caused by network, cell phone and wi-fi. Such apps have been available already for a couple of years, unfortunately only for Android but not for iPhone, and both the **COSMOS** and **GERoNiMO** are kind of considering to make use of them. Hopefully it will happen soon and the data of real radiation exposure will begin to be collected.

Tutorial on safety standards by IEEE-ICES in USA

On Tuesday morning **C.K. Chou** (retired; Fmr. of Motorola) gave a talk in the tutorial session "Standards development activities of the IEEE International Committee on Electromagnetic Safety". The presentation was really good and clear, showing procedures used by IEEE-ICES to evaluate scientific literature and to apply this knowledge in setting safety standards. However, there is something that IEEE-ICES does not consider much - the Conflict of Interest (CoI) issue. The Committee that sets safety standards for the telecom industry to follow, the Technical Committee-95 (TC95) consists of ca. 130 scientists from 27 countries. At some point I was also a member of this committee but I resigned in 2009 citing the Conflict of Interest within TC95 as my reason. My problem was that the membership of the IEEE-ICES-TC95 consists predominantly of the industrial scientists and the committee is chaired by **C.K. Chou** since the time he was employed by the Motorola. This means that **all safety standards being developed by IEEE-ICES-TC95 are, in practice, developed by the industry scientists for the use by the industry they are employed by.** The industry scientists have the majority on the committee and upper-hand in any process involving democratic voting. To me this is a clear CoI. No matter how the procedures are described in the documents governing the work of the IEEE-ICES-TC95 the final decision belongs to the voters, of whom the majority is employed by the industry they regulate. Out of the curiosity, Chairman of the committee SCC39 that supervises work of TC95 is **Ralf Bodemann** of Siemens... **While the IEEE has the excellent expertise in the area of telecom technology, the Conflict of Interest remains an unresolved issue that undermines, in my opinion, reliability of the IEEE safety standards**.

Chinese study – interesting but technically unreliable

Zhengping Xu from the Zhejiang University in Hangzhou, China, presented an interesting study "Mobile phone signal exposure triggers hormesis-like effect in $Atm^{+/+}$ and $Atm^{-/-}$ MEFs to maintain genome integrity".

Hormesis is a term used by toxicologists to refer to a biphasic dose response to an environmental agent characterized by a low dose stimulation or beneficial effect and a high dose inhibitory or toxic effect.

The research group from China considered response of mouse embryonic fibroblasts to 1800MHz RF-EMF to be hormesis-like and briefly described in the Technical Program as follows:

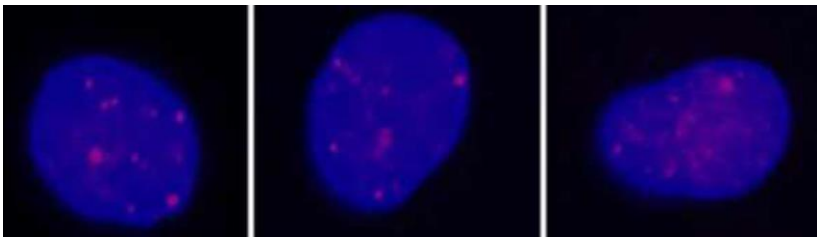
> "*We investigated the effects of 1,800 MHz RF-EMF on genomic integrity in ataxia telangiectasia mutated (ATM), a chief guardian of genome stability, sufficient (Atm+/+) or deficient (Atm-/-) mouse embryonic fibroblasts (MEFs). In Atm+/+ MEFs, RF-EMF at an average special absorption rate (SAR) of 4.0 W/kg induced significant DNA single-strand breaks (SSBs) at 1-hour exposure, and activated SSB repair mechanism, resulting in reduced DNA damage which is lower than the background level at 36-hour exposure. In Atm-/- MEFs, the same RF-EMF induced similar kinetics of both SSBs and double-strand breaks (DSBs). The observed phenomenon is similar to the hormesis of a toxic substance at low dose*."

In the brief discussion following the presentation a well-known expert in genotoxicity, **Vijaya** from Texas, USA, has strongly disagreed with the term used by Chinese scientists to describe the observed effect of RF-EMF as 'hormesis-like effect'.

The study has one major technical problem. The effects of RF-EMF on cells were determined by detection of the DNA damage as follows:

> "…*After RF-EMF exposure, the γH2AX foci formation was evaluated by indirect immunofluorescence staining and the γH2AX foci in the nuclei were observed using an Olympus AX70 fluorescent microscope with a 60 × oil immersion objective. The average number of γH2AX foci per cell was used as the index to evaluate γH2AX foci formation*…"

As simple as it may sound, counting of the γH2AX foci in microscope is not an easy job because the foci can be of different size, shape and some areas of cell will be crowded by them whereas other will have sparse distribution. Because the authors did not present any images of the nuclei stained for γH2AX foci, here are few examples of γH2AX foci staining from other studies performed by the group from China (images are not exactly sharp):



From observing the stained nuclei it becomes clear that any reliable counting of the number of foci is technically not possible. The only way to somewhat reliably estimate the differences in foci formation between cells is to make flow cytometry analysis.

For this technical reason, the results presented by the group from the Zhejiang University are technically unreliable and conclusions of the study are not sufficiently supported by the presented data. Formation of foci should be re-analyzed using e.g. flow cytometry before any reliable conclusions could be drawn.

Boris Pasche's work – what is the future?

In 2012, in my blog from the **Monte Verita meeting** (Switzerland) organized by **Niels Kuster**, I spoke for the first time about the work of **Boris Pasche** and his team in the USA. The tone of my comments was very positive and hoping for some breakthrough:

> "…*Buzz of both excitement and skepticism was elicited by the presentation of Boris Pasche (USA). He uses specific RF frequencies for treatment of cancer. As presented, the therapy appears to have impact and increases patients' survival time and even might cure some kinds of cancer. However, in the discussion were presented concerns that the energy deposited in tissues is extremely small. If such low energy would be confirmed to have impact on biological systems it would be a major breakthrough that would call for the revision of current paradigm. Dosimetry experts were very skeptical and if Boris would not have backing from the observed patient survival data, from the "heat of discussion" one could expect him to be "crucified". For now it did not happen. New research with good dosimetry support is being planned, both in vitro and in vivo, to confirm the existence of effects*…"

In my blog post from the **BioEM2013** the tone of my comments continued to be very positive, hoping for breakthrough by finding a proof of non-thermal effects:

> "…*talk was presented by Boris Pasche of the Department of Medicine, University of Alabama at Birmingham & UAB Comprehensive Cancer Center, Birmingham, AL, USA. In my earlier science blog where I gave my impressions from the 2012 Monte Verita meeting, I wrote about Boris' research. In short, his research indicates that the biological systems respond only to certain frequencies. The responses are frequency-specific, tumor-specific and genome-specific (individual variability of response between patients). The effects were observed consistently in cells grown in laboratory, in experimental animals (mice) and in cancer patients. It is important to note that this frequency-specific therapy was helping in some patients who otherwise did not respond to more traditional cancer treatments. What is still more exciting is that the effects were obtained at very low SAR and there were no observable side effects. Mechanism of this effect is unknown but effects are replicable.*
>
> *What is important, at least for me to assure the reliability of Boris' data, is that the exposures in his experiments are supervised by widely recognized expert – Niels Kuster.*
>
> *The lack of mechanism for the effect observed by Boris made people "nervous". At the same time it is difficult, based on the lack of known mechanism, to dismiss Boris' findings. As Boris himself pointed out it would be time to find out the mechanism for the effect he observes in lab and in clinic "where the demodulation of signal takes place?".*
>
> *The other important implication of Boris' study is that certain frequencies at very low SAR (non-thermal) are able to induce biological effects (e.g. effect on IP3/DAG signaling pathway) and even treat cancer. It means that the non-thermal RF exposures can non-thermally cause biological effects.*
>
> *I wonder how it is possible that low-level RF effects can be used in practice in clinical treatment but there is a very strong opposition to the notion that cell phone radiation and other wireless exposures could as well induce not-thermal effects in cell phone users*…"

Presentation of Pasche's work in my blog from the **BioEM2014** (South Africa) was somewhat less enthusiastic because of the problem with replication of his results in an animal study:

> "…*Last year, at the BioEM2013 in Thessaloniki, one of the hotly debated presentations was from Boris Pasche on cancer treatment using amplitude-modulated at discrete frequencies RF-fields. Pasche is already using this method to treat terminally ill cancer patients and is reporting positive results.*

> *This year, presentation from French scientists led by Yann Percherancier and Bernard Veyret, tested Pasche's method's validity in the animal study. The result of the French animal study was negative – scientists were unable to replicate Pasche's results.*
>
> *In the following discussion, it was asked and suggested that the results of the French animal study should be published in a peer-reviewed journal. Some scientists in the audience considered Pasche's results as not supported by the experimental evidence and, therefore, the successful treatment of some patients might be just a spontaneous recovery that happens from time to time and not the result of the treatment.*
>
> *Bernard Veyret, who presented the study in Cape Town, appeared somewhat uncertain about the publication of the results. Clearly, what he presented, was a pilot study and more experiments would be required to validate the result. As he put it, he did not want to get full-time involved in further animal study aimed at replication of the results of Pasche's work*…."

In my blogs from the **BioEM2015** (California, USA) I did not mention any more work by Pasche as I was disappointed with the presentation. Pasche was no more with the University of Alabama at Birmingham but with the Wake Forest Baptist Medical Center, Winston-Salem, North Carolina. However, most of the research was done in Brazil at the Hospital Sírio Libanês in São Paulo. If the work was appealing and had proven life-saving or life-extending ability at least according to the Pasche's team, why it was taken to a country with lower ethical standards than the researchers' own University of Alabama? Just puzzled…

This year, at the **BioEM2016** in Ghent, some in vitro experimental data were presented from Pasche's group. The overall conclusion of the study was that

> "…*Tumor-specific AM RF EMF are able to inhibit proliferation regardless of the presence or absence of external magnetic fields. This data implies that the antiproliferative effect is independent of the presence of external magnetic fields*…"

…and the voltage-gated calcium channel (T-type) was implicated as involved in mediation of the in vitro cellular effects because blockers of the T-type VGCC affected the response of cells to AM RF EMF treatment:

> "…*we show that the presence of Ethosuximide rescues Huh-7 cells and cancer stem cell population, from the antiproliferative effects of tumor-specific AM RF EMF. This underscores the fact that the antiproliferative effects of tumor-specific AM RF EMF is mediated by calcium influx through the T-type voltage gated calcium channels. This effect was not noted when an L-type voltage gated calcium channel blocker (Nifedipine) was placed in culture (data not shown). This indicates that HCC-specific AM RF EMF treatment mediates its antiproliferative effect via a T-type voltage gated calcium channels. This provides the first plausible link between changes in peripheral vascular resistance and antitumor effects*…"

There are few issues that weakened the enthusiasm towards Pasche's work:

- In discussion after the presentation, Niels Kuster, provider of the dosimetry for the study and co-author of the work, questioned the reproducibility of the presented results when he stated that for already one year the laboratory of Primo Schär has been unable to replicate the results of Pasche's work in vitro
- Claim that the therapy affects and eliminates cancer stem cells was weakened by the statement that patients, who respond to the therapy, live longer but the therapy has to be continuously applied. Once stopped the cancer returns. This means that the cancer stem cells are not entirely eliminated and, if therapy is stopped, the cancer stem cells regenerate the cancer.
- The first studies describing the therapy were published by Pasche's group in such prestigious journals as Cancer Research (2009) and British Journal of Cancer (2011 & 2012). However, the

latest publication, a review article, appeared in 'Chinese Journal of Cancer', an open-access journal published by the BioMedCentral.

- There is a question-raising peculiarity about the Pasche's review. As seen at the end of the article, the date of submission of the review is exactly the same as the date of acceptance it for publication. Was it really peer-reviewed within a few hours? This means that whatever the authors of the review wanted to be published was published but is it all correct we do not know as the peer-review was "skipped"(?).

Non-thermal effects of RF-EMF exposures

Several studies presented at the BioEM2016 examined the existence of the non-thermal effects of RF-EMF exposures. This is a very important issue, debated 'hotly' for already tens of years – are there any non-thermal effects or not? If non-thermal effects do not exist, there will not be biological and health effects caused by low level RF-EMF radiation emitted by cell phones in compliance with the current safety guidelines.

Therefore, proving or disproving the existence of non-thermal effects is of paramount importance.

It was disappointing to see that only one research group (from Bordeaux) presented research in this area. It was also disappointing to see the "quality" of the hypothesis in one of the two presented studies.

Biological effects at "non-thermal" levels have been reported but remain controversial. The best-documented effects have been the alterations in the EEG spectrum in human volunteers exposed to mobile phone RF-EMF. Suggestions that these effects are of thermal nature and occur by affecting thermal receptors of skin is controversial and still requires scientific proof. However, it is already being used to support the notion that exposures at ICNIRP safety levels do not cause no-thermal effects. Here is what I wrote from the Science and Wireless 2015 event in Melbourne, Australia:

> "*…Sarah Loughran presented a mechanism (still hypothetical) to explain the effect of RF exposures on the EEG, which has consistently been observed in several studies. The functional significance of this effect is unknown. There is also no information that the effect on the EEG would be in any way detrimental to human health. The effect occurs at energy levels insufficient to induce any thermal effect. Thus, if it is a non-thermal effect then it is not taken into account in the current standards and guidelines. The EEG effect was proposed to be caused by the RF exposure's effect on thermoreceptors present in human skin and in brain, which in turn affects the EEG. In conclusion it was suggested that exposures to RF at the levels well below the current safety limits can affect temperature of the skin and activate thermoreceptors and that the effect is only thermal in nature. This implied, according to Sarah Loughran, that the current safety limits take EEG effect into account as the other thermally induced effects.*
>
> *[DL/KL comment: this might be a false assumption that the current standards cover the safety for the thermal EEG effect. The effect occurs at the levels of RF exposure that, according to the current safety limits, should not cause any significant biological effect, neither thermal nor non-thermal. Repeated confirmation of the existence of the EEG effect should be considered as a proof of potentially inadequate protection provided by the current safety limits.]…*"

Research group from Bordeaux, led by **Bernard Veyret** and **Isabelle Lagroye**, examined the effect of RF-EMF exposures on TRPV1:

S1-1. Effects of radiofrequency fields on living cells at a molecular level using the real-time Bioluminescence Resonance Energy Transfer technique (BRET). H. Ruigrok, B. Goudeau, A. Hurtier, E. Poque-Haro, F. Poulletier DeGannes, I. Lagroye, N. Sojic, S. Arbault, P. Leveque, B. Veyret & Y. Percherancier

TRPV1, the transient receptor potential cation channel subfamily V member 1 (capsaicin receptor; vanilloid receptor 1) functions as detector and regulator of body temperature. TRPV1 provides also a "hot" sensation felt eating spicy food, caused by ingredients of e.g. chili peppers, mustard, or wasabi.

The justification/hypothesis for the study was

"…*We thus questioned whether some of the TRP channels are not only activated by the heat produced by RF but also by some specific "nonthermal" interaction with RF...*"

The authors observed the following outcome:

"…*Cells expressing the TRPV1-Luc and YFP-CaM probes were exposed to several signals at 1800 MHz at a SAR of 6 or 1.5 W/kg. In a typical experiment using the GSM signal at 6 W/kg, there was an expected rise in BRET signal due to RF-induced temperature elevation, but the BRET signal remained stable when temperature kept constant, showing no evidence of a specific RF effect on TRPV1 activation...*"

A few critical comments:

- First of all, the hypothesis does not sound convincing at all – why receptors, known for responding to a substantial increase in body temperature, would respond to the non-thermal exposure of RF-EMF? TRPV1 receptor senses and responds to temperatures of ca. 43^{o}C and higher. Such a temperature rise was apparently caused by the 6 W/kg but not by the 1.5 W/kg; hence the effect on TRPV1 was observed at 6 W/kg but not at lower SAR.
- This is a very unconvincing attempt to look for non-thermal effects of RF-EMF. While it may look as very advanced and novel scientific approach, using elaborate equipment set-up and advanced techniques to monitor function of TRPV1, the authors only found that TRPV1 does not respond to RF-EMF exposures that do not increase significantly (more than 1^{o}C) temperature of cells… and promised to examine several other TRP…
- Yet another elaborate study examined a single protein in cells and found out that protein activated by heat does not respond to lack of heating. With this approach there is work for several generations of scientists to examine all possible proteins in cells… why not?
- Examining one protein at a time is not an efficient way to find whether non-thermal exposures to RF-EMF cause any biological effects. Large scale screening of protein activation is the only sensible and efficient way to find protein targets and determine the signaling pathways governed by them that might be potentially affected by RF-EMF exposures. Studying one protein at a time and without reasonable justification, just because technology is available, is not any good way forward.

Another attempt at non-thermal effects was by looking for changes in the neuron firing activity in cells exposed to RF-EMF (GSM signal and CW signal):

S1-4. Decrease in burst activity of neuronal networks under exposure to RF as a function of SAR for the CW and GSM-1800 signals. C. El Khoueiry, F. Camera, R. Orlacchio, R. Renom, A. Garenn, F. Poulletier DeGannes, E.e Poque-Haro, I. Lagroye, B. Veyret, N. Lewis

Using cultures of cortical neurons from rat embryos and the microelectrode arrays to register burst and firing activity of neuronal networks in vitro, the following results were obtained:

"…*There was a decrease in MBR with time in the sham-sham experiments with a mean rate of 5% per phase. We performed RF exposures at a range of SAR levels from 0.01 to 9.2 W/kg. Figure 1 shows the average of data points at five SAR levels, obtained with GSM and CW*

exposures. The decrease in R is clearly non linear, fitted in Fig.1 as exponential decays (correlation coefficient ca. 0.9 for both signals).

At low SAR levels (ca. 0.1 W/kg), the inhibition of bursts was reversible, while at 4.6 W/kg, the inhibition continued in the P1 phase, and, at 9.2 W/kg, the activity was completely abolished over the E, P1, and P2 phases. Figure 1 also shows that there was a differential effect of CW and GSM, seen as model signals for non-pulsed and pulsed RF, respectively. Exponential decay constant was 0.34 and 0.56 for CW and GSM, respectively. This difference is not statistically significant…"

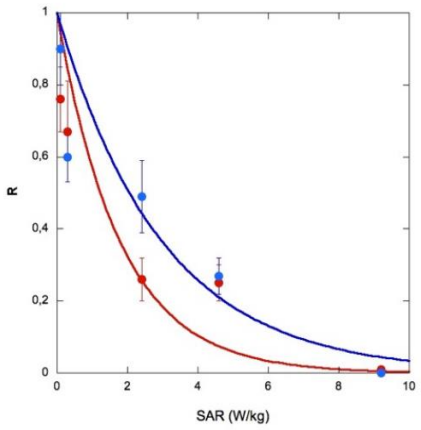


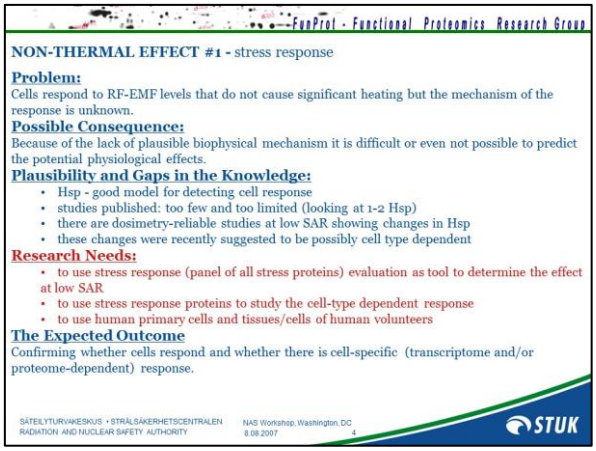
Figure 1. Inhibition R of burst rate in neuronal cell cultures exposed to CW (blue) and GSM (red) signals with nonlinear exponential curve fitting (Means± SEM).

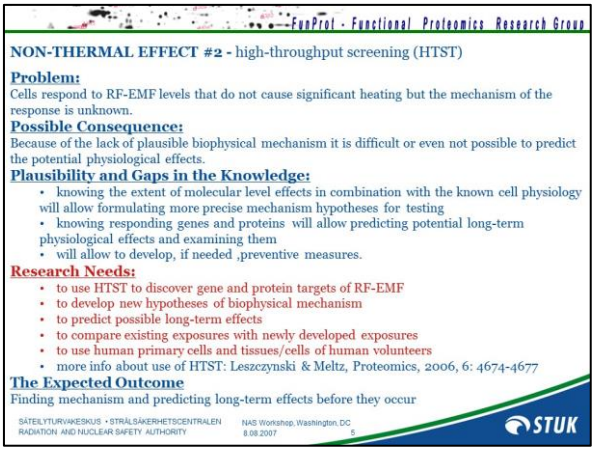
The authors concluded that:

"…we found a clear decrease in burst rate during exposure of neuronal networks to RF signals. The amplitude of the effect rose sharply with SAR and was greater in the case of the pulsed GSM signal. Based on these data, it is yet not possible to establish the contribution of a "nonthermal" specific mechanism. The fact that the GSM curve has a sharper rise in terms of SAR may indicate that this pulsed signal may have a specific contribution above that of the CW signal…"

Stress response as activation of heat-shock proteins and genes

Any response of a cell to an internal or external stressor is associated with the activation of the stress proteins – heat-shock proteins (Hsps). The activation is to protect cells from the damage. It has been shown in several studies that cells' response in non-thermal way to RF-EMF exposure indicates that the non-thermal effects likely exist. However, more work is needed because the responses are cell type specific – in different types of cells different stress proteins respond to different stressors. Therefore the "replication" studies undertaken using different cell types and different exposures (GSM vs. CDMA) and looking for activation of the same protein (e.g. Hsp27) have failed, because simply the design has been wrong. This topic is not "popular" anymore, and this is a mistake. Here is what I presented at the meeting at the US National Academies on Aug. 8, 2007 in Washington, DC:





In my opinion, one of the reasons for the current lack of interest in examining Hsps response might be the misconception, perpetuated by scientists unfamiliar with cell biology that the "heat-shock proteins" would respond only to the heat stimulus. This is not so. In order to activate stress proteins by a thermal change it is necessary to increase temperature up to 40^{o}C or above. Such temperatures are not caused by the RF-EMF exposures at levels of the current safety limits.

Upregulation of Hsps is mediated by a large variety of internal and external factors of which heat is only one kind of stimulus. Continuation of research on heat-shock protein mediated stress response is urgently needed as it might help to discover the mechanism by which RF-EMF affects living matter without significant increase (<1^{o}C) of temperature.

In the study

> **PB-166. Frequency dependent thermal effects of over 6 GHz radio frequency electromagnetic fields exposure in vivo**. S. Ohtani, A. Ushiyama, M. Maeda, K. Hattori, N. Kunugita, J. Wang & K. Ishii, Meiji Pharmaceutical University, Kiyose, National Institute of Public Health, Wako, Nagoya Institute of Technology, Nagoya, Japan

…the authors mistakenly assumed that when Hsps and heat shock factors (Hsfs) are upregulated by RF exposure it equals thermal effect:

> "*…the thermal effects of RF-EMF exposure on the transcriptional changes were thought to be '2.14 GHz > 6 GHz > 10 GHz' in the cerebellum*…"

It is not so. Hsps and Hsfs can and are upregulated not only in response to increased temperature but also e.g. in response to hormones or in response to malformation of proteins during synthesis on ribosomes.

Selected quotes from the extended abstract:

> "*…investigate the thermal effects of 10-GHz RF-EMF exposure, core temperature and gene expression of stress markers were analyzed during and following exposure for 3 days (6 h/day). As results, at WBA-SAR of 4 W/kg, the increase of core temperature was not observed, but some Hsp and Hsf genes were significantly upregulated in the cerebellum and skin. Comparison among 2.14-, 6-, and 10-GHz indicated that 10-GHz exposure showed quite different effects from 2.14- and 6-GHz exposure. Although the core temperature and transcriptional changes in the brain were less affected, the transcriptional changes in the skin were more affected. At 0.4 W/kg, there were no significant changes in the core temperature and these gene expression*…"
>
> "*…In this study, we expected that molecular genetic analysis of stress markers associated with thermal variations, such that the gene expression analyses of heat shock proteins (Hsp) and heat shock transcription factors (Hsf) could be a more accurate method to detect the thermal effects of RF-EMF*…"
>
> "*…A reverberation chamber system was developed for 10-GHz (sine wave) RF-EMF exposure. Whole-body average-specific absorption rate (WBA-SAR) was calculated by computer simulation*…"
>
> "*…Rats were divided into 4 W/kg, 0.4 W/kg, and sham exposure groups. Rats were exposed to RF-EMF for three consecutive days for 6 h per day at daytime (9 am to 3 pm), with freely available food and water*…"
>
> "*…During WBA-SAR of 4 W/kg at 10 GHz was exposed, increased core temperature was not observed, though intraperitoneal temperature increased by approximately 1.5°C compared with baseline under both 2.14 and 6 GHz frequencies. These results suggest that the core temperature was not almost affected by 10-GHz RF-EMF exposure unlike 2.14- and 6-GHz exposure*…"
>
> "*…Gene expression analyses showed that Hsp90aa1 and Hsf4 genes were significantly up-regulated in marginal region of the cerebellum and Hsp40 and Hsp90aa1 genes also in the skin. In case of the exposure of 2.14 and 6 GHz frequencies, many Hsps and Hsfs genes were up-*

regulated in the brain after 2.14-GHz exposure rather than after 6-GHz exposure, so that 2.14-GHz exposure would penetrate to deeper tissues than 6-GHz exposure. From these differences of gene expression among three frequencies, ***the thermal effects of RF-EMF exposure on the transcriptional changes were thought to be '2.14 GHz > 6 GHz > 10 GHz' in the cerebellum****. On the other hand, it was presumed that 10 GHz exposure would induce higher thermal effects than 2.14- and 6-GHz exposure in the skin. When WBA-SAR of 0.4 W/kg was exposed, increased core temperature and significant transcriptional changes in the cerebral cortex, cerebellum, and skin were not observed…*"

"*…These results suggest that there were no (or little) thermal effects on core temperature and the gene expression of Hsp and Hsf family under 2.14-, 6-, and 10-GHz exposure at WBA-SAR of 0.4 W/kg…*"

Dosimetry: assures the thermally-based safety limits… nothing else…

Dosimetry studies use modelling to determine whether exposures meet the safety limits. These modelling assessments are performed to determine whether the exposure causes thermal effects – crude warming up of the tissues or organ. The modeling does not show at all what low energy will, or will not, cause in cells and cellular structures. It is assumed that if the bulk temperature does not increase then there is no biological effect to be concerned about. It is also assumed that if the effect does not manifest itself fast then there is no reason for concern. Current modelling methods do not consider frequent and repeated exposures and effects that might be caused long after the exposure–exposure being a trigger to a cascade of events that is slow in manifesting because the repair mechanisms mitigate the damage, at least for some time. However, the models that represent biological structures are still very crude. The majority of modelling is based on dielectric properties of the tissues. While the electrical properties of tissues might be correct, these are crude representations of the complex biological structures. The tissues are represented as homogenous structures possessing certain dielectric properties but there is no consideration for the diversity of the cells in organs and tissues.

In 2009 I wrote about the problems with dosimetry. The same problems still persist. While it might be technically difficult to overcome them, the lack of knowledge about effects on cells and sub-cellular structures should not be misused, as it is being done now, to assure the users that the low-level RF-EMF exposures have no ability to cause any biological effects. From 2009:

"…In 1998, ICNIRP published the "Guidelines for limiting exposure to time-varying electric, magnetic and electromagnetic fields (up to 300 GHz)." (Health Physics, 1998, Volume 74, Number 4; http://www.icnirp.de/documents/emfgdl.pdf). In these guidelines, any biological effects of mobile phone radiation induced by temperature rise of up to 1 deg. C were considered as harmless and this approach became a basis for setting the safety standard that is still in force. At the same time the research field of non-thermal (athermal) effects was described as confusing, ***as stated in the ICNIRP guidelines****: "…****Overall, the literature on athermal effects of AM electromagnetic fields is so complex, the validity of reported effects so poorly established, and the relevance of the effects to human health is so uncertain, that it is impossible to use this body of information as a basis for setting limits on human exposure to these fields****.".*

According to the committees setting safety standard in Europe (ICNIRP) and USA (ICES) such small temperature increases of 0.1 - 0.3 deg. C induced by the mobile phone radiation exposure are meaningless when considering human health risk. The fact that the human body's temperature is in the morning ca. 1 deg. C lower than in the evening is commonly presented as a supportive piece of evidence. This is seen to suggest that the increase of the body temperature by up to 1 deg. C cannot be hazardous to health because it is within the normal

physiological range. However, entirely another question is if small temperature increases induced by mobile phone radiation could be meaningful, from the point of view of the potential induction of biological effects? And yes, the temperature increases are small but do we know enough about their nature and kinetics to be convinced that they are unimportant for the physiology of e.g. brain? I think that the issue might not be so simple. There are two "problems" to consider.

Firstly, the temperature of human body indeed rises over the course of the day by up to 1 deg. C and the process is harmless. However, this process cannot be directly compared with the local temperature increases caused by the mobile phone radiation. Such comparisons are omitting the time-scale of the event, its location and the involved physiological factors. To increase the temperature of the whole body it takes time (even hours). The process is preceded and accompanied by the production of humoral mediators that inform tissues and organs that the temperature increase is happening and cells have time to prepare protective responses. However, in case of the mobile phone radiation, the microwaves act locally by penetrating deeply into the body tissue (e.g. brain) and the temperature increase happens "instantaneously" and without any humoral mediators' warning. The exposed brain cells are suddenly, without any warning, warmed up. This is a non-physiological event for the brain cells to which these cells have not been prepared throughout the evolutionary development. Thus, the direct comparison of the slow and uniform increase in body temperature by classical heating (e.g. sauna, hot-tube or sun-bathing) or by physiological processes (e.g. daily temperature fluctuations, physical exercises or fever) with mobile phone radiation-induced rapid and localized increase in temperature might not be justified.

Secondly, the radiation emitted by mobile phones might induce temperature hot spots within the exposed biological material, i.e. small areas where temperature might rise more than in the neighboring areas. We can detect and measure hot spots on the macro-scale but we do not have yet technology to measure whether hot spots are created on the micro-scale (sub-cellular-scale). Presently, dosimetry and modeling of the distribution and intensity of mobile phone radiation in the brain uses as a model plastic container molded in the form of half-head and filled with "physiological solution" consisting of water, salt and sugar. Such model represents human head with skull (plastic mold) and brain (water solution of salt and sugar). However, it is a great oversimplification of the reality, made simple for the sake of mathematical calculations, and it certainly distorts the results. Such simplified models are claimed to be necessity but at the same time we might be "throwing the baby with the bath water".

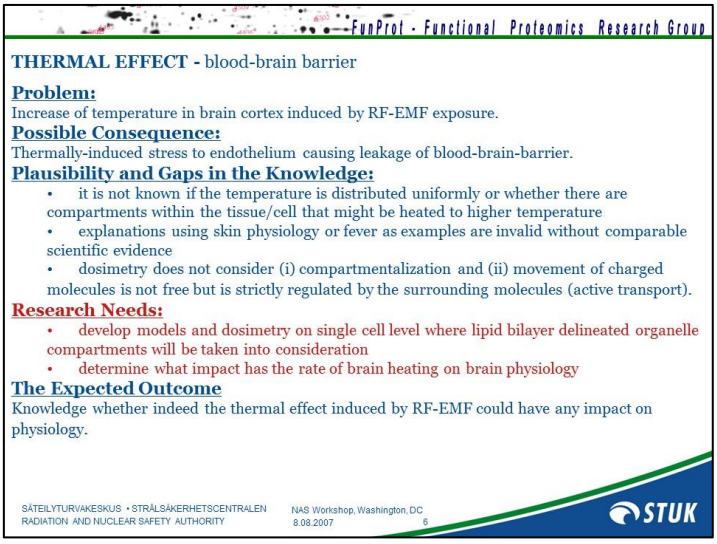
Living tissues and cells are not homogenous environments but they are compartmentalized into cells and sub-cellular size volumes (organelles) that are delineated by lipid-containing hydrophobic membranes. Charged biological molecules and ions, unlike in the above mentioned "head model", are not distributed within the tissue or cell uniformly and can't travel freely. Thanks to the membranes and their selective transport mechanisms the distribution of molecules and ions in cells is non-uniform and produces electric gradients that play a paramount role in physiological functioning. Strong electromagnetic fields can disrupt the function of selective transport mechanisms of the membranes and cause profound physiological changes (e.g. electroporation).

The question to be answered is what happens when such hydrophobically compartmentalized environment is exposed to weak electromagnetic stimulus like mobile phone radiation. Will such exposure lead to formation of thermal hot spots on sub-cellular scale, because the free flow of charged molecules and ions is prevented by the selective transport mechanisms? Formation of such sub-cellular hot spots could cause changes in certain functional areas of the cell that eventually could lead to alterations in cell physiology. Furthermore, there have been identified so-called temperature-sensing molecules in the cell membranes. When activated by temperature change these molecules send stress signals through e.g. the p38MAPK/Hsp27

signaling pathway. Such stress signals reach cell nucleus and may affect expression of genes and alter cell physiology. Activation of the above mentioned pathway by mobile phone radiation was identified in our study (Leszczynski et al., Differentiation, vol. 70, year 2002, pp 120-129). However, we still do not know whether the triggering event for this pathway activation was the activation of temperature sensing molecules in cell membrane or some another event.

In my opinion it is possible to expect that the mobile phone radiation affects cells by the combination of thermal and non-thermal (if they exist) mechanisms. Thermal effects, induced by mobile phone radiation, should not be automatically regarded as unimportant in context of health risk evaluation because their occurrence and kinetics are dramatically different from the harmless physiological warming up of the body. Unfortunately, the presently available technologies do not yet permit to measure temperature or field distribution on sub-cellular scale. On the macro-scale of groups of thousands of cells, that are presently measurable, such sub-cellular hot spots would not be detectable…"

Research in the area of micro-dosimetry is slow and it has never been named as a priority area by the WHO Research Agenda in RF-EMF. However, it is important area and should be pursued more efficiently. Here is what I wrote in my presentation at the US National Academies meeting on Aug. 8, 2007:



Skin and 5G technology

Modelling of such an important organ as skin, the largest organ of human body, is not possible using the most common voxel method. At the same time it is necessary to remember that skin is important not only because it is the largest organ of human body but because the radiation emitted by the 5G telecommunications technology will penetrate only skin deep. All radiation emitted by the 5G will be absorbed by the skin alone. We have no faintest idea what physiological effects such exposure will have. There was no research presented at the BioEM2016 on this subject. At the same time, worries are justified. Here is one example of research from the top-notch research group in Japan, examining effects of 5G exposures on human head.

The study examines only the thermal element of the exposure to justify implementation of the technology by proving it meets the current thermally-based safety standards. The abstract with images is here, exceptionally in full to illustrate the scarcity of our knowledge, in comparison with the push for very speedy implementation of the 5G globally.

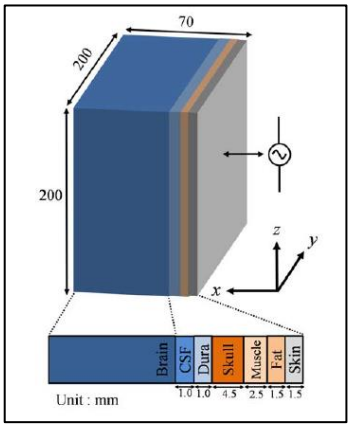
PA-39. Relationship between power density of external field and temperature elevation in a simplified head model for dipole and patch antennas. R. Morimoto, Y. Hashimoto, I. Laakso,

A. Hirata, K. Satoh & T. Onishi. Nagoya Institute of Technology, Nagoya and NTT DOCOMO, Kanagawa, Japan

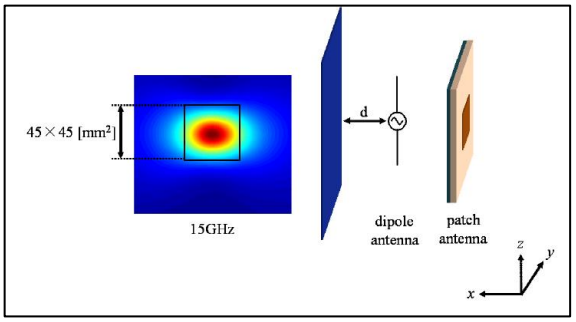
Some excerpts from the abstract:

"*…In this study, the relationship between power density and temperature elevation is investigated in a simplified head model from 3 to 30 GHz. The motivation for this investigation is that the power density is used as a surrogate of the thermal effect at frequencies > 3 GHz (IEEE) and > 10 GHz, its effectiveness has not been well investigated. Patch and dipole antennas are considered to discuss the variability for different field distributions…*"

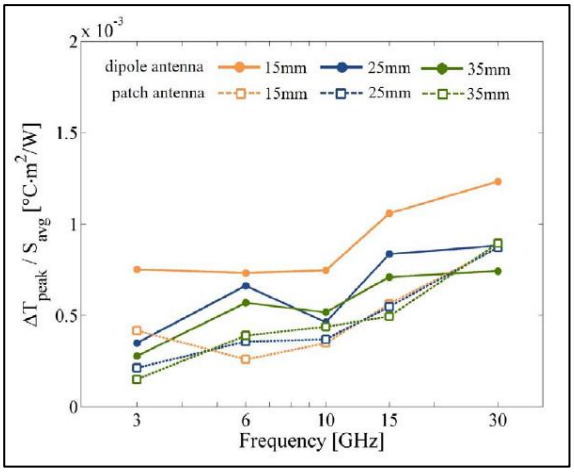
"*…In this study, simplified multi-layer cube are considered as a preliminary study. As shown in Fig. 1, a seven-layer model, consisting of the skin, fat, muscle, skull, dura, cerebrospinal fluid (CSF), and brain was considered as the model of the head. As antennas, half-wave dipole and patch antennas are considered as shown in Fig. 2. Then, the power density of external field is averaged over an area at a specific distance from the antenna, where the human head model is located.*



The SAR distribution in the head is calculated using the FDTD method for Maxwell's equations. Then, the temperature elevation distribution is obtained by solving the bioheat equation with the SAR as the heat source…"



"*…Figure 3 shows the ratios of the peak temperature elevation in the head to the power density for patch and dipole antennas. This ratio is defined as 'heating factor'. Three different separations between model surface and antennas were considered. As shown in Fig. 3, the heating factor increases gradually with the increase of the frequency. Similar tendency was observed when peak spatial averaged SAR is used instead of the power density [5]. On the other hand, this tendency is not the same for analytic solution using one-dimensional model [8]; almost independent on the frequency.*



When the separation between the antenna and model surface is small, the heating factors are large for the dipole antenna. Contrarily, the effect of separation on the heating factor is marginal for the patch antenna.

This tendency is attributable to the effect of the coupling between the antenna and head model. Note that the ground plane exists between the human head and the radiating element of the patch…"

"*…This study presented a preliminary* ***result on heating factor, the ratio of the peak temperature elevation in the head to the power density of external field, for dipole and patch antennas****. Further study is needed to investigate the applicability of the power density of external field as a surrogate of the peak temperature elevation for different exposure scenarios and practical antennas…*"

[1] ICNIRP, "Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz)," Health Physics, vol. 74, no. 4, April 1998.

[2] IEEE, "IEEE standard for safety levels with respect to human exposure to radio frequency electromagnetic fields, 3 kHz to 300 GHz, amendment 1," IEEE Std. C95.1a, March 2010.

[3] T. Nakamura, M. Iwamura, and H. Jiang, "Global research activities on 5G," IEICE vol. 98, no. 5, 2015 (in Japanese)

[4] Press Release, "DOCOMO's 5G Outdoor Trial Achieves 4.5Gbps Ultra-high-speed Transmission," https://www.nttdocomo.co.jp/english/info/media_center/pr/2015/0302_03.html, March 2015.

[5] R. L. McIntosh and V. Anderson, "SAR versus Sinc: what is the appropriate RF exposure metric in the range 1–10 GHz? Part II: using complex human body models," Bioelectromagnet., vol.31, no.6, pp.467-478, 2010.

[6] R. Morimoto, I. Laakso, V. De Santis, and A. Hirata, Relationship between peak spatial-averaged specific absorption rate and peak temperature elevation in human head in frequency range of 1-30 GHz (submitted).

[7] R. Morimoto, Y.Hashimoto, A.Hirata, K.Satoh, T.Onishi, Relationship between Power Density and Peak Temperature Elevation in Human Head in Frequency Range of 1-30 GHz, IEICE General Meet., B-4-1, 2016 (in Japanese)

[8] A Kanezaki, A Hirata, S Watanabe, H Shirai, "Effects of dielectric permittivities on skin heating due to millimeter wave exposure," Biomed. Eng. Online. Vol.8, article no. 20.

Exposure to RF-EMF and its impact on brain structure

A study performed in the UK suggested that a long-term exposure of mice to cell phone radiation at 1800 MHz at 0.5 and 1.0 W/kg might have an impact on animal behavior, potentially related with histological changes in brain microglia:

S4-2. Does exposure to radiofrequency fields in early life have an effect on behaviour? K. A. Broom, J. Jarvinen & Z. Sienkiewicz, Radiation Effects, Public Health England, Chilton, United Kingdom.

Some excerpts from the abstract:

"…Despite much research, there are still gaps in knowledge about the health effects of low level exposure to radiofrequency (RF) fields associated with mobile phones. This study is investigating the effects of exposure to RF fields used by 4G mobile phones on brain function and behaviour in young C57BL mice…"

"…Animals were exposed to controlled intensities to pulsed 1800 MHz fields at whole body specific energy absorption rates of 0, 0.5 or 1 W/kg for 30 minutes per day for 5 days a week, from gestation day 12.5 through to weaning; other animals were exposed to 0.5 Gy of X-rays on gestational day 18 as a positive control.

Following exposures, behaviour relating to long-term exploration, locomotion and activity patterns in the home cage were investigated in male mice using PhenoTypers.

A water maze task was performed in both male and female mice at 15 weeks and 30 weeks. Following assessments of learning and memory, brain tissues were examined using immunohistochemistry. All data shown is that of male mice at 30 weeks…"

"…Exposure had subtle effects on home cage behaviour, with the animals exposed at 1 W/kg making significantly increased number of licks, and they were significantly more active in the

running wheel. Compared to sham-exposed animals, exposure to X-rays increased cumulative movement in the cage.

Exposure also had a significant effect on acquisition of a water maze task at 30 weeks of age. Animals exposed at 0.5 W/kg had a significantly increased number of visits to the platform zone, but 1 W/kg had no effect. However, other parameters, including latency to first visit, distance travelled, and swim velocity were not significantly affected.

Immunohistochemistry at 30 weeks suggests exposure may impact microglial activation and neuronal activation, and could affect levels of Synaptophysin. Additional studies are underway for assessments of neuronal loss…"

Another study, with different results, performed in France, analyzed brain neuroinflammation following exposures to 900 MHz GSM and 1960 MHz UMTS. Brain-averaged SAR were 0.5, 5.0 and 15.0 W/kg. On contrary to observation of the UK researchers, no effect was found on brain structure.

S4-4. Neuroinflammation after GSM-900 or UMTS-1960 exposure. F. Poulletier De Gannes, E. Poque-Haro, R. Renom, A. Hurtier, M. Jany, J. Enderlin, G. Ruffie, Y. Percherancier, B. Veyret & I. Lagroye, University of Bordeaux, École Pratique des Hautes Études, Talence, ENSCBP, Pessac, France.

Some excerpts from the abstract:

"*…Animal exposure: Following a one-week acclimatization to the animal facility and another week of progressive habituation to confinement in exposure jigs, male Wistar rats (6 week old) were exposed head-only, using loop antennas, to GSM-900 or UMTS-1960 signals. Exposure lasted 2 hrs/day, 5 days/week, for 4 weeks at brain-averaged specific absorption rates (BASAR) of 0 (sham-exposed group), 0.5, 5, and 15 W/kg. We used a cage control group of non-exposed animals that remained in the animal facility during the whole experimental period. Three series of exposures for each RF signal were done*…"

"*…Effect of GSM900 exposure on neuroinflammation: The percentage of labelled area corresponding to GFAP positive cells in sham-exposed rats was 38.1±3.1 % in the prefrontal cortex and 50.7±4.7% in the hippocampus. In the exposed groups, the GFAP expression was not significantly affected in both areas. By contrast, Iba1 expression was significantly decreased in the prefrontal cortex of rats exposed at 5 and 15 W/kg and in the hippocampus of rats exposed at 15 W/kg. The CD68 population was scarce in both rat brain areas under investigation and not significantly affected in experimental groups*…"

"*…Effect of UMTS exposure on neuroinflammation: The percentage of GFAP positive cells in the group sham-exposed to UMTS was similar to that found in the GSM-900 experiment: 32.1±3.6 % in the prefrontal cortex and 45.2±3.5 % in the hippocampus. None of the experimental groups was affected by the tested conditions. No significant differences were observed for the expression of Iba1 and CD68*…"

"*…UMTS exposure did not globally affect the background levels of neuroinflammation markers. GSM-900 did not affected astrocytic gliosis*…"

"*… a decrease in Iba1 population in the cortex of rats exposed to GSM-900 at 5 and 15 W/kg and at 15 W/kg in the hippocampus was observed, while, no effect was seen on CD68. Temperature increase of 0.4±0.1°C and 1.0±0.0 °C were measured respectively at BASAR 5 and 15 W/kg under UMTS exposure. This temperature increase is expected to be similar with both signals for identical SAR levels, but the major difference is that GSM-900, but not UMTS is a pulsed signal*…"

"… ***no effect*** *was observed at 0.5 W/kg for either signals, at an SAR level in the rat brain considered as equivalent to the exposure level in the human brain when using a mobile phone at the ICNIRP exposure limit of 2 W/kg*…"

Telcom's concerns over information and misinformation

Internet is full of information and misinformation by experts and pseudo-experts. Thus, the telcom's concerns about the incorrect information about wireless technology are justified. However, telcoms do not address the problem of mistrust of information provided on the tecloms' websites.

A study from India and Hong Kong developed a preliminary chart of interrelations between telcom, technology users and news media in the current era of vast amount of reliable and unreliable information available freely on internet. While the health issue is not directly named in the study, the potential health effects of the radiation emitted by the wireless communication technology are one of the aspects that telecom is concerned with. In the worst case scenario, health concerns might affect the profitability of the technology:

> **PA-215. Consumer awareness framework – A risk mitigation architecture of EMF**. R. Pradhan, J. Rowley & M. Sagar, Indian Institute of Technology Delhi, New Delhi, India, and GSM Association, Hong Kong.

Some excerpts from the abstract:

"*…Aware consumer, informed choice are the two premises for a fast absorption of telecom technology. This framework is developed on the above premise. This consumer awareness framework represents the basic need of the hour because there are risks associated with the use of any technology. This framework will have high social impact for all the stakeholders of the telecom industry (Regulator, Operator, Government, and Consumer). This framework identifies the key factors, their linkages and hierarchy in developing the framework of consumer awareness of Radio Signal…*"

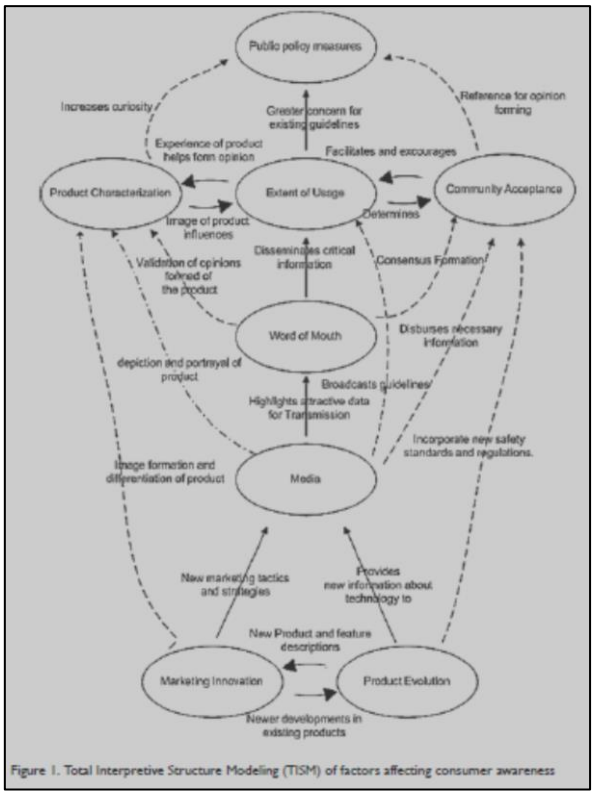


Figure 1. Total Interpretive Structure Modeling (TISM) of factors affecting consumer awareness

"*…The enormous increase in mobile phone usage over the past decade throughout the world has resulted in the development of various belief systems and misconceptions*..."

"*…The consumer of today is flooded with information from various sources that is propagated through various channels. It is therefore imperative for the existence of effective risk communication between technology provider and consumer in order to facilitate the consumer to make an informed choice regarding usage of a particular technology thus enabling the efficient absorption of the technology in a society…*"

"*…This study attempts to develop a consumer awareness framework in the context of the perceived risks surrounding the effects of radio signals used in mobile communication…*"

"*…This framework will have implications for industry associations, academia, telecom service provider policy planner, government authority and the public in large…*"

Wi-Fi and health – review with unfounded conclusions

Scientists from the 'EMF Portal' presented a review of the to-date published studies examining health effects of exposures to wi-fi. Conclusion of the study was that there is no health problem to be concerned about but, at the same time, our knowledge is still very limited. Unfortunately, scientists' conclusion was not justified by the presented evidence when the authors said

> "…***Summarizing our results so far, we do not derive substantial evidence of health implications from it.*** *Nevertheless, the large amount of studies of insufficient quality discovered in this review poses a serious problem in terms of substantial health risk assessment*…"

… but in the next paragraph the authors stated that

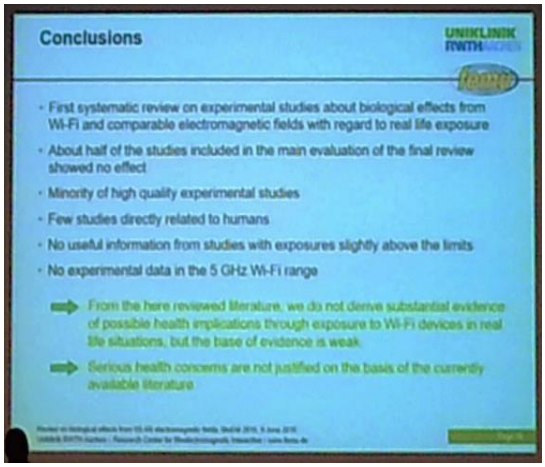
> "…***Studies on human subjects with exposures to WLAN RF fields or comparable fields are so far very rare. Due to the complete lack of experimental research on possible effects of weak 5 GHz fields, as used by WLAN devices under more recent standards, some appropriate research should be initiated***…"

T**his is the real problem**: the **insufficient research, the poor quality research, and lack of research studies is being interpreted as "evidence" for the lack of health effects. This is wrong.**

Interestingly, in a very short discussion that followed this presentation, **Martin Röösli** from Switzerland asked a simple question:

> "*…how authors can justify conclusion of no health implications from wi-fi exposures when there are only two human studies in this area of research?*"

Here is the conclusions slide and (below) the full abstract of the presentation [bold text was added by DL]. Because the photo of the slide is of poor quality, the last two statements of conclusions, marked in green text and with green arrows on the original Conclusions slide, are re-typed for clarity below:



- ***From the here reviewed literature we do not derive substantial evidence of possible health implications through exposure to Wi-Fi devices in real life situations, but the base of evidence is weak***
- ***Serious health concerns are not justified on the basis of the currently available literature***

Some excerpts from the abstract:

> **Is there evidence of biological effects from WLAN and comparable electromagnetic fields in everyday exposure situations? Systematic review of experimental studies.** F. Gollnick, L. Bodewein, D. Graefrath, K. Jagielski, T. Kraus & S. Driessen. Research Center for Bioelectromagnetic Interaction (femu), RWTH Aachen University, Aachen, Germany
>
> "*…We reviewed the evidence of experimental studies for biological or health effects by everyday exposure to RF fields of WLAN devices or exposures comparable to such RF fields. From 225 potentially eligible references, 65 relevant studies using exposures below, at, or slightly above the exposure limits were included.*
>
> *Just over half of those 44 studies of it using exposures below or at the limits showed an effect. The large majority of these 44 studies had medium or strong methodical weaknesses. More detailed evaluations are ongoing. So far no substantial evidence of health implications is*

derived from the results, but the mostly poor study quality impairs the informative value of the present available scientific database…"

"*…There is a long-standing public and scientific discussion about pulsed RF fields being potentially more biologically effective than continuous wave (CW) fields. In typical environments the radiated RF energy of WLAN devices is low compared to other wireless communication or transmission technologies (as e.g. mobile phones or broadcast), since the output power of the transmitters is mostly limited to 0.1 W by national regulation [2]. Regardless of this, there is continuing concern regarding possible adverse health effects through radiation from WLAN technology…*"

"*…Possible biological effects or health effects of electromagnetic field exposures from WLAN devices and networks, as well as the actual field distribution in homes, schools, offices, and outdoor environments, have been investigated in a number of scientific studies. In addition, there are many studies on possible effects by exposure to RF signals with field characteristics comparable to emissions from real WLAN devices. In the present systematic review we studied whether or not there is enough evidence of an association between those field exposures and any biological or health effects…*"

"*…Original peer-reviewed journal or book articles in English or German were considered. There were no limitations regarding biological endpoints of the studies. With regard to real life exposure scenarios, we considered only those experimental studies which were using adequately pulsed test signals in the relevant 2.4 GHz and 5 GHz frequency ranges (see above) and with field strengths below, at, or slightly above internationally recognized exposure limits. The relevant limit values were taken consistently from the guidelines of the U.S. Federal Communications Commission (FCC), the Institute of Electrical and Electronics Engineers (IEEE), and the International Commission on Non-Ionizing Radiation Protection (ICNIRP)…*"

"*…The literature search yielded a total number of 225 potentially eligible references, of which 160 were excluded from further review based on the applied technical exclusion criteria. From the 65 remaining publications, 44 studies with exposure levels below or just at the limits were included in the detailed final review. 20 of these 44 studies used exposures to real WLAN RF fields. 21 of the remaining 65 publications were evaluated separately with lower priority as a group of references with exposure levels lying clearly above general public exposure limits, but still low enough to provide some additional information about exposures in the limit range (i.e., lying in the whole body average SAR range of 0.1-0.4 W/kg or lying in the partial body SAR range of 2.1-4 W/kg)…*"

"*…Only studies using signals in the 2.4 GHz band remained in the final review, because all of the studies using signals in the 5 GHz band (i.e., 12 of 225 potentially eligible studies) had to be excluded, mostly due to too high power levels.* ***Only three studies on human subjects were identified among the relevant in vivo studies****…*"

"*…Just over half of the 44 studies finally reviewed showed an effect of the real WLAN or comparable to WLAN exposure. Overall, the most affected biological endpoints from a vast variety were oxidative stress, reproductive system functions including sperm quality, and heart rate variability. Most of the studies had medium or strong methodological weaknesses…*"

"*…In our systematic review, we evaluated the evidence from experimental studies for biological or health effects by the exposure to RF fields of WLAN devices and for the first time added evidence from experimental studies using exposures comparable to such RF fields.* ***Summarizing our results so far, we do not derive substantial evidence of health implications from it.*** *Nevertheless, the large amount of studies of insufficient quality discovered in this review poses a serious problem in terms of substantial health risk assessment.*

Studies on human subjects with exposures to WLAN RF fields or comparable fields are so far very rare. Due to the complete lack of experimental research on possible effects of weak 5

GHz fields, as used by WLAN devices under more recent standards, some appropriate research should be initiated. *Also, with regard to emerging new applications, the 60 GHz range (see above) should be regarded as a valuable objective of further research*…"

Closing words…

The BioEM meetings are the primary event for the scientists in this area of research. As every year some important issues are being omitted. This year the organizers arranged the last moment addition to the program – the hot-topic session on NTP study – kudos for this! Many participants of BioEM2016 would appreciate information from the WHO and ICNIRP on the status of the Environmental Health Criteria for RF-EMF. Unfortunately this hot-topic issue was missing from the program.

The meeting gives pretty good cross-sectional view of the diverse research ongoing in the area of EMF. This cross-section shows that some important topics are less and less in focus of researchers.

Yet again, there is seen a striking shortage in research on biological effects of EMF executed in human volunteers. Why such research is not being pursued? Yes, it is costly and must be ethically correct but… without research on biological effects of EMF executed in human volunteers it will be nearly impossible to prove the existence or lack of effects and assess their physiological significance.

In this report, unlike my reports from BioEM in 2013, 2014 and 2015, I used extensively opinions that I published in recent years to demonstrate that certain areas of research are not being pursued and the problems do not go away without research. Problems remain. Gaps in the knowledge need to be filled before we can make reliable and scientifically valid conclusions concerning EMF and public health. At this point, the debate on EMF and public health is more and more resembling a "shouting competition" where two opinions, neither of them being sufficiently supported by the scientific evidence, are being presented… and the groups presenting these opinions do not even want to speak to each other. The mistrust runs deep, and only good science would be the way to resolve the problematic issues.