

Editorial: Introduction of Dr. C-K. Chou—2006 d'Arsonval Awardee

It is my honor and privilege to introduce the 10th d'Arsonval award recipient, Dr. Chung-Kwang Chou. The award is the Bioelectromagnetics society's highest recognition of scientific excellence in our field of study. Dr. Chou, or C-K as most people know him, has been a member of the society since its inception and he has attended all 28 annual meetings. During this time he has contributed to the understanding of radio-frequency (RF) biological effects, RF dosimetry, and exposure systems, hyperthermia, as well as electrochemical treatment of cancer. He may be best known for his work on the auditory effect of RF exposure, but some 180 peer-reviewed papers map out a broad range of interests and accomplishments. In addition to his direct research work, Dr. Chou serves and has served on scientific advisory groups ranging from BEMS board and this journal's editorial board, to a number of IEEE committees shaping the current exposure standards. He is a fellow of IEEE and of the American Institute for Medical and Biological Engineering.

Dr. Chou's training in the engineering sciences started with a bachelor of science degree in electrical engineering from National Taiwan University (Taipei 1968), followed by a master's degree from Washington University (St. Louis, 1971), and a doctorate at the University of Washington (Seattle, 1975). He spent a year as an NIH post-doctoral fellow in the regional primate research center and the Department of Physiology and Biophysics at the University of Washington. He served as assistant professor and later research associate professor at the Department of Rehabilitation Medicine and Center for Bioengineering at the University of Washington (1977–1985). Dr. Chou then moved to direct the Department of Radiation Research at the City of Hope National Medical Center (Duarte, CA, 1985–1998). In 1998, he joined Motorola Florida Research Labs where he is now Chief EME Scientist and the Director of the Corporate EME Research Laboratory, responsible for RF product safety.

The text for the illuminated testimonial that Dr. Chou was presented with at the annual meeting in Cancún, Mexico was prepared by Dr. Asher Sheppard. It reads as follows: "The Board of Directors of the Bioelectromagnetics Society takes great pleasure in conferring the d'Arsonval Medal to Chung-Kwang Chou whose creativity and accomplishments



C-K. Chou—2006 d'Arsonval Medal Awardee

in Bioelectromagnetics have with genius blended engineering, physical science, and physiology to place new marks of distinction on the path first cut by Jacques Arsene d'Arsonval. With a keen ear for Nature's

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whispers, his probes were first to touch the cochlear rhythms struck by the tapping of electromagnetic energies in that chamber where the mind resides; his antennas have directed healing electromagnetic waves into bodies blighted by disease; his keen insight as author, editor, and reviewer has nurtured numerous scientific publications; his leadership has enhanced modern telecommunications; and with gentle rigor, he has fostered adoption of standards for safe use of electromagnetic energy. With delight in recognizing

these enduring deeds, and with gratitude for his warm friendship, we proudly confer this highest honor in Bioelectromagnetics on Monday the 12th day of June in the year 2006 in Cancun, Mexico on the occasion of the 28th Annual Meeting of the Society.”

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Thirty-five Years in Bioelectromagnetics Research

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For 35 years, I have been involved in various bioelectromagnetics research projects including acute and long-term radiofrequency (RF) bioeffects studies, dosimetry, exposure systems, MRI safety, cancer studies involving hyperthermia and electrochemical treatment, development of RF exposure and measurement standards, and product compliance. My first study demonstrated that effects on isolated nerve and muscle preparations were due to thermal effects of RF exposure. The recording of cochlear microphonics in animals shows the mechanical nature of the microwave auditory effect. In 1992, we published the results of a large-scale lifetime study in which 100 rats were sham-exposed and 100 rats were exposed for 21 h/day for 25 months to a pulsed RF signal. In dosimetry studies, human models were employed as well as many animal species including mice, rats, rabbits, monkeys, and birds of many sizes. Cancer hyperthermia studies demonstrated that knowledge of temperature distribution was crucial for successful treatment. Research on electrochemical treatment of tumors with direct current involved cellular, animal, and clinical studies. Over the past few decades, there has been rather extensive investigation of the public health impact of RF exposure. In my opinion, future research in bioelectromagnetics should place greater emphasis on medical applications. *Bioelectromagnetics* 28:3–15, 2007. © 2006 Wiley-Liss, Inc.

Key words: RF bioeffects; dosimetry; exposure system; safety; hyperthermia; standards

INTRODUCTION

It was indeed a surprise and an honor to receive a phone call from Dr. Stefan Engström, President of the Bioelectromagnetics Society, in the afternoon of February 7, 2006 informing me that I would be receiving the d'Arsonval Award. I thank the anonymous nominator(s) and others who wrote supporting letters as well as the Board of Directors for approving this award. Since I was a graduate student some 35 years ago, I have had the continuous good fortune of being a researcher on the biological effects, medical applications, and dosimetry of radiofrequency (RF) energy. I would like to thank three noble persons in my life who provided the opportunities for my research career in bioelectromagnetics. The first of them is Dr. Arthur W. (Bill) Guy, my mentor at the University of Washington from 1971 to 1985. The second is Dr. Kenneth Luk who, after our collaboration at the University of Washington, invited me to the City of Hope National Medical Center in Los Angeles to create a hyperthermia research program in 1985. The third is Dr. Quirino Balzano who recruited me in April 1998 to oversee the Motorola Electromagnetic Energy Research Laboratory and be responsible for RF product safety. During the past 35 years, I have had the privilege to work with many brilliant

minds on numerous projects on RF field bioeffects, dosimetry, exposure systems, hyperthermia, electrochemical treatment of tumors, MRI safety, compliance, standards and regulations. I appreciate this opportunity to discuss a selected number of projects to illustrate my endeavor in bioelectromagnetics.

In 1968, I completed my bachelor's degree in electrical engineering at the National Taiwan University in Taipei, Taiwan. After a year of military service, I came to the United States to join Dr. William Pickard's laboratory at Washington University in St. Louis, Missouri, for graduate training in biomedical engineering. The course work included cell biology, surgery and bioengineering classes, in addition to electrical

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engineering courses. After completing my Master's degree in 1971, I entered Bill Guy's laboratory in the Department of Rehabilitation Medicine (Dr. Justus Lehmann, Chairman) at the University of Washington. I originally planned to work on neural-controlled prostheses because my father owned a company in Taiwan making prosthetic and orthopedic devices. My interest in biomedical engineering dates back to my high school years when I accompanied my Dad on his trips to various hospitals. Other events changed these plans.

This was also the time when Jack Anderson of the Washington Post wrote about the Soviets beaming microwaves at the American Embassy in Moscow. It was thought that the microwave exposure might be an attempt to affect the health of the embassy staff. There was growing concern about electromagnetic (EM) emissions from consumer products (microwave ovens), medical applications (diathermy) as well as the adequacy of existing exposure standards. These events led to a call for research proposals on microwave bioeffects from the Bureau of Radiological Health which was a branch of the Food and Drug Administration. After obtaining a research grant, Dr. Guy asked me whether I would be willing to do my dissertation on microwave bioeffects instead of prosthetic devices. I accepted the offer and started my research career in bioelectromagnetics. Because of my 14 years at the University of Washington, some of the work that Dr. Guy talked about in his 1987 d'Arsonval Award speech [see Bioelectromagnetics 9(2), 1988] will be mentioned again here.

RF BIOEFFECTS

In Vitro Studies

Reports in the Soviet literature in the 1960s indicated that the nervous system is the most sensitive system to RF energy. For example, Kamenskii [1964] reported that isolated nerves exposed in a waveguide showed significant effects on nerve excitability and action potentials. The first project of my Ph.D. dissertation was an attempt to confirm these results using a temperature-controlled waveguide designed in our lab [Chou and Guy, 1973]. Taking advantage of being in a good medical school, I took many graduate courses in physiology and biophysics in addition to a series of electromagnetic courses from the distinguished Professor Akira Ishimaru.

In our laboratory, effects were found to be due to absorption of high levels of RF energy in the nerve exposed in air and parallel to the E-field in the center of waveguide (TE_{10} mode); although temperature meas-

urements with a thermocouple at the surface of the small nerve in the middle of a waveguide as done by Kamenskii showed no measurable temperature rise. When the experimental procedure was modified to keep the nerve in a temperature-controlled waveguide filled with physiological solution, no effect on action potentials other than thermal was observed; even with exposure to very high peak pulsed power levels with SARs up to 220 kW/kg [Chou and Guy, 1978]. Dr. Ken Courtney, a postdoctoral fellow from the Department of Physiology and Biophysics, used the same waveguide to show no RF effect on synaptic transmission [Courtney et al., 1975]. We concluded that the effects in Kamenskii [1964] were due to a thermal response because when the nerve preparation was exposed under temperature controlled conditions in our laboratory, the effects disappeared. Other experiments on muscle contraction gave similar results. Temperature control is vitally important for in vitro studies. In nerve and muscle preparations, a change in evoked response due to a 0.2 °C increase in temperature rise was observed. These studies also indicate that tissue temperature, not SAR, is the determining factor for a biological effect.

Another example of our studies illustrates the importance of temperature control. In an in vitro–in vivo study, conducted in the late 1970s in collaboration with Dr. Vernon Riley of the Pacific Northwest Foundation in Seattle, tumor cells were exposed in a coaxial line system to 30 MHz fields in addition to heating at 43 °C. The cells were then injected into mice to induce tumors with latency of tumor formation being the end point. The coaxial container for the cell culture was surrounded by a circulating mineral oil bath to keep the culture temperature constant. The temperature variation of the culture medium, which was monitored by a single non-perturbing VitekTM temperature sensor, was less than 0.2 °C. While this result indicated that the culture temperature was relatively constant at one location, this did not mean the temperature was constant at all locations. In our first experiments, we observed that the latency of tumor formation was different for different levels of RF exposure. Results showed that RF exposures protect the tumor cells from hyperthermia damage. The higher the RF exposure the shorter latency, which means more cells were protected. We attached a pump to circulate and stir the fluid containing the cells so that the cells would not sink to the bottom of the container. Without circulation, the cells would settle in the cooler region of the thermal gradient, caused by the cooling of the lower surface the cell container in contact with the mineral oil bath. Before we identified the thermal gradient problem, we thought we had found a non-thermal effect of RF fields and almost made a mistake of publishing the results [Chou, 2003].

In 1980, a visiting scientist K.C. Yee arrived from Zhejiang Medical University in China. His work addressed reports of effects on heart rate observed in Chinese RF factory workers, an effect also reported in the western literature [Frey and Seifert, 1968]. In a series of experiments, my temperature-controlled waveguide was used to study whether RF exposure would alter the beating of isolated hearts. A comparison of the results with different recording methods showed that bradycardia (decreased heart rate) of exposed hearts was due to induced-current perturbation artifacts, caused by the high electrical conductivity of the concentrated KCl or the metal wire electrodes used to record the heart rate [Yee et al., 1984]. With a modified and non-perturbing electrode method for monitoring heart rate and at a constant temperature, there was no 16 Hz modulated or pulsed RF exposure effect on the heart rate for SARs up to 200 W/kg [Yee et al., 1984, 1988, 1994]. Use of metal electrodes for physiological recordings during RF exposure can cause false positive effects, as shown by Dr. Guy in the cat brain study [Johnson and Guy, 1972]; therefore, high resistance carbon-loaded electrodes are recommended for EEG recordings [Chou and Guy, 1979].

Auditory Effect

The second part of my Ph.D. dissertation was on the microwave auditory effect, which was first described in 1947 [Chou et al., 1982a]. In the 1960s, based on a series of human and animal studies, Allan H. Frey concluded that microwave pulses trigger the auditory nerve resulting in the subject hearing buzzes or clicks when the head was exposed to short (less than 70 μ s) microwave pulses of various repetition rates. From discussions with Mr. Frey, we learned that a very quiet environment is necessary for the exposed subject to hear the microwave pulses. In fact, most subjects inserted ear stopples to reduce ambient noise so that the microwave-induced sounds could be heard. Dr. James Lin and Dr. Guy were the initial human subjects in our laboratory to confirm that indeed humans can hear microwave pulses [Guy et al., 1975]. Taylor and Ashleman [1974] from Dr. Guy's laboratory showed with evoked response method that the microwave auditory effect is mediated at the periphery as are the effects of conventional acoustic stimuli, because all evoked response disappeared after a destruction of the cochlea. I started a series of animal studies with the help of distinguished auditory physiologist, Dr. Robert Galambos of the University of California at San Diego. We successfully recorded cochlear microphonics (physiological potentials that mimic those induced by sound) from the round window of the cochlea of guinea pigs. The exposure system and recording techniques

were optimized to minimize the electromagnetic interference and improve the signal to noise ratio during the initial few hundred microseconds of the induced response [Chou et al., 1976]. At the beginning, I had trouble recording any signal from the guinea pig cochleae because these animals often have middle ear infection and are deaf. To measure microphonics, I learned to use guinea pigs with Pryor's reflex, that is, animals that displayed an involuntary flicking or twitching of the ears. With the appropriate animal model, the microwave-induced microphonics result matched well with the physical measurement results, obtained by Foster and Finch [1974] showing that the small energy absorption per pulse was adequate to launch a thermoelastic pressure wave. This wave activates the hair cells in the cochlea, which induces the hearing sensation. The microwave hearing effect was found not due to direct nerve stimulation as had been suggested by Frey. Further experiments on various head sizes of guinea pigs and cats showed that the frequency is dependent on the head size, and the auditory responses generated by short and long pulses have the characteristics of thermoelastic pressure waves [Chou et al., 1977]. Experimental observations following destruction of the eardrum, middle ear and cochlea on microwave- and sound-induced brain stem evoked responses confirms that the cochlea is the origin of the hearing sensation [Chou and Galambos, 1979]. Microwave hearing is a proven low-level microwave effect (at the threshold level, the temperature rise from each microwave pulse is a millionth of a degree Celsius) and the mechanism of interaction is known. Although the temperature rise is very small, the mechanism is still thermal in nature. Since hearing microwave pulses is similar to hearing very weak acoustic sound, the response is not considered adverse to human health. For details, please see a review and tutorial article on this subject published in the Journal of Acoustic Society of America [Chou et al., 1982a] and a recent review by Elder and Chou [2003].

Acute Exposures of Animals

In the early 1970s, in addition to the interest in RF bioeffects created by the Soviet exposure of the American Embassy in Moscow, there were concerns about microwave oven safety. Also, because of the oil embargo in the early 1970s, the Department of Energy funded work on the solar power satellite project. The plan was for satellites to contain equipment for transforming solar energy to microwave energy and beam the microwaves to earth where the energy would be transformed into electrical power. This project raised questions on microwave safety for humans as well as other animals and plants. During this time, we had

contracts from the American Home Appliance Association, Environmental Protection Agency (Ralph Smialowicz, Joe Elder, Carl Blackman), National Institute of Environmental Health Sciences (Mike Galvin, Don McRee), and National Aeronautics and Space Administration (Moris Shore, Mays Swicord), Office of Naval Research (Tom Rozzell, Mike Marron), and Air Force (John Mitchell). These contracts supported research on cardiovascular, behavioral, immunologic, and hematological effects in animals exposed for short periods of time to RF fields. I had a great time collaborating with many faculty members in the medical school of the University of Washington, such as Professors George Brengelmann, James Clagett, Karl and Ingrid Hellström, and Dr. Piro Kramar. Dr. Richard Lovely was a psychologist on our team responsible for behavioral effect studies. The Air Force also supported studies with both pulsed and continuous wave signals [Chou et al., 1982b] and I had the opportunity to work with Dave Ervin, William Hurt, Jim Marritt, Stu Allen, B. Jon Klauenberg, and Mike Murphy as well as the Air Force consultants Lou Heynick and Peter Polson.

In the late 1970s, there were reported effects of drug and RF exposure interaction effects and we started projects in this subject area in collaboration with Dr. Akira Horita of the Department of Pharmacology. Through this interaction, Dr. Henry Lai joined our research team in 1980 and he summarized many of our collaborative studies on the nervous system in his 1992 paper, presented at Dr. Guy's retirement symposium [Lai, 1992].

The Air Force had an interest in the so-called "stun effect" during the time we had a contract studying differences in bioeffects following pulsed and continuous wave exposure. There was a claim that a 3 °C temperature rise in the brain would "stun" rats. Using an exposure system modified from the auditory study and a high power RF source (10 kW), we exposed the head of rats to a single pulse (915 MHz magnetic field) of different durations (1 μ s–360 ms) to produce SARs as high as 4×10^5 W/kg. When the specific absorption exceeded 28 kJ/kg, regardless of peak power or pulse width, rats displayed seizures lasting for 1 min after exposure followed by a 4–5 min unconscious state. The rats recovered without apparent effect from the brief RF exposure. Thermography and thermocouple measurements indicated a maximum temperature rise of about 8 °C, that is, a final brain temperature of 46–46.5 °C. This study clarified that the stun effect is energy dependent and a result of a high temperature rise in the brain, that is, the threshold temperature rise is 8 °C, not 3 °C [Guy and Chou, 1982].

Chronic Exposures

The 1000-fold difference in Eastern and Western safety limits for RF exposure was a major reason for the USSR–USA scientific exchange program on electromagnetic effects research led by Dr. Don McRee of NIEHS (1976–1989). In this program, Dr. Guy was the US expert on RF dosimetry. It was obvious at the beginning of this program that the Soviet research was weak on RF dosimetry and the US and other Western countries had published few chronic exposure studies. To address the latter issue, we designed experiments to expose rats and rabbits to low-level microwave fields (<10 mW/cm²) for 3 months [Guy et al., 1980; Chou et al., 1982b, 1983]. Although there are no effects on body weight and health of rabbits exposed to RF energy, one interesting observation was a decrease in food consumption during exposure to 5 mW/cm² (5.5 W/kg in the head and 7 W/kg in the back) [Chou et al., 1983]. This effect was interpreted to be due to microwave energy being used by the animal as a food (energy) substitute.

Because of our experience with animals exposed to RF energy, our laboratory received an Air Force contract to investigate whether lifetime exposure to pulsed microwave signals simulating PAVE PAWS radar exposure can cause health effects. Dr. Jerome Krupp was our monitor throughout the 6-year study. More than 200 circularly polarized waveguides were built by our head technician Carrol Sorensen and his assistants. With the help of several consultants (Dr. Leo Bustad, Mr. George Sacher, and Dr. Edward Masoro), we designed a study exposing 100 rats (plus 100 sham exposed rats) to pulsed 2450 MHz fields for 21 h a day for 25 months. For the metabolism study, we invited Dr. Eleanor Adair to be our consultant. Robert Johnson led a group of technicians who worked in the specific pathogen free animal rooms where the animals were exposed. Pathology and hematological tests were subcontracted to Dr. Larry Kunz. Large amounts of data were analyzed by Desmond Thompson, a Ph.D. student in the Department of Biostatistics under the direction of Dr. John Crowley and Dr. Ross Prentice. This study was the first large-scale chronic exposure study in bioelectromagnetics. The original plan was to combine the 10 volumes of technical reports into one book, but this plan did not materialize. The results were published in the 1992 Bioelectromagnetics Special issue dedicated to Dr. Guy's retirement in 1991 [Chou et al., 1992]. Among the 155 parameters measured in the lifetime study, a statistically significant increase of primary malignancies in exposed rats versus controls (18 vs. 5) is a provocative finding, but the biological significance of the effect in the absence of truncated

longevity is conjectural. Overall, the results indicated no definitive biological effects in rats chronically exposed to RF fields at 2450 MHz at 0.15–0.4 W/kg averaged over the whole body. The Air Force funded three subsequent lifetime exposure studies specifically on cancer, one at the Georgia Institute of Technology and two at Trinity University; all three studies found no effect of RF exposure on cancer in mice and rats [Toler et al., 1997; Frei et al., 1998a,b]. The weight of evidence in these four lifetime studies is that there is no relation between RF exposure and cancer development, a result that continues to be supported by over 30 more recent animal cancer studies [Dasenbrock, 2005; Moulder et al., 2005].

In my paper published in a Russian journal [Chou, 2003], I pointed out the importance of sham controls (animals experiencing exactly the same treatment and handling as the exposed animal, but without RF exposure). [I take this opportunity to thank my Russian friend Professor Yury Grigoriev for his invitation to publish this article.] Some investigators have used either (a) historical controls (i.e., data collected at a different time, usually before), (b) cage controls (animals kept at a different location, e.g., the animal care facility, or the same location but not handled the same way as the exposed group), or (c) semi-sham controls (animals receiving simulated exposure but the exposure condition and handling are not identical to that of the exposed group). Comparison of any of these three “controls groups” to the RF-exposed animals can generate a “false positive” effect, that is, a statistically significant difference, just because the treatment or handling is not the same. For example, Professor Chiang Huai’s group in China recently published a paper showing cage controls had higher mammary tumor incidence than RF exposed rats and sham-exposed rats; however, when the correct comparison was evaluated, there was no difference in the cancer incidence in the RF-exposed and sham-exposed animals [Yu et al., 2006].

Some biological end points are very sensitive to slight differences in experimental procedures. For example, when we did the pilot study for the lifetime exposure study [Chou et al., 1992], we discovered an interesting effect on the stress level (using corticosterone as the indicator) between the exposed and the sham-exposed rats. Twenty rats (10 exposed and 10 sham-controls) were housed in individual circularly polarized waveguides on four shelves in each alcove of the exposure rooms [a total of 10 alcoves (200 rats) in two rooms]. All cylindrical waveguides had identical diameters and visual appearance to the rats, except those for the sham-exposed animals did not have transducers at the ends, and therefore, required less

longitudinal space. The exposed and sham-exposed waveguides were randomly arranged on these shelves, except that only sham waveguides could be in the center of the shelves because of the operation of the sliding door. Although we employed identical handling of the rats, because of the asymmetrical distribution of the exposed waveguides relative to the center, the sequence of opening the alcove doors for animal care caused a difference in stress hormone (later bled rats had higher corticosterone). Therefore, we implemented a random daily opening of the sliding doors (determined by computer) over the 25-month lifetime study in order to smooth out the bias of the door opening. Without knowing this fact, we could have found a repeatable, but artifactual effect, which was due to the door-opening sequence and not due to RF exposure.

In the 25-month exposure study, there were observed effects on corticosterone and immune system effects [Chou et al., 1992]. A follow-up study was conducted to confirm both effects. Neither effect was confirmed in two groups of 20 animals each exposed for 6 and 12 months, respectively, under the same exposure condition as the original study. An equal number of sham-exposed animals served as controls. The sample size of 20 animals per group was chosen to have good statistical power to detect the same magnitude of differences observed in the original study. The failure to confirm indicates that the original findings were not robust. Without this follow-up study, we had no confidence whether the immune system effect was repeatable.

DOSIMETRY

I had the fortune to learn and work in the laboratory of Dr. Guy who pioneered RF dosimetry. He has done extensive work in phantom development and thermography with the assistance of John McDougall and Carrol Sorensen. Because of this reputation, the lab attracted visiting scientists from many countries including China when that country opened its door to the US after President Nixon shook hands with Premier Chou En-Lai. As a Chinese, I had the privilege to work closely with them, not only technically but also personally. Mr. Yang Geng-Yuan of the Biophysics Institute in Beijing was the first to arrive in 1979. He investigated electric current distributions in animals and humans exposed to a uniform 60 Hz high-intensity electric field, and SAR patterns in spherical tissue models exposed to RF energy in a rectangular resonant cavity [Guy et al., 1982; Yang et al., 1984]. This work provided the background for exposure of human scale models in the resonant cavity and also in free space [Guy et al., 1984]. After returning to China, Mr. Yang

introduced dosimetry concepts to the Chinese National RF exposure standard GB8702–1988. Professor Chen Gang-Wu was in our lab for 1 year and participated in the development of phantom materials for simulating muscle tissue at 13.56–2450 MHz [Chou et al., 1984a]. These formulas for tissue simulating materials were later used in my hyperthermia studies when my work turned to medical applications. Professor Chen returned to Shangdong University and applied RF techniques for detecting oil underground. The third visitor was Professor Jiang Han-Bao from Sichuan University. Because of the one child policy in China, male contraception was one choice for birth control and one technique used microwaves to heat the testes for 1 h to produce a temporary sterility lasting about a month. He worked on a phantom male model to study heating patterns in the reproductive organ and found that circularly polarized fields were more effective in heating the testes than linearly polarized fields. In collaboration with another visiting scientist, Dr. D.J. Li of Henan Tumor Hospital, Professor Jiang also worked on several intracavitary applicators for vaginal and rectal cancer treatment [Li et al., 1984]. After his return to China, Professor Jiang developed other recipes for tissue simulants using food materials.

To quantify dosimetry in animals exposed acutely or chronically as described above, whole body and SAR distributions in animals of various sizes and orientations exposed in free space and in waveguides at various frequencies were studied. One experiment exposed birds of different sizes (parakeets to turkeys) to show how RF absorption in animals depends on size relative to the RF wavelength [Chou and Guy, 1985]. This paper describing this work received the best paper of the year award from the Journal of Microwave Power in 1985.

For the lifetime exposure study supported by the US Air Force, we used calorimetry for whole body SAR and thermography for SAR distributions in 100–700 g rats exposed at various orientations in 2450 MHz circularly polarized waveguide [Chou et al., 1984b]. With the same techniques, we studied dosimetry for seven different exposure conditions (including anterior and posterior exposures in a circular waveguide, near field, far field with E- or H-field parallel to the long axis of the body and dorsal exposure in a miniature exposure chamber with E or H field parallel to the body's long axis) [Chou et al., 1985]. Since the rat tail plays an important role in thermoregulation, it was interesting to show that the tail absorbed RF energy strongest when parallel to the E-field. Brain SARs measured by Vitek probes also showed large variations for different exposure conditions. This research demonstrated the complexity of RF absorption patterns in biological

objects and we have described techniques for measuring the RF absorbed energy at the target tissue. The data reinforced the conclusion that incident power density alone is not sufficient to interpret an RF induced biological effect.

In 1980, Mr. Ron Petersen of Bell Labs asked us to determine the maximum power that could be delivered to a UHF mobile cell phone antenna without exceeding the ANSI RF safe exposure limits. We built full size man and child models and placed them in the standing position next to an automobile or in sitting positions in the vehicle. The models were exposed from the vehicle mounted antenna in a $12 \times 12 \times 24$ ft anechoic chamber to 10 kW UHF power emitted from top or trunk mount antennas. Thermometry and thermography techniques were used to measure localized SAR values at various anatomical sites. We found that a maximum of 3.5 W input could be delivered to the antenna without exceeding the 1982 ANSI RF protection guide for humans exposed either inside or at closest approach to the vehicle [Guy and Chou, 1986].

About the same time, Mr. Petersen also asked us to test the shielding effectiveness of an RF protective suit [Guy et al., 1987]. After the initial research results were obtained, Werner Rhode of Milliken & Company continued to support the project to test additional developed materials and suits until 1985 [Chou et al., 1987]. A full size homogenous muscle man model was exposed in the far field to high intensity RF energy with and without protective suits made of different metallic fabrics and different designs. Electric fields at different anatomical surface locations on the model were measured and attenuations were calculated. Results showed that the suit must fully enclose the entire body to be effective. For example, a laboratory coat-like design gave poor protection because the RF fields could propagate into the body through the openings. A Navy protective suit provided by Dr. Elliot Postow performed the best because it was completely enclosed; however, we found that the material was very flammable. Upon learning this Dr. Postow told me that he once wore the RF protective suit to a Halloween party but that he would not do it again.

In 1982, we studied induced current in humans exposed to VLF fields from US Navy and Coast Guard antennas in the states of Washington and Hawaii. We used ourselves as guinea pigs by measured induced currents in our bodies when exposed to VLF fields very close to the antennas. We parked rented cars of various sizes on metal wire mesh (chicken wire) ground planes under large antennas emitting 10, 24, or 100 kHz signals. We measured RF currents passing through our bodies when in contact with a vehicle, when wearing shoes with soles of different materials, and when

standing bare foot in a puddle of water. I experienced a lot of shocks during that week. I felt the current all the way to my upper arm, while Dr. Guy and Carrol Sorensen were measuring the current passing through my legs. I did not have any side effects from the RF induced currents in my body, but I did have serious skin burn from exposure to the Hawaiian sunlight. I was so tanned that my wife almost could not recognize me when I returned home.

When I moved to the City of Hope National Medical Center in 1985, I was very fortunate to convince John McDougall to join me. Kwok Chan, newly graduated from the University of Arizona and with extensive experience in thermometry and instrumentation, joined our newly formed hyperthermia research team. During 13 years at the City of Hope, many dosimetry projects were performed related to exposure system design and medical applications, which will be described in a later section.

Now I will leap to 1998 and my Motorola experience, in a laboratory started by Dr. Quirino Balzano in the late 1970s. The team now consists of very capable engineers working on dosimetry and antennas. Most of the dosimetry work is related to RF product compliance issues. For example, we developed head tissue simulants for various frequencies which have been included in IEEE 1528 and IEC 62209-1 standards [Kanda et al., 2004a]. Mike Kanda and Maurice Ballen were the main contributors. Because of the long SAR measurement time required to do three-dimensional scans for mobile phone compliance testing, Dr. Mark Douglas and Mike Kanda developed a two-dimensional scanning method which is 70% faster and shown to be accurate enough for preliminary testing [Kanda et al., 2004b]. This method has been implemented in a commercial system known as MOTO-SCAN.

While the company laboratory is primarily for product compliance related projects, interesting research studies have also been conducted. The first example is on the usefulness (or uselessness) of protective shields for mobile phones. We tested seven brands of "Radiation Shields" using the standardized method of SAR testing for a GSM phone with and without the shields [Oliver et al., 2003]. We found no difference in the RF absorption in a phantom human head model exposed to a mobile phone with or without the presence of the shield. Some of the advertisements for the shields claimed that the material could block 97-99% of the RF energy. This statement may be true for energy incident on the material itself, but the shield is only a small piece of material and cannot block majority of the RF energy emitted by the phone. Before mobile phones can be shipped to customers in different

countries, all phone models are tested at maximum power and must be within international exposure limits specified by receiving countries. There is no need for any "radiation shield" on a mobile phone. If any shield were to be effective, it would adversely affect the phone function and the battery would lose power faster because the phone would need to operate at a higher power to communicate with a base station. Such a shield would defeat the phone's adaptive power control that enables the phone to operate at the lowest possible power level when communicating with a base station.

Another study addressed the media report from the United Kingdom claiming that use of hands free kits can increase RF energy absorption in the brain by three times. We did experiments and calculations which showed that this was due to improper measurement methods in the studies reported to the media [Bit-Babik et al., 2003]. A third example is on the controversial issue of whether children's heads when exposed to mobile phones have deeper energy penetration than in adults as shown by Gandhi et al. [1996]. Dr. Giorgi Bit-Babik in our laboratory, in collaboration with Dr. Guy, Professor Jian-qin Wang, and Professor Osamu Fujiwara of Nagoya Institute of Technology, tested several human head models and found that penetration depths for children and adults are about the same [Bit-Babik et al., 2005]. This conclusion is consistent with other recent publications [Martinez-Burdalo et al., 2004; Christ and Kuster, 2005; Lee et al., 2005; Wiart et al., 2005; Beard et al., 2006; Keshvari et al., 2006].

EXPOSURE SYSTEMS

At the University of Washington, we developed various methods and exposure systems to expose mice, rats, guinea pigs, cats, rabbits, monkeys, and birds to RF energy. While at the City of Hope, I had the pleasure to work with Dr. Guy again from 1994 to 1998 when we were funded by the Wireless Technology Research Program (industry supported). The work involved the development of unique RF exposure systems. One system would be used to expose only the head of animals to simulate mobile phone use, and another system would be a temperature controlled in vitro system for exposing cell cultures to RF energy. John McDougall provided experimental expertise and Kwok Chan provided numerical computer analysis effort in the development of a loop antenna design for a head only exposure system. With the help of Dr. Balzano and Danny McCoy of Motorola, tunable loop antennas were shown to produce very efficient energy coupling to the rat brain exposed to high power cellular and PCS band RF energy. The system was successfully used for

an acute DNA effect study, a contract monitored by Dr. Don McRee. This design also was adopted by scientists in Europe. The *in vitro* exposure system consisted of two temperature-controlled TEM cells built by Carrol Sorensen. Originally, the system was designed to expose cells in Petri dishes in a cell culture study on p53 tumor suppressor protein in normal human fibroblasts [Li et al., 1999]. Later, the system was modified to hold test tubes instead of Petri dishes. Papers describing both exposure systems were presented in Dr. Carl Durney's retirement symposium and published in *Bioelectromagnetics* [Guy et al., 1999; Chou et al., 1999a].

When I arrived at Motorola in April 1998, a system was being designed to expose a large population of mice to GSM frequency fields to study whether chronic exposure can cause increased lymphoma incidence; the system would be used in the follow up study to the Repacholi et al. [1997] paper, describing increased lymphoma in mice exposed to mobile phone signals. The final exposure system [Balzano et al., 2000] was used in Australia to expose 600 mice simultaneously in the morning and another 600 in the afternoon for 2 years. The results published in 2002 showed no effect of RF exposure on lymphoma incidence [Utteridge et al., 2002]; thus, these results did not confirm the earlier reported effect. A detailed dosimetry study of the exposure system, in collaboration with Dr. Tadeusz Babij and two graduate students of the Florida International University, was recently published [Faraone et al., 2006].

MEDICAL APPLICATIONS

Hyperthermia

After researching RF bioeffects for many years and finding only thermal effects, my interest in using RF energy for beneficial applications resulted in my attendance at the 1980 hyperthermia meeting in Colorado Springs. At this meeting, I met Dr. Kenneth Luk of the University of California, San Francisco and Dr. D.J. Li of China. Dr. Luk inquired about the University of Washington because he was being recruited to start a hyperthermia clinic in the Radiation Oncology Department. I encouraged him to accept the position so we could work together because it was difficult for me as a bioengineer to work alone on a medical project without a medical partner. Our collaboration started in 1982 and we treated many large tumors with a 915 MHz applicator designed by Dr. Guy to provide efficient RF heating of the tumor, while providing forced air cooling of the skin and surface tissue. Two years later, Dr. Luk accepted a Chairman

position at the City of Hope National Medical Center in Los Angeles and he proposed that I also join him to start a new hyperthermia program. After long consideration, I accepted the offer and moved to Los Angeles in August 1985.

It was an interesting experience to build a new laboratory and to work with radiation oncologists, medical physicists, and nurses. With the assistance of John McDougall and Kwok Chan, we treated patients who had head and neck tumors, breast cancer, cervical cancer, esophageal, and superficial tumors with external, intracavitary, interstitial, and ferromagnetic implant methods. In addition to radiated RF energy, we also used RF current (500 kHz) and ultrasound for inducing hyperthermia. Our team also had biologists led by Dr. Steve Saparato studying the thermal response of tumor and normal cells. We experimented with whole body heating with a system originally designed by Mr. Bill Harrison, by applying 27 MHz fields to a phantom man model and pigs. The first few years, we spent a lot of time investigating heating patterns so as to understand how to more effectively elevate tumor temperature while keeping the temperature of normal tissues below harmful levels. We observed many surprising heating patterns and learned why safe and effective hyperthermia is so difficult to achieve. We also learned the meaning of the phrase "dump and pray" used in the field of hyperthermia because the heating capability of the clinical heating tools was not well characterized before treatment. A summary of the applicator evaluations has been published [Chou, 1992].

In 1991, I obtained a 4-year grant from the National Cancer Institute (NCI) to study intracavitary hyperthermia and combined RF/ionizing radiation treatment of esophageal cancer. We designed a seven-lumen intracavitary tube for applying hyperthermia from an RF source and ionizing radiation from iridium seeds. The hyperthermia part was tested on phantoms, rabbits and pigs before it was applied to patients. Due to the few esophageal cancer patients in Los Angeles, we treated only three patients in 2 years. In 1994, after obtaining permission from NCI to conduct a phase I/II clinical trial in China, I led a team consisting of a radiation oncologist (Dr. Nayana Vora), a medical physicist (Dr. Cecil Staud), and engineers (McDougall and Chan) to China. We treated 25 patients in 3 weeks at the Jingling Hospital in Nanjing, my hometown. The Department Chairman of Radiation Oncology, Dr. Ren Ru-long was instrumental in getting the study completed on schedule. He came to the City of Hope in 1995 and worked with me until I left in 1998. Results of the clinical trial in China were published in the *International Journal of Hyperthermia* [Ren et al.,

1998]. Summaries of more recent clinical results on hyperthermia and RF ablation are reported in a book chapter [Chou, 2006].

Electrochemical Treatment

In 1992, I attended the First International Symposium on Electrochemotherapy of Cancer in Beijing and was intrigued by the results of this technique. Electrochemical treatment (EChT) of cancer utilizes direct current to produce chemical changes in tumors. Dr. Xin Yu-ling of China Japan Friendship Hospital led the effort in China and had treated thousands of patients with a modification of the method promoted by Dr. Björn Nordenström of the Karolinska Institute, Sweden. Dr. Xin modified the method by inserting both cathode and anode platinum electrodes into tumors of conscious patients. A constant voltage of less than 10 V was applied to produce a 40–80 mA current between the anode and cathode for 30 min to several hours, delivering 100 coulombs per cubic centimeter. Professor Li Kai-Hwa showed that electrolysis, electrophoresis, and electroosmosis are the mechanisms of cell killing. At the time, the newly formed NIH Office of Alternative Medicine issued a call for proposals. I successfully obtained a seed grant to investigate the method with mice first and then with rats. Results were encouraging and consistent with the patient data in China. I introduced the subject of EChT in the *Bioelectromagnetics* [volume 18(1); Chou, 1997] and this issue included two EChT papers I invited from China, written by Dr. Xin and Professor Li. Our own animal study was also included [Chou et al., 1997a]. In collaboration with Dr. Yun Yen, a medical oncologist, we studied cellular responses to EChT [Yen et al., 1999]. My Ph.D. student, J.R. Li presented a poster in 1995 at the BEMS meeting in Boston and won the best poster award. In 1994, before we went to Nanjing for the esophageal cancer treatment, I took Dr. Vora and the team to Beijing to observe Dr. Xin's treatment of his patients with EChT. Dr. Vora was impressed by its simplicity and remarkable follow up results. After the trip, I initiated a Phase I clinical trial on recurrent superficial measurable malignant tumors, but it took 2 years to get approval from the local institutional review board, after the FDA Investigational Device Exemption was granted. We treated our first patient with multiple small superficial tumors on October 3, 1996 in the presence of Dr. Xin; however, a total of only seven patients were treated during the last 2 years I worked at the City of Hope [Chou et al., 1999b]. We were treating patients who have failed all other treatments, including surgery, radiation, and chemotherapy. Although we saw some positive local responses on these terminal patients, a small local response is not

enough to save a patient with metastatic disease. While struggling to get protocol approval, a 3-year grant from the Army Breast Cancer program supported our studies on mechanisms and dose relationship until I left for Motorola.

MRI Safety

In 1994, Cochlear Corporation asked us to help determine whether patients with metallic cochlear implants can be safely scanned with MRI. We built a full size human fiberglass model with a brain, bones including the skull, and muscle made of phantom materials. Dielectric properties of the phantom tissues were prepared accordingly for simulating tissue exposure to 63.8 MHz in the 1.5 T scanner. The cochlear implant was installed in the model using the method I learned at the House Ear Institute in Los Angeles. Temperature rises during MRI scans were monitored by 12 channel Luxtron optical sensors. The results showed no observable heating of or from the implant during exposure. The company then asked us to test a new product for totally deaf patients which could be implanted in the brainstem to stimulate the neural tissue beyond the cochlea [Chou et al., 1995]. The FDA approval for this device required data on RF safety during MRI scans. A month after we submitted a report showing no RF heating, the FDA approved the product. We had the pleasure to contribute to the introduction of a new device to treat many totally deaf patients.

In 1996, Dr. Bruce Simon of Electro-Biology Inc. wanted us to test the safety of a spinal fusion stimulator which has been used to increase bone fusion in 50,000 patients (as of 1997) during MRI scans. We modified the phantom to suit this study. When the stimulating electrodes were properly implanted, the maximum temperature rise was less than 2 °C. If the leads were broken, the maximum temperature rise was up to 14 °C. We therefore recommended that radiological examinations are necessary to ensure the integrity of the implant before a patient can be MRI scanned [Chou et al., 1997b].

The third request from DePuy ACE Medical Company led to an evaluation of RF tissue heating attributed to cervical fixation devices during MRI scanning. We designed an experiment to determine whether titanium fixation pins can cause excessive heating in a phantom model. If so, inserting a high resistance ceramic section into skull fixation pins would reduce, or eliminate, skull heating by these devices during MRI scans. Seven cervical fixation devices (different halos and tongs) and two types of skull pins were evaluated. For an open back halo with standard titanium skull pins, the temperature increase was up to 48.3 °C. With a less conductive carbon open back halo,

the temperature rise was only 5.6 °C. A closed back aluminum halo with standard titanium skull pins resulted in a 6.8 or 2.8 °C rise, depending on the halo orientation in the MRI bore. With titanium/ceramic skull pins, temperature rise with all halos and tongs was less than 1 °C (with air temperature correction). These results showed that during MRI scans, excessive heating of patients due to RF induced current may occur in conductive halos, tongs, and skull pins. RF tissue heating depends on the conductivity, shape, and orientation of the fixation device. Heating may be significantly reduced by using insulated skull pins, which isolate RF induced current from the head. However, if titanium/ceramic skull pins are unavailable, an electrically closed halo can also appreciably reduce RF heating. Due to legal concerns of overheating patients, the sponsoring company did not want me to publish the paper. When the concerns were over, I submitted the paper for publication, but the method was criticized by a reviewer for not following a standardized procedure that was published 5 years after our study was completed! This was the only study that I could not get published.

SERVICE

IEEE

In 1979, I assisted Dr. Guy in his role as Chairman of the ANSI RF safety standard committee; a new standard incorporating dosimetry was published in 1982. I again assisted Dr. Guy who chaired the revision of this standard that led to the publication of the IEEE C95.1–1991 RF safety standard. In 1997, while at the City of Hope, Dr. Om Gandhi recommended that I replace him as the IEEE SCC28 SC4 Co-Chairman; this committee was responsible for revision of the 1991 standard. When I changed jobs in 1998 to work for Motorola, I tried to resign from the co-chair position, but my resignation was not accepted by the IEEE SCC28 Executive Committee. I continued to co-chair the subcommittee with Dr. John D'Andrea and the work culminated in the publication of the IEEE/ICES C95.1-2005 RF safety standard on April 19, 2006. It was a rewarding experience to work with so many experts in the field of bioelectromagnetics. I worked extensively with Ron Petersen, Richard Tell, Mays Swicord, Joe Elder, Eleanor Adair, Patrick Reilly, Robert Cleveland, Lou Heynick, Dennis Blick, Robert Curtis, Marvin Ziskin, John Osepchuk, Sakari Lang, John DeFrank, Ken Foster, Howard Cyr, Jules Cohen, Asher Sheppard, Sheila Johnston, Marty Meltz, Vitas Anderson, etc. The subcommittee consisted of 132 members from 24 countries. To get so many

different opinions to agree with more than 75% consensus as required for IEEE approval was not easy. During the last several years, I represented ICES SC4 and presented updates on the RF safety standard revision in many scientific meetings, including WHO EMF standard harmonization and government regulators meetings.

In addition to the RF safety standard, I have participated in mobile phone SAR measurement standard work since 1997 and served as section editor for the phantom model chapter. It was a pleasure to work with Howard Bassen, Niels Kuster, Anssi Toropainen, Antonio Faraone, Mark Douglas, and others on the standard. After extensive discussions for several years, IEEE Standard 1528 was published in December 2003. In 2005, IEC published 62209–1 which is completely harmonized with IEEE 1528. Mark Douglas worked with Matthias Meier and played a big part on this harmonization.

COMAR

From 1994 to 1999, I served as Vice-Chair, Chair and Past Chair for the Committee on Man and Radiation (COMAR) of the Engineering in Medicine and Biology Society of IEEE. COMAR's primary area of interest is biological effects of non-ionizing electromagnetic fields. The committee examines and interprets biological effects and presents its reports usually in Technical Information Statements (TISs) or Position Papers. I have contributed to a few COMAR reports published in IEEE Engineering in Medicine and Biology Magazine on video display terminals, wireless communication devices, base stations, high definition TV, RF sealers and heaters, medical equipment interference, RF overexposure, and use of protective devices for mobile phones [<http://ewh.ieee.org/soc/embs/comar/>]. In 1996, I led a task group to publish a tutorial review paper on RF experimental dosimetry [Chou et al., 1996].

BEMS

In 1978, I participated in the committee to organize a joint 1979 meeting of URSI, IEEE Antennas and Propagation, and the Bioelectromagnetics Symposium at the University of Washington in Seattle, which was the first BEMS meeting. I have attended all 28 annual meetings of the Bioelectromagnetics Society. I served on the BEMS Board from 1981 to 1984. In 1985, I joined the Editorial Board and in 1987 I began a 16-year position as an Associate Editor. During this time, I learned so much from three Chief Editors: Richard Phillips, Don Justesen, and Ben Greenebaum. When I switched jobs from academia to industry in 1998, I submitted a letter of resignation as an Associate

Editor, but my resignation was not accepted by the Board of Directors. During the years, I served as guest editor for the Bill Guy retirement special issue [Bioelectromagnetics, 13(2), 1992]; the issue on electrochemical treatment of tumors [Bioelectromagnetics, 18(1), 1997]; assisted Om Gandhi with the Carl Durney retirement issue [Bioelectromagnetics, 1999 (Supplement 4)]; and assisted Ben Greenebaum with the Eleanor Adair retirement issue [Bioelectromagnetics, 2003 (Supplement 6)].

Mobile Manufacturers Forum (MMF)

The MMF was formed in 1998 to facilitate joint funding of key research projects and industry cooperation on standards, regulatory issues and communications concerning health and mobile phones. I have served as a Science Advisor for MMF and have worked extensively on media, standard, and regulatory issues in China and other parts of Asia.

CONCLUDING REMARKS

In closing, I would like to summarize the lessons I have learned from my 35 years in bioelectromagnetics research.

- (1) RF energy interaction with biological tissues is very complicated. Collaboration among experts in biological sciences and engineering is necessary for credible RF biological effects studies and successful medical applications of RF energy.
- (2) For bioeffects studies, learning how to design an experiment and how to properly expose animals or specimens are critical. Artifacts are difficult to reveal. Sham exposure must be done properly. Double blind procedure is much preferred.
- (3) When an effect was found, I checked to see whether the effect was repeatable and look for reasons to explain the effect. So far, my own studies have not shown any effect which is not related to heating. Because there is no known mechanism at *low* RF exposure levels that can explain effects other than heating (except electrostimulation at low RF frequencies, pearl chain, and electroporation, etc, occur at high RF intensities). To prove an effect is not due to heating is not easy.
- (4) For medical applications using heat, knowing temperature distribution pattern in a complex human body with sophisticated cooling capacity is crucial for successful treatments.

While there are differences in approaches and methods, science should converge and not diverge in

finding the safe level for exposure to EMF that is not adverse to human health. This is reflected in the new IEEE C95.1–2005 standard, which is substantially harmonized with the 1998 ICNIRP guidelines (basic restrictions in the RF range), and the conclusion of biological effects is consistent with the 1995–2006 reviews of more than 20 independent expert groups worldwide, that is, there is no credible evidence that RF exposures within internationally accepted limits cause any adverse health effects.

As the progress in technology continues and human beings are enjoying an increased quality of life, it is essential for scientists to ensure that safety is not compromised. Scientists must be very careful in reporting their findings. Mistakes must be minimized and stopped at the first level of scientific research. As in an Egyptian saying “it takes one person to throw a rock into the well, and it will take 10 people to get it out.” Let us make sure that what we do is right the first time. If there is a mistake, one should be courageous to admit it promptly. Scientists should aspire to explore the unknowns through sound and well-planned research and not to make the situation worse through reporting what might be erroneous conclusions that take a long time to clear up. As stated by the Biological Effects Policy Advisory Group of the Institution of Engineering and Technology in Europe: “. . .scientists have an overriding responsibility to ensure that their findings are robust before publication, notwithstanding the various pressures to publish their work.” [IET, 2006].

Communicating with media is important. Currently, media reports are rarely reviewed by the source, unlike the peer review process in scientific publication. Media reports are mostly on the spotlight stories instead of on weight of scientific evidence. In my opinion, accumulated misinformation from the media is the source of electrophobia in the general public. It is the responsibility and moral obligation of scientists to bring “verified” information to the public through media.

After more than 50 years of studies looking for EMF bioeffects, it is time for the Bioelectromagnetics research community to clarify the identified gaps in knowledge on EMF bioeffects as listed in the WHO research agenda and move on to study what EMF can do for people. Dr. d’Arsonval would have been pleased to learn that what he started in the late 19th century on medical applications of EMF holds promise for much fruit in the 21st Century.

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