A Conversation Between Yasuhito Sasaki and Thomas Beyer

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Thomas Beyer, a professor of Physics of Medical Imaging at the Medical University Vienna (Austria), talked with Yasuhito Sasaki, MD, PhD, Director of the Research Center for Radiation Oncology in the Clinical Research Center at Shonan Kamakura General Hospital, which is affiliated with the Graduate School of Yokohama City University (Japan). Dr. Sasaki is also president of the Radiation Effects Association. He was trained as an internist and specialized in nuclear medicine at the University of Tokyo (Japan) and Johns Hopkins Hospital (Baltimore, MD). His research activities have spanned in vitro and in vivo nuclear medicine research, including development and application of catheter-based semiconductor detectors, ^{14}C- and ^{13}C-labeled breath analysis techniques, prototype PET/CT instrumentation, and radioimmunoassay of drugs for therapeutic monitoring. Dr. Sasaki has chaired departments of radiology and nuclear medicine at several universities in Japan, including Gunma University and the University of Tokyo. He also served as Director General of the National Institute of Radiological Sciences (NIRS; Chiba, Japan), where he promoted carbon beam radiotherapy.

Dr. Sasaki has also been actively involved in the field of radiation health effects and radiologic protection in positions with international organizations. In 2000, he received the SNM Presidential Distinguished Service Award for his contributions to collaborative activities between the United States and Japanese nuclear medicine communities. In Japan, he received the Honorable Recognition of Contribution to Disaster Prevention from Prime Minister Yasuo Fukuda in 2008 and the Order of the Sacred Treasure Gold and Silver Star from Emperor Akihito in 2007.

Dr. Beyer: *Dr. Sasaki, thank you very much for talking with me. Could you tell us a little bit about yourself and the reasons for becoming a medical doctor?*

Dr. Sasaki: My father was an internist, and my grandfather was a pediatrician. My father was called to the army when I was only 4 months old. He was later killed in the war. Since my childhood, the expectation of my mother and grandparents was that I would follow in the family tradition. Quite naturally I did and never regret it.

Dr. Beyer: *You studied internal medicine in the early 1960s and became a research fellow in nuclear medicine 5 years later. What drove you from internal medicine to nuclear medicine at the time?*

Dr. Sasaki: I happened to be in charge of a patient with late effects from Thorotorast, a contrast agent containing $^{232}ThO_2$ that was used in the 1930s and 1940s and found to cause liver cancer 20–30 years later. I learned many things through that patient, such as γ-spectrometry, whole-body counting, and microautoradiography, that an internist ordinarily does not learn. My professor assigned me to be a member of the radioisotope group and sent me to Johns Hopkins to be trained by Henry Wagner, Jr., MD.

Yasuhito Sasaki, MD, PhD, FSNMMI

Dr. Beyer: *Throughout your career you held multiple clinical and managerial positions in clinical nuclear medicine and radiology. How would you say this field of diagnostic medicine changed over the years?*

Dr. Sasaki: Obviously the changes were caused by the progress of science and emergence of new medical technology. Nuclear medicine started to evaluate regional physiologic function, which was expanded to metabolic and molecular functions for more precise diagnoses. The progress is amazing, but uncertainty has remained. Medicine cannot cure all patients, because humans must die eventually. Nevertheless, it appears that patients today expect to be cured, just as broken machines and toys are repaired by an engineer. There is less trust in the medical profession. We need to seek a way to recover trust between patients and medical professionals.

Dr. Beyer: *Why do you think that with technologic progress patients have less trust in medicine?*

Dr. Sasaki: Paternalism dominated medical practice half a century ago. Today we are in the era of informed consent and self-decision. Now doctors must explain every possible choice, and patients choose how they want to be treated. It is nice that technologic progress made this possible. Quite often, however, patients are at a loss to make these decisions and may feel that doctors are trying to avoid their responsibilities.

Dr. Beyer: *We spoke about radiology and nuclear medicine as specialties of the field of medicine. Do you see a change in the public perception of the value of ionizing radiation? And what do you think caused this?*

Dr. Sasaki: People fear radiation and radioactive substances, regardless of doses. Some express concerns about the health effects of radiation, and, in recent years, their numbers may have grown. Apparently in western countries quite many patients refuse radiology examinations—is this true?

Dr. Beyer: *I believe there is an increasing but still small fraction of patients who do so, but this is an issue with which doctors are faced. I can only speak for Germany and Austria, where I sense a very strong public fear of radiation. Patients ask for low- or no-exposure examinations. You mentioned already the experience of the Japanese public. You were 8-year-old when*

Hiroshima and Nagasaki were bombed. Do you have any memories of that time and its public reconciliation?

Dr. Sasaki: All schools were closed in Tokyo and other large cities in 1945 because of the war. It was compulsory to move to the countryside. I lived with a farmer's family, who were family friends. I did not hear any news of the atomic tragedy in Hiroshima and Nagasaki when it happened. I lived a peaceful life in the countryside until August 15, 1945, when Japan lost the war, which I recognized observing the sorrowful looks of the adults. I learned the tragedy of Hiroshima and Nagasaki several years later. So, there is no link between my selection of a professional career and the A-bomb.

Dr. Beyer: *So because of your seclusion in the countryside you were not a witness to these torments when they actually happened?*

Dr. Sasaki: No. Much later I served as Chair of the Atomic Bomb Survivors Health care Commission, with a mandate to review applications for special medical allowance submitted by A-bomb survivors, or *hibakusha* in Japanese. I also served as Councilor of the Radiation Effects Research Foundation (RERF), so I'm quite familiar with the consequences of the atomic bomb. When A-bomb survivors became ill, for example with cancer, and needed treatments, they could claim a special medical allowance. If the illness was deemed by the commission to be caused by A-bomb radiation, they would get an allowance of around €1000 per month. When I was the chair, 50 to 70 submissions for the allowance were made per month. The commission had to decline the majority because the probability of causation by radiation exposure was not high enough. But most applicants did not accept their rejections, and many of them sued the country.

Dr. Beyer: *Where did the committee get its data on dose profiles and dose-risk relationships?*

Dr. Sasaki: Dose estimates had been performed by a joint United States–Japan committee of experts. Today, dose–risk relationships come from RERF's study of survivors. The Life Span Study (LSS) gave us a lot of information from which we calculated the probability of causation, which formed the basis for compensation decisions. Over time, the committee had to relax the standard for authorization of allowances. This cycle has been repeated for the past 75 years. This is one consequence of the A-bomb attack, which has been exhausting for our society. I am afraid that this situation is going to resurface in the aftermath of the Fukushima nuclear power plant accident.

Dr. Beyer: *Do we know the actual consequences after the nuclear attacks? Do we know with a high certainty how many people developed leukemia or thyroid cancers?*

Dr. Sasaki: One third of the population (210,000 people) of Hiroshima and Nagasaki was estimated to have died by the end of 1945. The national census of 1950 revealed 285,000 survivors eligible to be registered as *hibakusha*. In 1958, the LSS was launched. It included 93,000 exposed survivors and 27,000 nonexposed controls. Mainly the long-term health effects of acute exposures to moderate- and low-level radiation have been studied, because most highly exposed survivors died of acute effects. Since then, the actual numbers of cancer deaths as well as excess relative risks (ERRs) of the LSS cohort have been reported (*1*). For example, the ERR of leukemia was 3.1/Gy (316 deaths) compared with 0.47/Gy for all solid cancers (10,929 deaths). The ERR for thyroid cancer within the LSS cohort was estimated as 1.28/Gy (371 cases) (*2*).

Dr. Beyer: *Have these A-bomb events affected the public opinion of radiation in and beyond Japan? Have they affected the public opinion of the usefulness of diagnostic and therapeutic medicine?*

Dr. Sasaki: Naturally, all Japanese people have sympathy for victims of atomic bombings. There are people who are actively fighting against nuclear power in support of the A-bomb survivors. They are also against radiation. They insist that radiation is very dangerous. But, as I already said, most people receive medical radiologic examinations and treatments without opposition.

Dr. Beyer: *Let's talk about your personal involvement. You have been the director of NIRS in Japan. I suppose that in this capacity you've been involved as a witness and expert, solicited by the government whenever there was a critical incident. Could you tell us—also in light of Hiroshima and Nagasaki and the knowledge acquired—a bit about your involvement?*

Dr. Sasaki: We experienced a criticality accident on September 30, 1999, in a uranium processing factory in Tokai village. While enriching ^{235}U, a chain reaction of nuclear fission occurred and reached critical levels, which continued for 20 h, thereby emitting neutrons and γ-rays. I was responsible for the medical treatment of 3 workers who were exposed to high radiation doses ranging from 2 Gy to 18 Gy equivalents, mainly from neutron beams. I observed those 3 victims from the day of the accident, when they were transferred to the NIRS hospital. Two of them, who were exposed to 10–18 Gy and transferred to the Tokyo University Hospital, struggled for life for 82 days and 210 days, respectively, before they died. I witnessed the horrible effects of high-dose radiation exposure: the so-called harmful tissue reactions or deterministic effects. Our medical teams fought to treat acute radiation syndromes. I would like to emphasize that there are 2 different effects of radiation: tissue reactions (or deterministic effects) and cancer risk (stochastic effects). Many nonmedical people in Japan do not distinguish clearly between these 2 categories of radiation effects.

In Fukushima, where the nuclear power plant accident occurred after the big earthquake and gigantic tsunami on March 11, 2011, people were confused about tissue reactions vs. cancer risk. For inhabitants in Fukushima, where the dose was very low (much less than threshold doses), there is no possibility for tissue reactions to occur. But there were rumors that nasal bleeding caused by radiation had been frequently observed in Fukushima. Many people believed such rumors, which caused serious problems.

Dr. Beyer: *You said people were confused after Fukushima, which happened more than a decade after the critical event in Tokai. Can you tell us about this confusion and how the people who knew about the difference between stochastic and deterministic risks reacted to it?*

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Dr. Sasaki: Diverse comments and explanations made by so-called specialists caused lots of confusion among people who did not know what to believe. Soon after Fukushima, Dr. Ohtsura Niwa and I visited major newspapers and TV stations to explain the concept of radiation health effects, including the 2 categories, as well as the International Commission on Radiological Protection (ICRP) 2007 recommendations, so that they could deliver appropriate news about radiation. We acted in the capacity of former and current ICRP main commission members. Such efforts need to be made by professionals in order to share common knowledge with the general public.

Dr. Beyer: *Would you agree that we should do this not only when there is an incident but continuously?*

Dr. Sasaki: Yes. This is a very important point. When the criticality accident occurred, some 200 people lived near the Tokai factory and were exposed to a subtle radiation dose. Researchers went to talk with these people, who were very much concerned about health effects. When they came back, everyone told me that once an accident happens people do not believe scientific explanations. So, it is important to share appropriate knowledge on radiation and radiation health impacts and its protection in everyday life.

Dr. Beyer: *You mentioned that after Hiroshima and Nagasaki, long-term studies were initiated to investigate the risk profiles or risks associated with low-dose as well as ultra-high exposure. Were there similar studies initiated independently after the Tokai and Fukushima events?*

Dr. Sasaki: The acute Tokai incident affected 3 workers. We know very precisely what happened to them. The 2 million inhabitants living in Fukushima were exposed to low-dose radiation, and health check-ups have been performed. I think they should not be concerned about cancer risk—but they are very much concerned, in part because so-called specialists warn that their exposure was much more dangerous than predicted based on the international standard. Studies to estimate doses received by the inhabitants on the basis of behavior registrations and model analyses revealed that doses were $<$ 10 mGy during the year after the accident.

Dr. Beyer: *This leads us now to the heated debate about the linear-no-threshold (LNT) model and alternative models, particularly in low-dose situations. Do you think we have enough evidence today to comment on the absolute risk of low-dose exposure?*

Dr. Sasaki No. There is no scientifically proven low-dose risk estimate.

Dr. Beyer: *But don't we need such an estimate in view of the diagnostically exploited use of low-dose exposure? Shouldn't we know more about the risk, if any? Or could we safely say that based on our experience from past events, we cannot see a risk?*

Dr. Sasaki: There have been lots of discussion about the LNT-model. Some people think that this model is inappropriate for making rules. The LNT model is just one of many different models of dose–response curves in the low-dose range. I believe that the LNT model should be used only for radiological protection purposes, because of its prudent nature and its managerial convenience. We do not know what is happening in the low-dose range, because there are big statistical limits. The LSS study includes around 100,000 exposed people. That study revealed linear dose–response relationships for exposures of $>$ 100–150 mGy, but many survivors received $<$ 100 mGy, and the LSS study cannot reveal any statistically meaningful dose–risk profiles for them. That is because the subcohort is too small. Radiation is a relatively weak carcinogen, so you cannot distinguish radiation-induced cancer from cancers from other causes when the radiation dose is $<$ 100 mGy.

Dr. Beyer: *Do you think we will ever be able to resolve the true dose–risk relationship?*

Dr. Sasaki: A famous epidemiologist said that epidemiology cannot give the answers as to which is the correct dose–response curve for low-dose radiation but that the combination of radiation biology and epidemiology may give the answer in the future.

Dr. Beyer: *In Europe, companies promote new imaging equipment, like CT or PET/CT systems, largely for dose reduction. This exploits the public perception that it is always good to reduce the dose. But shouldn't we instead go the other way? Should we not strive to use new imaging equipment to increase our diagnostic value rather than to maintain the diagnostic value at a lower injected activity to the patient?*

Dr. Sasaki: When a decision is made to use radiation for diagnosing patients, the most important thing is to provide good data for precise diagnosis. After that, we have to think about reducing dose to patients. The ALARA principle—when applied in medicine—is quite different from other situations in which we try to reduce the dose to workers and the general public. The priority should be always on making appropriate diagnoses. ALARA is not for us to take literally.

Dr. Beyer: *In your opinion, is there any evidence that medical diagnostic radiation increases cancer risks?*

Dr. Sasaki: There have been increasing numbers of epidemiological studies focusing on patients. As an example, several epidemiological studies have included children who received CT examinations. But the cohort numbers are still too limited to tell the effects of a very low dose, for example, 10 mGy.

Dr. Beyer: *We talked about patient fears and also changes in the patient–doctor relationship. What do you think we should do to provide the best care to our patients while addressing their most irrational fears?*

Dr. Sasaki: Communication with patients is very important to get rid of irrational fears about radiation. I believe that the rational explanation is not enough; we also need empathy and trust for mutual understanding. We need to explain technical matters in simple terms.

Dr. Beyer *Thank you. Dr Sasaki, you have witnessed almost 70 years of medical development. Do you think the next 70 years will be as exciting as the ones that you actively witnessed?*

Dr. Sasaki: I hope so. I know I will not see it, but emerging sciences will bring new developments in future medicine, which should be very exciting.

Dr. Beyer: *Thank you very much for your time and insights.*

REFERENCES

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