Future of Nuclear Medicine

R. D. Ganatra (1982)

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Dr. R.D. Ganatra was a remarkable Nuclear Medicine Physician who pioneered Nuclear Medicine in India during its formative years. He established the Radiation Medicine Centre in Mumbai, one of the best training centers for nuclear medicine and started the first University based postgraduate degree course in nuclear medicine in the world way back in the year 1965. Subsequently he went on to become the Head of Nuclear Medicine at the IAEA, Vienna, during the eighties. A great teacher, a visionary and a leader in the true sense of the word, he revitalized the programs and activities of nuclear medicine at the IAEA by introducing several new concepts for promoting nuclear medicine in the developing countries of the world. This is the transcript of a lecture he delivered at the Annual Conference of the Society of Nuclear Medicine (India) in the year 1982. Read it. It is quite "inspiring". After 27 years, his thoughts are still relevant to the practice of nuclear medicine anywhere in the world to-day. Also read the related Editorial in this issue of WJNM.

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When it comes to setting up nuclear medicine in a developing country, there is a group of people, who feel that such high technology has no place in a developing country. Their nihilistic argument runs as follows:

The boom of the sixties is over for nuclear medicine in many countries, even those which are not "developing". The new imaging devices, starting with the gamma camera with computer on line and going on to SPECT and PET, are beyond the reach of many countries, which in the sixties were full of rectilinear scanners and enthusiasm. Obtaining up-to-date radiopharmaceuticals is also a big problem, as many of the radionuclides used today are not easy to produce locally, even in countries which have spent large sums on nuclear research. Many of the developing countries, depend on few commercial suppliers, from the advanced countries, for their supply of radiopharmaceuticals. In some of these countries, customs regulations are so cumbersome, that clearing radionuclides through customs represents a real achievement.

The current global economic situation has kept health expenditure to almost zero growth in many countries. Many countries spend only 10 - 50 US dollars per inhabitant/year for total health care; a good majority of the developing countries spend less than $10. This amount on health care is totally inadequate, particularly when the developing countries are committed to:

(a) provide potable water for a large percentage of the population;
(b) organize a primary health care network;
(c) vaccinate all children against the prevalent diseases;
(d) fight against diarrhoeal disease using oral rehydration and against other specific endemic diseases, such as malaria, schistosomiasis, amoebiasis, etc.;
(e) improve maternal and child care, as well as nutrition;
(f) provide essential drugs;

In this context, the decision to purchase, for example, a SPECT machine is not easy to justify. Justification for SPECT is even more difficult when competing alternatives offered are more cost-effective. For US $50 000 you can have a large variety of ultrasound diagnostic machines, real time or more complex with Doppler facilities, with image recording systems, measuring possibilities, guidance for interventional procedures, etc.

Looking at nuclear medicine during the sixties and early seventies, this imaging technology was widely applied in investigations of thyroid, liver, brain, kidneys, lungs, bones, pancreas, etc., particularly for space-occupying lesions, and in limited cases for function testing. The new imaging modalities available have changed this situation: ultrasound has almost taken over the field of liver and gall bladder imaging, kidney and urinary bladder, pancreas and is now entering the area of thyroid, brain lesions **in infants,** etc.; computed tomography has superseded nuclear medicine in brain imaging, is gradually becoming more accurate in bone metastases evaluation and is starting to compete with nuclear medicine in the area of heart.

Even in the advanced countries, every one does not feel that future of nuclear medicine is so bright. There are cries of despair and disappointment. Nuclear medicine is a specialty based on a technology. Any scientific discipline tied to a specific technology or a disease cannot be everlasting. For instance, specialties related to tuberculosis will vanish as soon as a cure for tuberculosis is discovered. The moment a technology is found that does what nuclear medicine does in a better way, is more sensitive and more specific, less invasive in terms of cost or adverse effects, the nuclear medicine as a specialty would face a bleak future.

Fear of radiation is not going to disappear easily from the minds of public. NMR has to camouflage itself as MRI. That fear is not entirely irrational, and there is every reason to fear that in years to come, it will increase and not diminish.

Specialties like cardiology or nephrology do not face this problem, because heart or kidneys are not going to disappear from the human body. "Who does what" disputes between cardiologists and nuclear medicine physicians are not likely to be settled in our favor. Our claim is based on the premise that a radio-thallium is used for cardiac diagnosis. That, by itself, does not give us a right over any territory. A nuclear medicine physician cannot be a cardiologist and a nephrologist and a neurologist - a super specialist. If we do

Nuclear Cardiology, we can not avoid being subservient to cardiologists.

In vitro nuclear medicine is considered our prerogative because radioimmunoassays form a principal part of in vitro work. As soon as a non-radioactive label is as successful as a radioactive label, we are going to lose that ground to clinical chemistry which has no reason to fear extinction.

There is no denying the extremely useful role that the radiotracers play in medical research. It will always remain unique and unsurpassed but then that does not make nuclear medicine. The radiotracers would certainly survive in the research setting. The role of nuclear medicine as a diagnostic service facility is recent and likely to be short lived. In advanced countries, nuclear medicine is trying to expand in new directions, like PET and immuno-scintigraphy. They would remain largely as research areas for years to come but not likely to form a major part of diagnostic nuclear medicine.

Wide spread use of radiolabeled monoclonal antibodies in the detection, let alone the treatment of malignant disease, is doubtful. The "magic bullet" is still going to remain a dream only. Monoclonal antibody research may produce interesting and useful radiopharmaceuticals such as white blood cell labeling agents and will probably produce in vitro tests for the presence of tumour. The problem is that there is no particular reason why the latter should require radioactive labels.

Nuclear medicine claims that its unique strength is its ability to do functional studies, yet very few are being done. WHY? They are not likely to be possible without significant development of a new generation of radiopharmaceuticals.

Nuclear medicine will survive. The scientific and intellectual activities of nuclear medicine will thrive. The party is over for nuclear medicine as a large volume prosperous specialty of wide diagnostic application. What nuclear medicine needs is an investigation like chest X-ray or blood count which can be ordered by any physician uncritically for each and every patient that attends a hospital. There is nothing on the horizon like that. Nuclear medicine is not going to be a money spinning specialty, which is usually the yard stick, by which success or failure is measured, in the advanced countries.

In the initial days of nuclear medicine, there was no imaging. Scientists were not thinking in terms of imaging. It was an excitement and enthusiasm of doing tracer studies. Hevesy called his book "adventures with radioisotopes" with a sub-title "their applications in Biochemistry, Physiology and Pathology". The word imaging does not even appear in the Index. Nuclear medicine did not start with imaging. It was there even before imaging became possible. It will be there even after imaging goes away from nuclear medicine.

The gamma camera was developed in 1954 but became the instrument of choice, only when Tc-99m became available, after a decade or so. For us, in nuclear medicine, the tracer, the radiopharmaceutical has always remained of paramount importance. The detector has always remained secondary.

"I am carrying the ocean on my shoulders and looking for the shores. Put down the ocean, put down the burden of imaging and you will find the shores you are looking for".

Only when you get rid of the burden of the preconceived notions, you can find the shores. The last thing to be discovered about science is what the science is about.

"To **carry the burden of the instrument, count the cost of the equipment and never to know that it is** for music, is the tragedy of life's deafness."

Nuclear medicine is not only about imaging. It is about detecting the ever changing distribution of a radioactive substance in the body measured in quantitative terms, in relation to time. In CT, density does not change with time; dead or alive it is same. In US, the acoustic impedance does not change. In MRI, the nuclear spin does not change. You can have beautiful images - frozen flower vases, exquisite, but motionless.

If one wanted to count the shortcomings of nuclear medicine as an imaging modality, it will be like that famous Belafonte song "there's a hole in the bucket". First of all, the nuclear medicine imaging needs radiopharmaceuticals as well as the instruments to produce an image of an organ; the radiopharmaceuticals are short-lived and need to be imported periodically, or rather every few days from abroad; the photon yield from the radiopharmaceuticals in an organ is not of the same order of magnitude as that arising in the case of a radiograph; moreover, the image is a two dimensional display of a three dimensional distribution of the radiopharmaceuticals in an organ!

However, the radiograph and the nuclear medicine image of the organ differ as much as a `photograph' and a `mirror': a photograph shows a physical image, where time is static, a moment of time frozen in a frame; mirror shows a physical image where the time element is dynamic, all the antics of the subject can be visualized, while they are happening! Oscilloscope becomes a mirror of functional changes happening inside the body. Who would like to tell the flying bird not to fly? Who wants to freeze the ever changing dynamic processes in the body? We are not photographers. We are like a mirror, tracing every moment of the body, without freezing the motion. A photograph confines you to the frame of the observer; the mirror is limited only by the antics of the tracee. We reconstruct anatomy out of the function. We conceptualize abnormality rather than visualize it. In nuclear medicine, time is our third dimension.

93% of the American Hospitals with more than 100 beds have gamma cameras. There is an 8 % rise in the nuclear medicine investigations annually even now. Every third patient in an American hospital undergoes a nuclear medicine investigation. Third world countries have a lot to do to catch up. Our instrument companies have realized this. Low cost of nuclear medicine is going to be its redeeming feature. Do not mention the still lower cost of ultrasound. As long as the US pictures look like a lunar landscape, we have some hope.

"A dew drop knows the sun in its own tiny orb."

What kind of spectrum we see there for the nuclear medicine? Biochemistry of the brain. Thyroid, anyway, is our private preserve. There is no other better way of detecting pulmonary embolism. Radionuclide scan is still an investigation of choice for liver imaging in most of the developing countries. Renogram is a superb test for screening patients with hypertension. Bone pathology is still best detected by bone imaging. Nuclear Cardiology can not be bypassed, if coronary insufficiency is suspected. Anything that moves during the course of time, we can image. Time domain may be slow in a dynamic functional study like RBC survival; or very rapid as in Nuclear Cardiology. Time is our third dimension.

RIA is also a pharmacokinetic distribution of a labeled substance in a test tube in its interaction with a clinical isolate, in the same way as a colloid distributes in vivo in the presence of a liver. RIA done repeatedly gives a functional profile of an organ.

To challenge the function of any organ adds a special dimension to nuclear medicine studies. It is not enough to have a servant, the servant must respond to the command. It is not only possible to show the function of an organ in nuclear medicine, but also the functional reserve can be studied by the challenge tests.

The dynamic functional studies, the epitome of the present day nuclear medicine, can be done with simple instruments also. The very first study in nuclear medicine, where circulation time was measured was done with "Bi and a cloud chamber. Thyroid uptake studies when done serially are dynamic studies, because they provide quantitative information in temporal terms. RBC survival is a dynamic study although spread out over a number of days. Radioimmunoassays done serially in the same patient also provide dynamic information.

Instrument has never been our concern. Cloud chamber, single probe, scanner, oesophageal probe. In nuclear medicine, "we change oars, but we do not change boats."

CT and MRI are instrument based specialties. They are like escalators. It can take you that far and no further. We are not moving on the escalator. We are climbing mountains making our own way, finding our own radiopharmaceuticals and devising new instruments to suit our radiopharmaceuticals. Sometimes we move, sometimes the road moves, but we are constantly in motion.

What is there in future?

Several new radiopharmaceuticals have become available in recent years, e.g. new hepatobiliary agents, new cerebral perfusion agents, new Tc based myocardial perfusion agents, monoclonal antibodies labeled with Indium-111 - it is an unending list. Cyclotron is adding a totally new breed of radionuclides.

The Ace in our hands is, of course, the non-imaging part of the nuclear medicine, which was so far neglected and relegated to the background, but which had a marked upswing and recognition because of the Nobel award to the discoverer of the principle of the Radioimmunoassay. The achievements of the Radioimmunoassay is a glorious chapter of nuclear medicine, where without administration of any radioactivity to the patient a large number of biologically important substances can be estimated in the circulating blood.

This is what Rosalyn Yalow has to say on the future of RIA: "Those promoting non-nuclear tests are not necessarily suggesting that these have any technical advantage, but rather that regulatory procedures and the fear of radiation at any level would make the radioisotopic label less desirable. Nonetheless, radioimmunoassay is likely to remain the method of choice for measurement of the peptide hormones, since their concentrations are well below 10" M and the sensitivity of the RIA is essential”?

RIA is likely to remain the method of choice for the research laboratory. The use of radioisotope label has many advantages compared to the use of an enzyme marker. Generally, iodination is simpler than the preparation of an enzyme labeled substance, especially since there has been no agreement as to which enzyme is best for substances as small as steroids or as large as viruses. In addition, there may be some change in the configuration of the enzyme or the substance to be labeled during the conjugation procedure.

Monoclonal antibodies can provide virtually unlimited amounts of homogenous antibodies against a specific antigenic site. The heterogeneous antibodies are more likely to provide more sensitive assays than the monoclonal antibodies, although assays employing the latter are likely to be more specific. The optimal choice of the antiserum may depend on whether sensitivity or specificity is required for the assays.

RIA is now used in thousands of laboratories around the world to measure hundreds of substances of biological interest. Even now, a quarter century after the introduction of RIA, there remains many additional fields that can be explored with its help.

We are not reaching a limit; we are finding that we are limitless. The rumors of the death of nuclear medicine are somewhat exaggerated. The curtain is not being brought down, it is being raised. Don't send your ocean into my pond to drown my little boat. We do not want MRI into NM.

When radionuclides were introduced first in medicine, they were heralded as a discovery as great as a microscope, a tracer technique which can be turned inward to find out what is happening inside the body. There are so many research problems of relevance to the developing countries, which can be resolved by application of radioisotopes as research tools. For example, in vitro assays can be applied for the diagnosis of the communicable diseases, absorption studies can be useful in problems related to nutrition, and even myocardial ejection fraction can be studied by a single probe. Depending on the interests of the clinical group and depending on what instruments are available, a variety of clinical research problems can be tackled in the developing countries.

"In the autumn of my life, I am still announcing new dawns. The same sun is newly born in new lands in a ring of endless dawns."