

Nuclear cardiology for developing countries

Simple devices may answer practical needs

by L.E. Feinendegen

The "power of the atom" — of radionuclides — is the primary tool of nuclear medicine for observing the vital functions of cells and tissues. As applications and detection devices have diversified, and especially since the gamma camera has become available, many have taken up the advancement of the art of imaging as a unique possibility for describing organ structures and functions in a way that somewhat resembles, but cannot be achieved by, conventional radiography. In fact, radiology departments began to call themselves imaging departments.

Over the past few years, imaging with ultrasound has been added, and together with nuclear magnetic resonance, is now gaining rapid acceptance because of its unprecedented quality. In view of these fascinating developments, one needs to examine the role of nuclear medical imaging in the future of clinical practice and research.

Currently, many physicians, administrators, and funding groups believe that nuclear medical imaging is being threatened or is becoming more and more obsolete in competition with the more recent imaging techniques. No doubt this is partly true if the emphasis is placed on imaging itself, image quality, and the infrastructure needed to produce it. This question of competition between imaging techniques is of great importance, since resources are limited and one must aim to achieve the most favourable cost-benefit ratio for long-term planning.

Attempts should be made to assess this situation, and to make suggestions for development, that are of particular interest where large numbers of people lack full medical care, where the spectrum of diseases is quite different from that in industrialized countries, and where funding must follow priorities set by the desire to avoid

as much suffering as possible with sometimes extremely limited financial resources. The case of managing cardio-vascular disease is especially suitable as a subject, and its discussion here is meant to apply to nuclear medical imaging in general.

Assessment of imaging

Of course, nuclear medical images are a primary expression of the information obtained by observing the pathway of radionuclides in the body. It is this fate of radionuclides, or more specifically of radioactively labelled substrates, that interests physicians most; indeed, images should be viewed as windows through which one can examine this fate. One may even say that nuclear medical images are fully exploited only when they unravel this fate, in the sense that radioactively labelled cells or metabolites can permit the observation of the cellular and molecular level of organization of the body. In this way, nuclear medical images have the power to make the body biochemically transparent as no other imaging technique can do. This is one important aspect that should be stressed. It is, therefore, necessary to first emphasize what the objectives of a diagnostic investigation are, and then to turn to the proper techniques and tools to achieve them.

If one wants to emphasize structure — or more precisely, organ spaces — it does not appear to be optimal to turn to nuclear medical imaging, provided other means are available that are effective and cost less. But if one wishes to investigate correlations between organ spaces and time of passage of a tracer through them, then nuclear medical imaging may be the only alternative.

If measuring the passage of a tracer is more important than the resolution of the space to which it applies, then simple, single-probe counters of radioactivity may fully suffice without adding the luxury of an image. If passages of larger masses through an organ space are required without the need to avoid disturbing the observed system, nuclear medical tracer techniques may remain the preferred method because of economy, speed, lack of hazard, and better quantification. This is

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A gamma camera in use at Pakistan's Atomic Energy Medical Centre in Lahore. (Credit: Pakistan AEC)

in comparison with other non-invasive approaches, such as radiology, ultrasound, and nuclear magnetic resonance imaging.

These considerations, of course, apply directly to cardio-vascular diseases.

Special case of nuclear cardiology

Primary aims of nuclear cardiology are assessments of (1) the pumping function of the heart, especially that of the left ventricle; (2) myocardial perfusion; and (3) myocardial metabolism. Additional needs may arise for quantifying the capacity of the peripheral circulation to adapt especially the pulmonary circulation and reserve.*

Are these diagnostic demands very urgent in developing countries?

The answer appears to be "yes" and "no" at the same time: "Yes" for those many individuals who need the diagnostic work-up, and "no" for those many individuals who, because of other serious illnesses, do not, or very rarely do, develop cardio-vascular disease.

The next question then is: Can the specified diagnostic demands be met? Here are the main problems: Finances are limited; training is often not sufficient; maintenance of equipment is most difficult for infra-structural and climatic reasons; supply of radiopharmaceuticals is constantly in jeopardy. Nevertheless, this does not advise taking these difficulties as justification to abstain from nuclear medical investigations wherever they are uniquely in demand.

There are two reasons for this statement: The first is the need for evolution, from which no one should be excluded. This demands openness, motivation to engage oneself and to be efficient in a team with colleagues, administrators, and society as a whole. The second reason is a psychological one: It would be disastrous to widen the gap between developing and industrialized, or wealthy and poor, countries. Planning should be helpful here to co-ordinate investments so efficiently that centres of excellence can be maintained. On the one hand, these are a source of pride, and on the other hand, they are an opportunity for training in self-sufficiency as demands arise and can be financed.

Nuclear cardiology, because of its diversity and its particular role in clinical practice, poses a challenge for the good.

Examining cardiac function

Examinations of cardiac function may resort to complex imaging procedures, such as parametric imaging of the left ventricular ejection fraction and of wall motion. Both of these, however, can now be analysed to some degree by ultrasound, even if quantification still leaves much to be desired. Cardiac functional assessment by the fastest flow times and the minimal transit times is

relatively simple and precise as well. The latter investigation does not necessarily demand complex imaging; single-probe devices may be quite useful, or even better for this purpose.

A single-probe device for specifically measuring the left ventricular performance (in terms of the ejection fraction, time and rate, and the filling time and rate) is the "nuclear stethoscope".* It will be referred to briefly later in this article, when a new simple device is explained that may answer a practical need in developing countries.

Imaging agents

There is no doubt that the diagnosis of coronary artery disease has immensely profited from the use of thallium-201 myocardial perfusion imaging. Differentiation between the images obtained immediately after a proper exercise load and after a 2 to 3 hour rest period has fully proved its clinical significance. It has a sensitivity of close to 90% for the practically risk-free and time-saving diagnosis of coronary artery disease, when conventional methods, excepting angiography, have failed to clarify the suspicion.

However, thallium-201 is not only expensive, but also hampered by a gamma energy emission that is not quite optimal for conventional gamma cameras. New tracers are actively sought. Recently it was found (first announced at a nuclear medicine conference in Kuwait from 17 to 21 February 1985) that iodinated orthophenyl-pentadecanoic acid is a superb myocardial imaging agent. It is easily prepared and, when labelled with iodine-123, gives image qualities superior to thallium-201. It is avidly incorporated by the well-perfused myocardium and then becomes trapped there, so that images may be repeated for hours. This compound is hardly, if at all, catabolized, in contrast to others.**

* "The nuclear stethoscope: A simple device for generation of left ventricular volume curves", by H.N. Wagner, R. Wake, and E. Nicholoff, *Journal of Cardiology*, 38, 747 (1976).

** Iodinated para-phenyl-pentadecanoic acid or iodinated omega-heptadecanoic acid, both of which were found to be most useful for evaluating myocardial metabolism. See "Myocardial imaging and metabolic studies with (17-123-I) iodo-heptadecanoic acid in patients with idiopathic congestive cardiomyopathy", by A. Höck, Chr. Freundlieb, K. Vyska, B. Lösse, R. Erbel, and L.E. Feinendegen, *Journal of Nuclear Medicine*, 24, 22-28 (1983); "Kinetics of different 123-I- and 14-C-labelled fatty acids in normal and diabetic rat myocardium in vivo", by T.E. Beckurts, W.W. Shreeve, R. Schieren, and L.E. Feinendegen, *Nuclear Medicine Comm.*, 6, 415-424 (1985); and "15-(ortho-123-I-phenyl)-pentadecanoic acid, a new myocardial imaging agent for clinical use", by M.A. Antar, G. Spohr, H.H. Herzog, K.P. Kaiser, G. Notohamiprodjo, E. Vester, B. Schwartzkopf, B. Lösse, H.-J. Machulla, W.W. Shreeve, and L.E. Feinendegen, *Nuclear Medicine Comm.* (in press).

Myocardial metabolism can be assessed by planar scintigraphy and long-chain fatty acids (such as I-omega-heptadecanoic acid) labelled with iodine-123, if the labelled catabolites are corrected for by the proper image-subtraction technique. Results are practically identical to those obtained by positron emission tomography and ¹¹C-palmitic acid.

* *Clinical nuclear cardiology*, edited by D.S. Bergman and D.T. Mason (Grune & Stratton, New York, London, Toronto, Sydney, San Francisco, 1981).

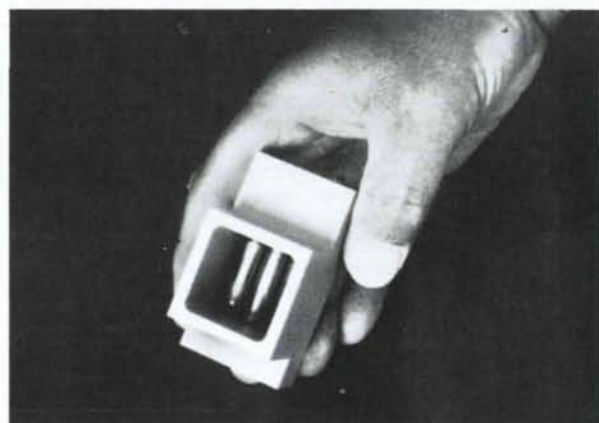
One special advantage of metabolic imaging of the myocardium appears to be the differential diagnosis between coronary artery disease and cardiomyopathy, even in an early stage of development. Even subtle, induced changes in myocardial metabolism — for example, by alcohol or insulin — have been easily observed. Even though metabolic imaging of the myocardium is at present a special test reserved for solving difficult diagnostic problems, it appears that cardiomyopathies are more common than so far generally believed.

There are challenging questions here, especially in regard to malnutrition, vitamin deficiencies, trace element deficiencies or overburdens, and to changes induced by drugs, toxic chemicals, or infections. Particularly in poor countries, one knows little of the effects of living conditions on myocardial metabolism. Are there at least certain minimal requirements for normal cardio-vascular performance? These are research questions with potentially great practical consequences.

A simplified nuclear cardiology

As previously mentioned, there is a need for evolution, response, and adaptation to practical needs. Such a response is the suggestion of a compact radiocardiograph that was developed by the Institute of Medicine at the Nuclear Research Centre, Jülich, in the Federal Republic of Germany. Named the parametric gamma-scope, the instrument combines the performance of the nuclear stethoscope with the capacity to measure the cardiac minimal transit time, and to observe changes in cardiac, pulmonary, and hepatic blood volume, both at rest and during graded exercise. These three cardiovascular tests are made in one examination. They measure sequentially the left ventricular performance, the entire central circulation from the right atrium to the aortic root including the pulmonary segment, and finally the response of the cardiac-pulmonary-hepatic blood volume distribution during graded exercise. The equipment is compact, robust, easily movable, and electronically designed to withstand considerable alterations in room temperature, humidity, and changes in electrical current. The device relies on single-probe measurements; curves are produced and evaluated by a small computer with currently available hardware.*

* For further technical information, see the author's paper in *Nuclear Medicine and Related Radionuclide Applications in Developing Countries*, proceedings of the IAEA/WHO symposium, IAEA STI/PUB/699, Vienna (1986). Also see "A compact radiocardiograph for simultaneous measurement of left ventricular function and cardiopulmonary minimal transit time", by V. Becker, M. Schitteck, M. Rosen, and L.E. Feinendegen; and "Multiple non-gated blood pool analysis for measuring central hemodynamics at rest and exercise", by G. Spohr, A. Höck, A. Schmid, and L.E. Feinendegen, *Nuklearmedizin — Darstellung von Metabolismen und Organfunktionen*, edited by H.A.E. Schmidt, W.E. Adam, F.K. Schattauer Verlag, Stuttgart, New York (1984); and "The minimal transit times", by L.E. Feinendegen, K. Vyska, H. Schicha, V. Becker, Chr. Freundlieb, *Der Nuklearmediziner* (Supplement 1979).



Overall view of parametric gamma scope and one of its probes.

Challenges and needs

The role of nuclear medicine in developing countries must be oriented to local needs for clinical practice, the health care of large populations, and the demands for research with, sometimes extremely limited resources. To help define the locally different needs, it should be reiterated that nuclear medicine provides the unique opportunity to observe the body at the molecular level of organization and, thus, makes the body biochemically transparent.

Depending on the particular diagnostic demands, complex computer-assisted imaging with gamma-camera scintigraphy or emission tomography may be the only method of choice in some instances, but for the others it may be an unnecessary luxury. Nuclear cardiology, with the purpose of non-invasively assessing cardiac function, myocardial perfusion, and myocardial metabolism, is a particular challenge in both respects for developing countries. Given such requirements, single-probe devices with multiple purpose application are less expensive than gamma cameras and promise advanced diagnostic uses.

Developing countries should be encouraged to participate in nuclear medicine's evolution and to assure that centres of excellence are maintained, not only for treatment, but also for the purpose of training.

IAEA's role in the field

Agency programmes continue to attach a great deal of importance to appropriate development and dissemination of current technical know-how for radiation sterilization, in particular with regard to health and welfare interests of technologically less advanced developing Member States. Particular emphasis has been given to helping development of suitable practices pertinent to indigenous medical and pharmaceutical items, with regard to local conditions and environment. Action plans are developed and implemented through periodic panels, expert advisory groups, topical symposia, research support, and co-ordination programmes, publications, and, primarily, through an elaborate technical co-operation and support service to Member States.

Encouraging results are noticeable, particularly in some developing countries of Asia and the Pacific region in implementation of various integral steps for radiation sterilization practices of medical supplies (see accompanying map). Following successful commissioning of two cobalt-60 irradiation facilities in India, in 1974, and in the Republic of Korea, in 1975, a spurt of interest in this nuclear technology was evident in most other countries in the region.

Today in the region, large-scale cobalt-60 irradiation facilities are operating in Bangladesh, Indonesia, Malaysia, Singapore, and Thailand, while smaller pilot gamma-cell facilities are in research and development stages in Burma, Pakistan, Philippines, and, more recently, in Sri Lanka. Since 1985, Chinese cobalt-60 facilities, respectively in Beijing and Shanghai, have sought and received IAEA assistance in research support, as well as in provision of microbiological standard preparations for dosimetry and process calibration. Through these recent developments, the "radiation sterilization map" in Asia and the Pacific region has better bridged the gap between Japan and Australia. Further progress is expected in the region.

The map also gives an overview of the status in developing regions of Europe, the Middle East, Africa, and Latin America. Africa, the Middle East, and Latin America are marked by a high degree of heterogeneity and inadequacy, leaving much scope for future development. In the African region, Egypt and Saudi Arabia have already commissioned and are operating cobalt-60 facilities producing sterile medical supplies for indigenous health care. In striking contrast, many other countries in the region do not even have at the elementary level a technical and manpower infrastructure, while some others (e.g., Algeria, Ghana, Morocco, Zaire, and Zambia) are in an advanced planning stage. A promotion of regional co-operation is desired.

Recently some countries in Latin America have been considering possible regional co-operation in industrial uses of radiation processing, for which medical supply sterilization is a likely candidate.

Almost all cobalt-60 facilities installed in developing Member States through IAEA support are located administratively in the respective governmental establishments, such as the Atomic Energy Commission or the Ministry of Science and Technology. Consequently, their operation involves the "service sterilization" of medical products derived from local manufacturers. This implies that a close co-operation be maintained with facility customers at all stages, including education and technical guidance for specifications, compatibility, and standardization through good manufacturing practices and national regulation. Advisory group meetings and workshops, including one in Sri Lanka later this year, and regional co-operative projects for Member States help fulfil such promotional objectives and development of radiation technology well suited to upgrading local health care.



Nearly half of medical supplies and devices such as these are being sterilized by radiation in some countries. (Credit: Isomedix)

Legend:

- Gamma irradiator for medical supplies and/or food irradiation
- ▲ Research, technical assistance, and/or training

