

NUCLEAR APPLICATIONS IN HEALTH CARE LASTING BENEFITS

BY STEFFEN GROTH

Nuclear applications in health care have a time-honoured record of being highly cost-effective in addressing important health problems such as malnutrition, cancer, infectious and circulatory diseases. Today they are providing lasting benefits for patients, physicians, medical researchers, and health care practitioners throughout the world.

Many nuclear applications have become so well-established and documented that they are preferred to other methods. This is because they frequently provide unique medical information, or are among the least expensive approaches to a problem.

Some applications -- originally introduced as nuclear techniques -- have developed into applications that have no "nuclear" component as such. (For example, many routine radioimmunoassays, or RIAs, have later developed into enzyme-linked immunoassay, or ELISA methods.) This development often occurred for reasons of high-speed automation and/or simplicity. At the same time, however, robustness and precision often were sacrificed.

Nuclear applications in health care can be roughly divided into *diagnostic*, *therapeutic*, and *preventive* applications. This article describes a series of successful

and well established applications in view of new directions that are emerging.

MEDICAL DIAGNOSIS

Diagnostic applications comprise *in vivo* and *in vitro* methods. The *in vivo* applications are characterized by the administration of a radiopharmaceutical to the patient and usually subsequent external detection with a gamma camera or some other detector. The *in vitro* applications involve analysis of samples taken from the patient, most often blood samples.

In vivo Applications. *In vivo* applications are a major nuclear medicine technology. The principal role of these procedures is the assessment of organ function. Radionuclides or compounds that are labelled with radionuclides are administered to the patients to allow specific organ function to be evaluated by tracing the dynamic biodistribution of such a compound in specific organs. Tracing of the compound is achieved by external detection of the photon emitted from the

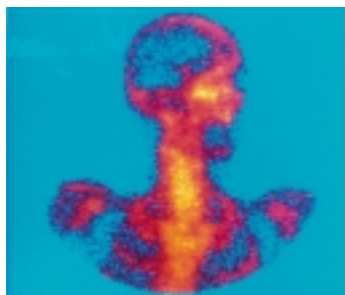
radionuclides by using instruments like rectilinear scanners or gamma cameras.

Probably the major characteristics of *in vivo* nuclear medicine procedures is that the amount of radiopharmaceutical needed for *in vivo* diagnostic studies is very tiny and always in the range of physiological quantities. For instance, for a thyroid scintigraphy, the amount of radioactive iodine employed is over a thousand-fold less than the amount of iodine daily taken up with food. It therefore has no measurable interference with thyroid function and no side effects.

Also, the radioactive dose received by the patient for scintigraphies is, in most cases, negligible. As a rule of thumb, it approximates the dose received from one year of natural background radiation per examination.

The *in vivo* method provides for studying a number of organs and systems. The major fields of application are oncology, endocrinology, cardiology, and nephro-urology. The most widely applied instruments and *in*

Mr. Groth is Director of the IAEA Division of Human Health. Contributors to the article were Mr. Ajit Padhy, Head of the Division's Nuclear Medicine Section; Mr. Victor Levin, Head of the Division's Radiation Biology & Therapy Section; Mr. Venkatesh Iyengar, Head of the Division's Nutrition, Health, & Environmental Studies Section; Mr. Pedro Andreo, Head of the Dosimetry & Medical Radiation Physics Section, and Ms. Baldeep Khan and Mr. Soo Ling Ch'ng, staff members of the Division.



vivo technologies for nuclear medicine diagnostics constitute a formidable list. (See box, pages 38 & 39.)

■ **Bone scanning** is probably the technique most commonly performed. This is a very efficient approach to look at the function of the bones: any significant injury to the bone will cause an increase in bone metabolism that can be detected by the bone scan. The method is the most efficient way to search for bone metastases in many types of tumours. It is also used in orthopaedics for the study of fractures, osteomyelitis or joint replacements.

■ **Myocardial perfusion scanning** is another frequently performed nuclear medicine technique. This test informs about the presence of heart infarction. If a patient suffers from chest pain, the test will help clarify whether it relates to reduced blood flow to the coronaries (arteries of the myocardium).

■ **Renal scintigraphy** provides a detailed description of renal function, from blood supply to urine formation and excretion. It is very useful for the study of kidney function in patients suffering from elevated

blood pressure, diabetes or kidney stones.

■ **Thyroid scanning** is commonly used for the screening of hyperthyroidism and searching for possible malignant thyroid tumours in patients with nodular goitre.

■ **Brain scanning** provides important information in patients with stroke, epilepsy and Alzheimer's disease.

■ **Perfusion lung scanning** in combination with ventilation lung scanning, is the most efficient technique for the study of pulmonary embolism. This is a dangerous condition originating from blood clots that requires early intensive treatment.

Diagnostic procedures in inflammatory or infection diseases play an increasingly important role in nuclear medicine. In most cases inflammation can be diagnosed by clinical examination and routine laboratory analysis. Not infrequently, however, nuclear medicine techniques are required to confirm and evaluate the presence, the extent, and the severity of the process.

Emerging Directions. Nuclear techniques developed particularly over the past decade hold great potential for future applications. These include an explosion in the use of positron emission tomography (PET) and the development of receptor ligand radiopharmaceuticals.

PET allows a more accurate visualization of the organ under study than can be obtained with the usual gamma camera. It can also provide information on metabolic functions that is impossible to obtain with other techniques. For the time being,

PET is available only in a limited number of developing countries since the technology is expensive and the radiopharmaceuticals difficult to produce. It is envisaged, however, that following the current clinical success, the technology will continue to be made widely available, especially in oncology, neurology, and cardiology.

The receptor ligand radiopharmaceuticals bind selectively to specific cells or tissues. They bear the unique feature of allowing *in vivo* identification of the presence of specific types of tissue whose presence is suspected (such as infected tissue.)

Also being developed is a series of new tumour seeking radiopharmaceuticals. By a single injection of the relevant radiopharmaceutical, the entire body can be scanned for the presence of tumour cells. For certain kinds of tumours called neuroendocrine tumours, these techniques are already dramatically changing the diagnostic approach to the patient.

In vitro Applications. These applications include:

■ **Radioimmunoassay (RIA).** Immunoassays in a variety of forms have gained widespread usage in both nuclear medicine and clinical pathology. Four main attributes account for their successful application in diagnostic services, these being their sensitivity, specificity, precision, and convenience. The first three are inherent consequences of the fundamental properties of the interactions between antibodies and their ligands which form the basis of immunoassay systems.

Photo: Nuclear imaging techniques provide key information for diagnosing a wide range of illnesses. (Credit: IAEA)

Immunoassay is an analytical technique for quantification of the biomolecule at picogram/femtogram concentration. RIA is used to detect and quantify drugs, intermediate metabolites, steroids, peptide hormones, enzymes, cancer markers, viral antigens, cellular receptors and deoxyribo nucleic acid (DNA) molecules for early clinical laboratory diagnosis of new diseases or recurrence of previous pathologies. In monoclonal antibody work, it is the most sensitive and cost effective method for screening hybridoma cell line which produces the antibody. Currently it is one of the preferred conventional methods used in pharmaceutical work on new drug development.

Since it is an isotopic assay, the radioactive signal of the probe is not subjected to usual interference; for example, by water impurity, enzyme poisons and other unforeseen side reactions. The method is therefore regarded as the gold standard by the practitioner of the art of immunoassay. It can be modularly automated using a robotic sampler for large-scale screening of treatable diseases using minimal human resources.

Emerging Directions. The emerging trends in RIA point to greater sophistication. They include optimization of monoclonal antibody secretion, synthetic novel binders, novel immobilisation techniques, detection of new markers of neoplastic, degenerative, metabolic and endocrinological diseases, screening technology, global validation and cognitive apprenticeship of clinical RIA

data, and evidence-based RIA.

■ **Molecular Biology Techniques using Radionuclide Methods.**

Over the past several years, the development and application of molecular diagnostic techniques has initiated a revolution in the diagnosis and monitoring of diseases. Polymerase chain reaction (PCR) is one of the best and most commonly applied examples of clinical applications of molecular techniques in human health. The heart of the technology relies on the repeated enzymatic amplification of the targeted sequence of DNA fragment. The final product can be visualized by ethidium bromide staining after electrophoretic separation by means of a radioisotopically labelled DNA probe (*see photo*) or detected by direct sequence analysis. Phosphorus-32 and sulphur-35 are the commonly used radioisotopes.

PCR has found many applications in both basic research and clinical settings. In the Agency's programme, PCR technology is being used for the diagnosis of infectious diseases such as Chagas disease, Leishmaniosis, Hepatitis B and Tuberculosis. Reverse transcriptase PCR is being used to detect Hepatitis C virus.

PCR is also being used for detecting sub-species variation which can be important in the prognosis of cervical cancer and of Hepatitis B & C.

The efficacy of treatment can be effectively monitored through quantitative PCR in hepatitis. Direct detection of mutations responsible for drug resistance in malaria and tuberculosis is being carried out using mutation specific PCR, and PCR coupled with what is known as Dot-Blot hybridization, respectively. Diagnosis of genetic defects -- for example, in thalassemia and muscular dystrophy, the latter using multiplex PCR -- also is being carried out. It has enabled some countries to set up genetic counselling programmes.

Besides PCR, other molecular techniques include single strand confirmation polymorphism (SSCP) and protein truncation tests. They are being used to further refine diagnosis in muscular dystrophy. PCR is being used to detect malignant cells in patients with leukemias that are characterized by consistent translocation break points.

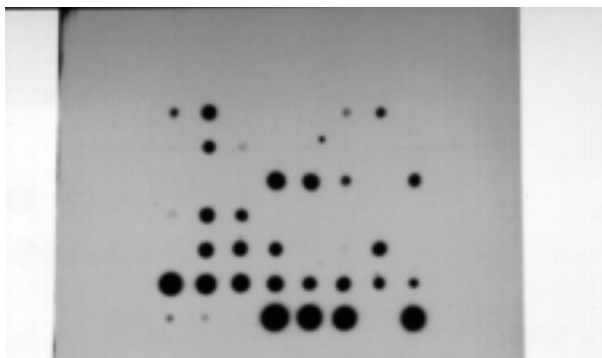


Photo: An autoradiography of Hepatitis B samples using phosphorus-32 and the Dot-Blot hybridization technique.

Primers that span the breakpoint are added to a bone marrow sample and subjected to multiple cycles of PCR. Even one cell in a million with translocation can be detected.

Emerging Trends. In the near future, more than one hundred thousand genes will be characterized under the human genome project. Bacterial, protozoan, helminth, viral and fungal genomes have already been or will be elucidated very soon. The most important application of this variety of sequences will be expected to be in diagnostics.

Other increasingly important applications will be the detection of prognostic markers for cancer, drug resistance indicators, predictive markers for malignant and degenerative disorders, models for molecular modelling for drug design, gene therapy, detection of minimal residual disease, molecular epidemiological information and control measures and detection of new emerging diseases.

A number of technologies are most likely to be used in the above applications. They are: quantitative, multiplex and *in situ* PCR; multiplex DNA sequencing and diagnostics by hybridization with enriched stable isotope labels using mass spectrometry; peptide nucleic acids probes that provide faster results than traditional DNA probes; DNA bio-chip technology where distinct probes can be linked to an inert support and hybridized with the test DNA from clinical samples; phosphor-imagers that detect beta and gamma radiation more rapidly; protein truncation tests; and functional genomics.

■ **Measurement of Stable Isotopes.** Measurement of stable isotopes by nuclear and related techniques have gained widespread strategic application in a variety of health problems through analysis of trace elements. (See box, page 37.) These techniques are now generally considered the best methods for measuring the uptake and bioavailability of many important vitamins and nutrients.

Commonly used techniques applied for these purposes include neutron activation analysis (radiochemical and instrumental), Inductively Coupled Plasma Mass Spectrometry, Particle-Induced X-ray Emission, dual energy X-ray absorptiometry, Particle-Induced Gamma-ray Emission, Energy Dispersive X-ray Fluorescence Analysis, and Total Reflection X-ray Fluorescence.

Emerging trends. Isotopic techniques in many cases have just begun to be applied in developing countries. Their use carries the potential of benefiting millions through improved nutrition and nutrition monitoring techniques. They can also serve to yield specific indicators of broader social and economic advances. Important areas for strategic monitoring include health care for the elderly, and for young children and women.

Health care for the elderly will be a growing concern, since by 2025 there will be 1.2 billion elderly people in the world (60% of them in developing countries). Hence preventive measures through nutritional and other health monitoring will gain

importance. Similarly, up to 300 million adults are likely to be affected by diabetes in the next two decades and therefore, prevention and management of overweight (obesity) is of critical importance.

For women and children, deprivation of proper nutrition has enormous consequences. There is clear evidence of developing countries having higher prevalence of low birth weight babies compared with developed ones. The prevalence of intrauterine growth retardation in most developing countries also is recognized as a public health problem of great concern.

MEDICAL TREATMENT

Therapeutic applications of nuclear and radiation techniques are advancing. Radiation does not selectively kill cancer cells; with sufficient dose it kills all dividing cells. Developments in imaging using computer tomography (CT) scanning and magnetic resonance imaging (MRI) have improved the definition of the margins of cancers. This, in turn, has stimulated efforts to develop therapy planning systems and equipment capable of treating the tumour to higher doses without increasing the dose to healthy surrounding organs.

The most common techniques involve delivery of radiation from a distance -- called teletherapy -- and inserting radioactive sources into cavities adjacent to tumours or even invasively directly into tumours -- called brachytherapy. Other applications involve open radioactive sources for radiation therapy of cancer, and some

STRATEGIC HEALTH APPLICATIONS OF STABLE ISOTOPES

■ **Targeting Malnutrition:** Nearly 200 million children (over 150 million in Asia and about 27 million in Africa) under 5 years of age are affected. Assessment of vitamin A is an important requirement in this context. About 90% of the body's vitamin A is stored in the liver, and direct measurement of liver vitamin A would require invasive procedures (for example, biopsy of the liver). The IAEA has been developing far less invasive isotopic tracer techniques for measuring whole body vitamin A under conditions of supplementation (Ghana, Peru), food fortification (Peru, Israel) and dietary improvement (China, Thailand, Philippines and India) for addressing problems of vitamin A nutrition in children and pregnant or lactating women. Similarly, assessment of iron absorption from diets to evaluate its bioavailability is an important nutritional measurement. Stable isotopes provide the only direct way for measuring iron uptake and bioavailability and are regarded as a kind of "gold standard" for iron studies in humans. Isotopic methods are very useful for measuring absorption of zinc from foods, and measurement of breast milk intake by infants.

■ **Osteoporosis:** This disorder affects elderly people (particularly post-menopausal women). The IAEA has helped several developing countries in applying dual energy X-ray absorptiometry (DEXA) for bone density measurements for investigating how bone mineral density varies with age, sex, ethnicity and geographical origin of subjects.

■ **Obesity:** This is linked to cardiovascular diseases, hypertension, and maturity on-set diabetes mellitus, among many others; stable isotope-based techniques are



becoming effective tools to assess obesity. There are no alternatives to the isotopic methods for measuring energy expenditure under everyday living conditions. The doubly labelled water method ($^2\text{H}_2^{18}\text{O}$) is the only technique that can accurately determine the energy needs of people in their own environments and is one of the most reliable methods for determining food energy intake. This method is gaining wider acceptance since it is inexpensive, accurate, and can be applied under field conditions.

■ **Helicobacter pylori (Hp):** Young children in developing countries suffer from high prevalence of this infection that makes them susceptible to diarrhoeal diseases. According to 1993 statistics, persistent diarrhoea accounted for over 60% of infant diarrhoeal deaths in Brazil, 47% in India, 36% in Senegal, and 26% in Bangladesh. Stable isotope techniques have been recognized as the best and most cost effective modes of diagnosis of Hp through a simple breath test using carbon-13 enriched substrates and measurement of labelled carbon dioxide.

Photo: Health practitioners in many countries are being trained to use isotope techniques effectively.

thyroid diseases. (See table, page 40.)

■ **Teletherapy:** Teletherapy has evolved from treatment using X-ray tubes, to treatment involving cobalt machines, where radiation was derived from radioactive cobalt sources (gamma rays), and then back to using X-rays that now are produced by linear accelerators. These machines produce more penetrating and very sharp beam edges capable of

reaching deeper-seated tumours with improved accuracy.

Earlier treatment equipment was highly effective for smaller superficial tumours; it was so effective that skin tumours treated by radiotherapy or surgery are expected to be cured and only melanomas of the skin are included in cancer registers. Increased emphasis is being placed on cosmetic results and retention of

function. Early cancers of the larynx are treated with radiotherapy to preserve the voice, and early breast cancer is treated by removal of the lump and radiation rather than mastectomy.

As imaging and treatment improved, this trend towards minimal surgery augmented by radiotherapy has increased for deeper tumours. Sites ranging from the prostate to the head

NUCLEAR APPLICATIONS IN HEALTH CARE

■ Static Gamma Camera Imaging

Principle: Gamma camera converts photons emitted from a radiopharmaceutical administered to a patient, presenting an image of the element's distribution. *Application:* Static and dynamic imaging of organ functions. *Comparative Advantage:* High-quality images.

■ Single Photon Emission Tomography (SPECT)

Principle: Distribution of radiopharmaceutical administered to patient is measured from many different angles by a rotating gamma camera head. *Application:* Main interest in heart perfusion imaging and brain imaging. Examination of liver and spine also is frequent clinical application. *Comparative Advantage:* Improved gamma camera imaging. Permits absolute three-dimensional localization of radiopharmaceutical distribution with 3-D representation of the imaged organ.

■ Positron Emission Tomography (PET)

Principle: When a positron combines with an electron, the action produces two 511-keV annihilation photons moving in opposite directions. By recording their simultaneous arrival in a detector system surrounding the patient, the origin of the emission can be located in three dimensions, resulting in extremely high-quality images. Basic organic elements, such as carbon-11, nitrogen-13, oxygen-15, and fluorine-18 are positron emitters. These elements are tagged to common molecules found in the body and therefore can be made specifically for a target organ. *Application:* By combining a positron

emitting isotope with a tracer that is selective for a specific biochemical pathway, it is possible to estimate absolute rates of biological processes, such as rates of glucose utilization, protein synthesis, oxygen consumption, and blood flow. *Comparative Advantage:* PET is unique in its ability to create "functional" images of blood flow or metabolic processes. They surpass conventional structural or anatomic images produced by X-ray examination, magnetic resonance imaging, and even SPECT.

■ Rectilinear Scanning

Principle: Moving detectors that map the location of radiopharmaceuticals in a patient's body. Scanner moves across the organ in one or more planes until the organ or the area under examination has been completely surveyed by the scintillation counter. *Application:* Thyroid imaging. *Comparative Advantage:* Thick crystals and high-energy collimation provide high efficiency and resolution, particularly with radiopharmaceuticals such as iodine-131.

■ General Gamma Probes

Principle: The activity of a radiopharmaceutical is detected using a collimated scintillation probe detector aligned with the organ under examination. *Application:* Thyroid uptake of iodine. Single probe counting systems that employ only one crystalline detector are useful. *Comparative Advantage:* Thyroid uptake as an index of thyroid function remains a routine diagnostic tool, even though more sophisticated procedures are available.

and neck are being treated with less extensive surgery combined with radiotherapy. Easily damaged organs such as the eye, brain or spinal cord can be accurately distinguished from the tumour.

Emerging Directions

Sophisticated planning systems now design each treatment beam to minimize dose to these structures while escalating the tumour dose. These planning systems control the dose output (intensity) and treatment apertures to deliver so-called

"conformal therapy".

Stereotactic radiosurgery (single fraction) and stereotactic radiotherapy (multiple fractions) are developments of this conformal therapy. But they place an emphasis on tumour positioning.

While these techniques were initially developed for proton accelerator beams or a gamma knife (a very elaborate teletherapy unit with over 200 cobalt sources) this has now become more generally available with the use of add-on

components to a conventional linear accelerator. The use has rapidly expanded for smaller, often benign lesions within the brain where surgery is hazardous. Typically arterio-venous malformations, acoustic schwannomas and meningiomas of the brain are well managed with this technique, with control rates exceeding 80%.

■ Radiotherapy Services

Radiotherapy services have expanded rapidly over the last decade. The most developed countries make few

■ Surgical Gamma Probes

Principle: A hand-held surgical detector is used to detect and survey the positive accumulation of a radiopharmaceutical that is administered before surgery. *Application:* Allows surgeon to identify the first lymph node downstream from a tumour, usually melanoma or a breast tumour. *Comparative Advantage:* Improves effectiveness of surgical treatment, which invariably depends upon the complete removal of all tumour tissue. The metastasis of melanoma or breast cancer will pass down the lymph system and deposit some cells in the first or "sentinel" lymph node. By localization of this node, the spread or lack of cancer cells can be identified and appropriate treatment can be applied to the patient.

■ Radionuclide Clearance Studies

Principle: Basically, the rate at which a particular radioactive substance, usually administered to patients intravenously, is cleared from the plasma can be determined by calculating the concentration of the substance in plasma and/or urine. *Application:* Studies offer the ability to do combined examinations of renal function and anatomy. *Comparative Advantage:* Radionuclide Clearance Studies reflect much more precisely the functional state of kidneys. Conventional chemical analysis tends to be diagnostic in applications for severe renal cases and therefore inadequate for patients with only moderate loss of renal function.

■ Radionuclide Dilution Techniques

Principle: Techniques involve the administration to the patient of a radionuclide that diffuses

throughout the compartment being studied, and whose distribution can be traced. *Application:* Measures with great accuracy total body water, red blood cell mass, survival and sequestration, total exchangeable potassium. Tritiated water is generally preferred for body water determinations. Chromium-51 sodium chromate is used for labelling red blood cells. *Comparative Advantage:* Measurement is simple and accurate. Radionuclides used are not toxic.

■ Therapeutic Applications

Principle: Radiotherapy of cancer involves the targeting of radioactivity to tumour cells rather than the cells of normal tissues. Beta or alpha emitting radionuclides can be labelled to some compounds which deliver radiation with cellular damaging effect to local tissue, where it accumulates. Selective uptake in particular tumours or organs occurs with these radionuclides or labelled compounds. *Application:* Many different radiopharmaceuticals that seek out tumours are being used for therapy by different routes and a variety of targeting mechanisms. Treatment of thyroid cancer or hyperthyroidism with iodine-131 has been used for more than 50 years. Some radiopharmaceuticals selectively accumulate in metastatic sites of bone tissue which enables the management of pain. *Comparative Advantage:* Treatment specifically targets tissues, is non-invasive, and holds relatively little early and late side effects. Tracer studies further enable assessment of the uptake and retention of radiation in the tumour before treatment begins.

compromises in accessibility of basic radiation oncology services. They have centres where the highest level of technology can be applied, when necessary. Though high technology techniques are only required for a minority of patients, their use can result in a major improvement in control or reduction of morbidity in appropriately selected patients.

Developing countries over the last decade show a threefold increase in the

amount of equipment available for use. Of the IAEA's 130 Member States, only 10 of the least developed countries now lack basic radiotherapy technology. The IAEA initiated radiotherapy in five of these Member States over the past five years. The sixth is currently being established. The challenge for the next decade will be to raise the standards to levels where the best modern techniques can safely be incorporated into their treatment practice.

Emerging Directions. A new challenge presented to radiation oncologists is the increasing number of cancers associated with AIDS seen in the clinics. The role of radiotherapy remains in the control of these cancers but the objectives of treatment have undergone radical revision. No longer is cancer cure, obtainable in about 45% of patients in developed countries, the prime objective. Quality of life issues, always of importance to the patient and

RADIOTHERAPY CENTRES & UNITS WORLDWIDE

REGION	POPULATION (MILLIONS)	RADIOTHERAPY CENTRES	COBALT-60 UNITS	CLINICAL ACCELERATORS	TELE MACHINES (TOTAL)	TELE- MACHINES (RATIO*)
North America	300.9	1903	207	2251	2458	8.2
Central America	134.1	139	115	30	145	1.1
Tropical South America	276.2	266	219	122	341	1.2
Temperate South America	54.3	139	128	46	174	3.2
Caribbean	29.4	18	23	1	24	0.8
Western Europe	387	1027	410	1109	1519	3.9
Eastern Europe	390.6	334	508	182	690	1.8
Northern Africa	138.2	59	54	41	95	0.7
Central Africa	358.6	22	25	2	27	0.1
Southern Africa	56.5	21	19	27	46	0.8
Middle East	221.3	91	64	56	120	0.5
Indian Subcontinent	1245.1	221	286	46	332	0.3
South East Asia	477.2	81	71	59	130	0.3
East Asia	1430.9	1107	606	948	1554	1.1
Australia & Pacific Islands	22.6	49	5	113	118	5.2

* Average number of tele-machines per million people in region. Source: Directory of Radiotherapy Centres, November 1999.

the treating oncologist, become even more significant when faced with a limited life expectancy from a more lethal disease.

■ **Brachytherapy.** Advances are rapid in this application. The original radium sources of Marie Curie have mostly been replaced with caesium sources which are safer to handle and involve easier disposal. While a few millimeters may initially appear small, the introduction of these sources into cavities and tissues is difficult. New micro high-dose rate sources under one millimeter in diameter and having high activities in the order of 10 Curies have paid dividends. They have made procedures for insertion easier, shortened treatment times to typically 10 to 20 minutes instead of 2 to 5 days, and opened new possibilities. These sources can be directed into small bronchi of the lungs, bile ducts and even small heart vessels (coronary arteries). The older brachytherapy units, on the other hand, were almost exclusively confined to the treatment of the uterine cervix.

Cancer of the cervix remains the most common cancer in many developing countries.

About 80% of all patients with this malignancy receive brachytherapy as part of their treatment. Cure rates range from 80% in tumours confined to the cervix to 35% in tumours at stage III. These may be over 10 centimeters in size and yet highly curable using combined tele- and brachytherapy with brachytherapy as the major component.

As teletherapy is usually administered on a daily basis as an outpatient, the advent of micro high-dose rate therapy now has eliminated hospital admission during treatment.

Emerging Directions.

Endovascular treatment for the prevention of coronary artery restenosis after bypass surgery or dilatation of constricted heart vessels has now brought brachytherapy into the field of management of "benign" diseases by radiation. Results indicate that the significant restenosis rate may have dropped by a factor of four for different surgical interventions.

REALIZING THE POTENTIAL

Advances in the medical application of nuclear technologies hold significant

potential for improving health care in many countries. The most widespread diagnostic *in vivo* applications worldwide remain gamma camera examinations of organ functions.

Promising applications, however, are emerging in this field, including PET and new classes of radiopharmaceuticals. *In vitro* applications of radio-immunoassay, molecular biology, and measurement of stable isotopes by nuclear and related techniques are examples of highly successful technologies that are far from being mature, and hold considerable potential for growth.

For therapeutic applications, radiation treatment by teletherapy and brachytherapy are still the treatments of choice to be offered to most cancer patients. But new developments in conformal therapy and of surprisingly effective cancer-seeking radiopharmaceuticals for treatment by open radioactive sources seem promising. Another exciting development -- intravascular treatment of arteriosclerosis by radiation -- may confer a new dimension to the treatment of what is the number one killer disease in the industrialized world. □