PACT: The IAEA's plan to stem the "cancer crisis" in developing countries

BY DICK KOVAN

In 2003, with the growth in the incidence of cancer in the developing world moving toward crisis, the World Health Organization (WHO) and the International Union Against Cancer (UICC) issued a call for action "through concerted efforts by all sectors to prevent and treat cancer throughout the world." In response, the International Atomic Energy Agency (IAEA) Secretariat developed the Program of Action for Cancer Therapy—PACT—an ambitious project that builds on the agency's long experience in providing radiotherapy to developing countries. PACT was approved this year by the IAEA's governing board and endorsed by the General Conference. Pedro Andreo, director of the IAEA's Division of Human Health, provided information about how PACT developed, as well as its plans and goals.

The IAEA's Program of Action for Cancer Therapy is working to provide radiotherapy treatment facilities and expertise to the developing world.

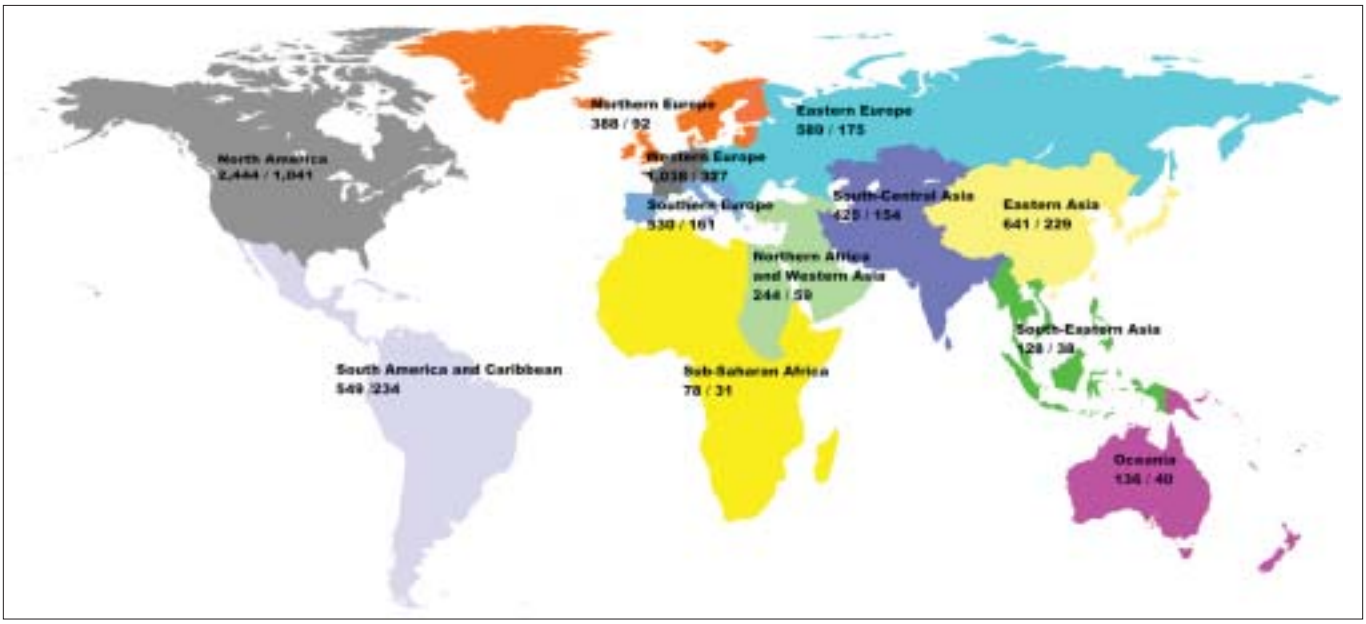
THERE ARE NOW more new cancer cases every year in developing countries than in industrialized countries, and by 2020 the developing world is expected to account for two-thirds of the projected 10 million annual cancer deaths. This "cancer crisis" is due to a combination of a rapid increase in incidence and the scarcity of radiotherapy equipment and expertise in many of these countries.

The increase is tied to the fact that people are living longer, which is the most important factor in the growth in the number of new cases of cancer. Unfortunately, the developing world is also plagued by high levels of smoking and other lifestyle risk factors adopted from the more industrialized countries.

The importance of radiotherapy in dealing with this crisis, Andreo said, should not be underestimated. According to WHO, "Radiotherapy is fundamental to the optimum management of cancer patients, and provision of radiotherapy services is central to national cancer control strategies." This is particularly true in the developing world.

In the industrial world, the use of each of the three main treatments for cancer—surgery, chemotherapy, and radiation therapy—is more or less equal. In the developing world, however, radiotherapy accounts for more than half of cancer treatments. The reasons for this are that chemotherapy is expensive (requiring a more extensive industrial infrastructure) and that surgery is often not available and is very expensive. On the other hand, radiotherapy is relatively cheap; the cost of a single "radiation dose" (a radiotherapy treatment session) can be as low as a few dollars. And it is an efficient tool. It not only can cure many patients, but it also offers palliative care: A single "dose" can relieve a lot of pain that otherwise would be treated with morphine over a period of several months.

Nevertheless, the hope offered by radiotherapy is unavailable for most cancer patients in developing countries, leaving more

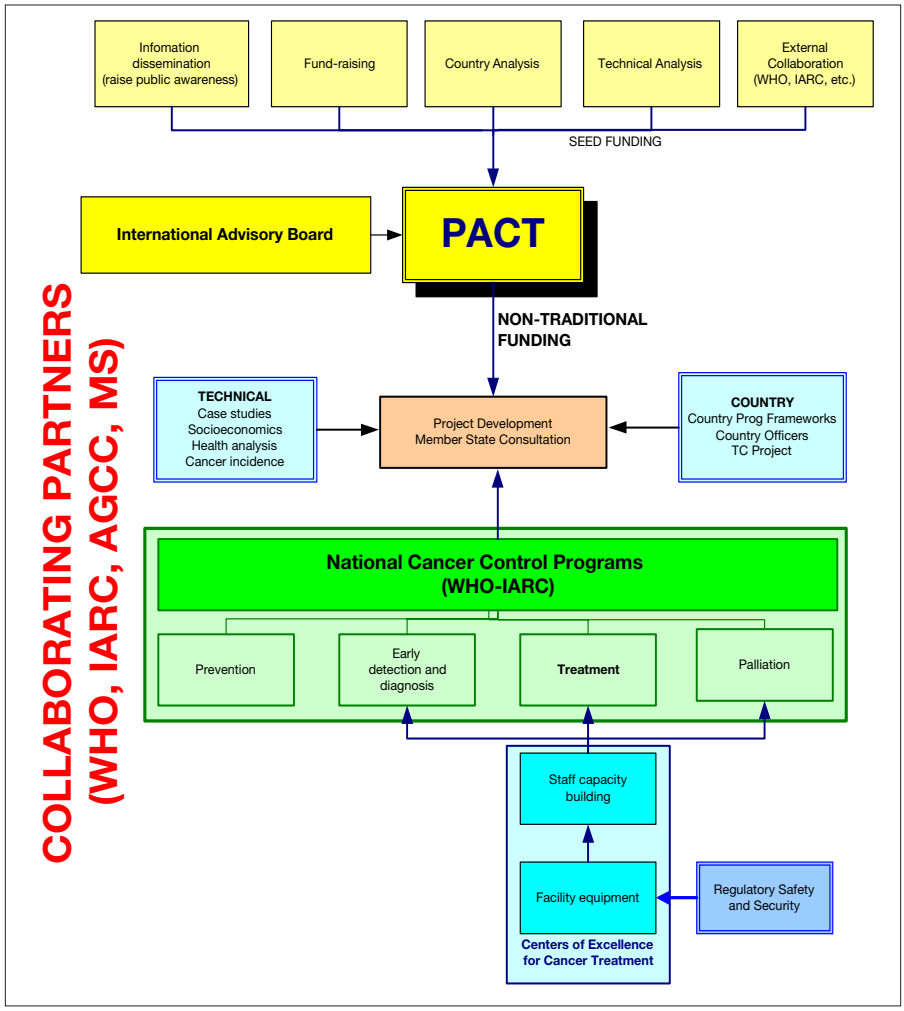


Worldwide distribution of radiotherapy equipment (teletherapy/brachytherapy) as registered in the IAEA/WHO database, DIRAC (Directory of Radiotherapy Centers). DIRAC contains information on equipment for treatment, dosimetry, patient dose calculation and quality assurance, and staff strength at the installations (radiation oncologists, medical physicists, technicians, etc.). (All graphics: IAEA)

than 3000 such patients to die every day. At the end of 2004, there were only about 2500 radiotherapy centers in the developing world, with approximately 3700 machines for cancer therapy. This can provide treatment for about 1.85 million patients per year. Although radiation therapy would be medically appropriate for about 3 million of the almost 6 million people in developing countries who will develop cancer this year, there is a deficit of approximately 2700 radiotherapy machines in these countries. Eliminating this shortfall would cost at least $1 billion to $2 billion.

Of course, the deficit is not just one of machines—trained radiotherapy staff are also required. "With machines alone you can do almost nothing," Andreo said. "You cure more people with your brain and a simple machine than with very sophisticated equipment and poor training." A national program also requires an infrastructure that can provide appropriate policies, administration, and planning and can ensure that the treatment is applied safely and effectively. Getting that in place requires a high level of understanding by the top government officials.

The lack of radiotherapy resources is not a new problem, and it is an area in which many member countries ask the IAEA for assistance. Over many decades, the IAEA has developed extensive technical expertise and has acquired unrivaled experience in the delivery of radiotherapy to developing countries. It provides assistance in all relevant aspects of a national cancer radiation therapy program, such as planning, training, econometric analysis, implementation, radiation protection, safety, and security. Over the past five years, the agency has invested $10.4 million annually in radiotherapy projects under its Technical Cooperation (TC) programs. There are currently about 100 active TC projects involving radiotherapy, ranging in duration from two to five years. These projects are supplemented by activities carried out under the regular programs of the IAEA's Department of Nuclear Sciences and Applications and the Department of Nuclear Safety and Security.



The PACT road map shows how the program brings together the collaborating organizations, funding, and technical expertise to treat cancer worldwide.

PACT

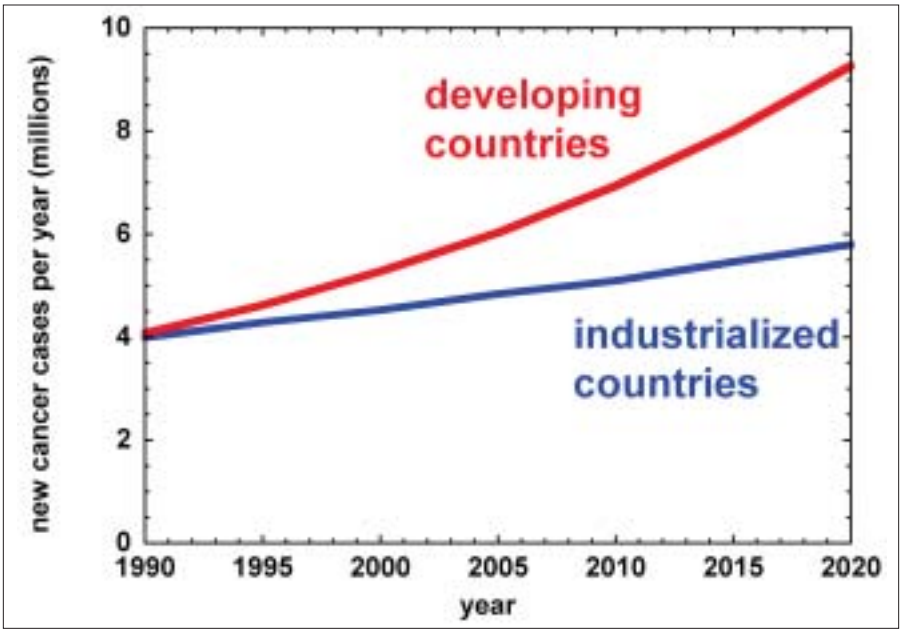
"About one-and-a-half years ago," Andreo explained, "we realized that with a budget of only $10–12 million per year, the ongoing program could clearly not do enough. Furthermore, we are the only UN organization that has a program in radiation therapy or nuclear medicine. So all the radiotherapy assistance that member states get is what we provide."

Faced with the increasing rate of the incidence of cancer, as well as budgetary limits, it was clear that a different approach was needed if the agency were going to increase its activities well beyond what it is doing today. "Otherwise, a lot of people are going to die," Andreo said. At the heart of PACT is the need for greater resources, well beyond what has been available through the normal agency financing arrangements. This has led to what is probably the most groundbreaking aspect of PACT—reaching out to nontraditional donors, such as foundations and charities. "For that, we will have to raise the awareness of potential new donors, as well as our traditional donors, to the cancer crisis and the fundamental role of radiotherapy as a mature technology that can help alleviate the crisis," Andreo said. In this regard, it is also important to stress the linkage of health to poverty reduction and long-term economic growth, which is much stronger than is generally understood.

Another important element of PACT is the building of partnerships with new organizations. Normally, the IAEA's contact with member states is through national nuclear commissions. Under its ambitious new plan, the agency sees the need for collaboration with organizations that have more direct links to health provision in these countries, particularly those operating at local levels. It is especially important to coordinate activities with WHO and its regional offices and the UICC, both founding members of the Alliance for Global Cancer Control, which the IAEA joined in 2003; the International Agency for Research on Cancer; and other international agencies, such as the Pan American Health Organization. Working with the private sector and appropriate nongovernmental organizations will also be encouraged. To facilitate this, PACT plans to establish an international advisory board that can reflect all elements of the health community.

Program elements

The overall objective of PACT is to develop a sustainable national capability to provide cancer therapy to patients in developing countries. This means having all of the necessary elements in place: operational radiotherapy and treatment facilities in the context of a sound national cancer control strategy, trained radiotherapy professionals, and effective management, safety, and quality control programs. There is a particular need to bring ministers and government planners on board and to ensure that the technical, legal, administrative, and regulatory arrangements are in place. "Many policymakers do not attach enough importance



Estimation of the number of new cancer cases per year (in millions) by the Globocan (2000) computer package developed by the International Agency for Cancer Research. In 1990, the number of cases was approximately the same in developing and industrialized countries. The predicted dramatic increase in cases in the developing world is associated with people living longer, high levels of smoking, and life-style risk factors—such as diet and lack of exercise—adopted from the more industrialized countries.

to the provision of good radiotherapy. This is important to ensure the integration of radiation therapy into national policies and programs," explained IAEA Director General Mohamed ElBaradei, in his report to the IAEA's Board of Governors.

With these aims in mind, the near-term objectives of PACT are focused on the following:

■ *Policy-level capacity building*—To raise awareness and broaden understanding among policy- and decision-makers of the part played by radiation therapy in the treatment of cancer patients and its implications for developing national policies and strategies. PACT will seek to increase capacity within ministries of health and other health sector institutions to analyze options, formulate policies, and set priorities to put in place appropriate cancer therapy programs.

■ *Centers of excellence for radiotherapy*—To design, plan, and implement regional and subregional institutions with the technical capacity to serve as training and reference centers for radiation therapy procedures, practices, methods, and applications, as well as the technical, legal, and regulatory arrangements appropriate for radiation therapy. PACT plans to establish as many as 25 such centers.

■ *National cancer therapy planning*—To prepare national cancer-control strategies based on case studies that will review country-specific and regional circumstances, including mechanisms for regional cooperation. The studies will assess the burden of cancer and the status of programs, policies, regulatory frameworks, and standards relating to radiotherapy applications for each selected country. Based on these studies, along with national goals and policies, and through a process of multi-stakeholder consultations, national plans of action will be formulated.

Plans of action may include, for example: upgrading arrangements for radiation protection (for the public, as well as medical staff and patients), safety, and security; setting up systems for collecting cancer statistics and monitoring performance at the hospital level; strengthening human resources through group training events, fellowships, scientific visits, and expert missions; upgrading hospital services, such as surgical pathology, surgical oncology, oncological imaging, teletherapy, brachytherapy, immobilization, treatment-planning computer systems, and record and verification systems; and implementing quality control and quality assurance procedures.

Starting up PACT

Having received the green light from the IAEA Board of Governors and an endorsement by the General Conference, ElBaradei was able to start the program. PACT is now being organized, with a focus on fund-raising, which includes raising awareness and preparing cases to submit to potential donors, Andreo said.

The agency has already received seed money from the United States, which makes it possible to hire some staff specifically for PACT. One manufacturer has donated equipment for a first radiotherapy clinic. Other countries have offered their institutions to provide education and training.

Andreo explained that the development of the PACT proposal had been undertaken by an in-house task force that is now focusing on establishing the structure of PACT, which should take a few months. The new structure will include a number of professionals with a range of expertise, including technical, public health, and resource mobilization specialties. Official contacts—"country officers"—are also needed to ensure input from the member states.

Although PACT will be closely connected to the IAEA's Division of Human Health and the Department of Technical Cooperation, it is important that it should

Many people around the world get cancer, and too many patients lack access to appropriate radiotherapy treatment. Facilities such as the one shown lack the up-to-date equipment found in developed countries. Cancer treatment—or the lack thereof—is what the IAEA calls "the silent crisis."

At left, technicians prepare a patient for treatment with a cobalt-60 teletherapy machine at the Kandy General Hospital's cancer treatment facility, in Sri Lanka. The man in the photo at right was treated for a brain tumor at the facility, which was started in 1998 with assistance from the IAEA's Technical Cooperation Program. Because of treatment, he is expected to be able to live a normal life.

have its own identity, particularly in regard to its fund-raising role.

"We are now developing the material to go to the donors, including well-documented country cases. These include analyses of what needs to be done, which means finding answers to a number of questions, such as: What is the cancer incidence in the country? Is there an ongoing program for prevention and early diagnosis? What are the perspectives for the future (for example, how many patients do we think can be helped with a therapy center)? and so forth. We need to have a lot of data about what is available. We are still in the early stage of this process, and there is a lot of enthusiasm," Andreo said.

A model clinic

While the regional centers will have many roles, the bulk of the work will be done at local radiotherapy clinics. A model setup for such a facility in a developing country is shown in the diagram. At the minimum, Andreo said, a basic clinic would have at its heart a cobalt-60 teletherapy machine or a simple accelerator (an accelerator would require an assured power supply, which is not always available in developing countries). A brachytherapy machine is also desirable, particularly in areas with a high incidence of cervical cancer. Then there is the necessary ancillary equipment for dosimetry and film processing, and facilities for designing and producing fixation devices for positioning patients during treatment. Also needed is a simulator to precisely determine and visualize the treatment.

The staff would include radiation oncologists, who conduct examinations and prescribe treatment; medical physicists, who calibrate the machines and determine how the radiation dose is distributed inside the patient to ensure minimal dose to other organs and structures, as prescribed by the radiation oncologist; and radiation technicians, who deliver the treatment itself to ensure that the patient's position is properly reproduced from day to day. A trained staff of 10–12 or more people would be needed to optimize the use of the facility. Quality assurance along the entire radiotherapy process, as well as radiation safety and security, must be guaranteed.

Such a setup does not include sophisticated equipment, said Andreo. The aim is to provide robust and well-proven technology. A cobalt-60 teletherapy machine has been the basic workhorse for treatment throughout the world. It is well-suited for constant use day and night. Any hospital in a major city in the West would have five or six such machines, which would likely be more sophisticated than what PACT seeks, he explained.

In theory, one cobalt-60 machine could treat 500 patients per year, operating 12 hours a day, five days a week. In many countries, however, the machines are not available because of shortages and mechanical problems. That is why the agency also helps provide maintenance.

The IAEA already has an extensive program to educate and train radiotherapy professionals. There is a particular problem with the lack of radiotherapy technicians, which jeopardizes the goal of 12 hours of uninterrupted treatments. The shortage of medical physicists poses a risk for the success of the treatment and for safety issues. Agency experience suggests that some 20–30 percent of the professionals trained abroad do not return to their country of origin following their training. They are often hired by manufacturers and vendors, or are recruited for research. This "brain drain" is understandable from the perspective of the professional, said Andreo, but requires the training of more professionals than are needed to compensate for the loss.

Resource development and tools

The IAEA also plans to strengthen a variety of resources and tools that will be useful for PACT.

The Directory of Radiotherapy Centers (DIRAC), a project undertaken together with WHO, is a worldwide database of radiotherapy equipment, ancillary equipment, and radiotherapy professionals. It includes sources used in teletherapy and brachytherapy; equipment used for dosimetry, patient dose calculation, and quality assurance; and numbers of staff (including radiation oncologists, medical physicists, and technicians) at radiotherapy installations. DIRAC is to be made available on the Internet.

Econometric models for estimating the costs of radiotherapy and making equipment choices are under continuous development. These models compare the costs of various kinds of equipment, the cost of constructing the bunker (the structure that houses and provides shielding for the irradiation machine and treatment area), the cost of personnel, and even the running costs for any combination of palliative and radical radiotherapy. In order to apply resources effectively, a thorough understanding of the costs and benefits of starting or improving radiotherapy treatment in differing conditions is needed. Local and regional circumstances should be taken into account, including the socioeconomic impact of radiation therapy for cancer in differing contexts.

To support continuing professional development of clinical staff, PACT will provide fellowships in fields such as cancer statis-

Australia to expand radiopharmaceuticals production

A major project to refurbish and extend the radiopharmaceuticals production facilities operated by the Australian Nuclear Science & Technology Organization (ANSTO) was officially launched in August by Australia's Science Minister Peter McGauran. The project, costing Aus$17.9 million ($13.4 million), is being carried out in conjunction with the 2006 opening of a new research reactor being built to replace HIFAR (the High Flux Australian Reactor), which has been operating for more than 45 years. The pharmaceutical facilities are located about 50 meters from the reactor at ANSTO's Lucas Heights site in Sydney.

The new Replacement Research Reactor (RRR) will be a small pool reactor rated at between 14 and 20 MW, compared with HIFAR's 10–15 MW. The new reactor, which will be fueled with 20 percent enriched uranium in place of HIFAR's 60 percent fuel, will be a multipurpose facility for radioisotope production, irradiation services, and neutron beam research.

The new production facility will allow ANSTO, Australia's only manufacturer of radionuclides, to produce a broader range of radioisotopes, many not currently available to the Australian public. The organization, which also produces radionuclides at its 30-MeV National Medical Cyclotron, now supplies over 70 percent of radiopharmaceuticals used in nuclear medicine procedures for some half a million Australians every year. ANSTO's annual revenues from radiopharmaceutical production is now above Aus$20 million ($15 million). These figures are expected to increase dramatically, as the RRR will have the capacity to produce four times more radionuclides than HIFAR currently does.

The manufacture of radioisotope products is largely carried out in Building 23 at Lucas Heights. Originally planned as a research facility, the building has evolved into a full production facility. ANSTO has continually improved its production facilities over the years. Last year, the organization completed a major upgrade of the Isotope Handling Plant, which contains four handling cells used principally for the production of molybdenum-99, which is used to manufacture technetium-99m generators, the workhorse of nuclear medicine.

ANSTO's Building 23: An artist's conception of the expanded facility

Despite this continual upgrading, the expected growth in demand for radiopharmaceuticals meant that a much greater increase in production capacity was needed. Furthermore, there were problems with the present layout, facilities, and services infrastructure, which reflected the incremental development of Building 23. This process has led to operational, health, and safety concerns, brought about, ANSTO explained, by aging infrastructure, inefficient production workflow, inability to significantly increase production, and inflexible, outmoded, and inadequate materials-handling solutions. In fact, present work methods are still manually based and labor-intensive.

With the expectation of much greater radionuclide production from the RRR, ANSTO decided that it was time for a major extension to Building 23. The new complex will be on three levels, adding approximately 3700 m^2 of usable floor area. Besides new production equipment, the new building will feature modern quality-controlled chemistry laboratories, service and instrumentation rooms, production clean-room facilities, packaging and shipping facilities, storage facilities, and component wash bays. The renovation also will include modifications to existing microbiological and clean rooms, intermediate solutions preparation clean rooms, and a sterilization room. It will provide for improved work methods and production efficiency through the introduction of appropriate materials-handling devices, computerization, and automation. Other improvements include a new ventilation system that meets best practice for nuclear applications. The project will also provide improved amenities and support facilities.

ANSTO also undertakes research in radionuclide and radiopharmaceutical production. For example, its researchers are working on a process for producing molybdenum-99 using low-enriched uranium more effectively. The process includes state-of-the-art methods for managing liquid and gaseous by-products. The process will initially be used in HIFAR and transferred to the RRR to ensure an uninterrupted supply of the isotope.

ANSTO has also carried out trials of a radio-labeled benzamide as an effective marker of malignant melanoma that may lead to its use in treating the disease.—*D.K.*

tics, clinical oncology, surgical pathology, surgical oncology, oncological imaging, teletherapy, brachytherapy, immobilization, quality assurance, computerized treatment planning, and palliative care.

Internet- and CD-based interactive distance-learning tools will be developed to support training. This will include an Internet-based information platform within the IAEA that will provide member countries with up-to-date information on the status of cancer therapy applications, relevant infrastructure requirements, guides to essential practice, and evidence-based guidelines.

Agency programs will also be available for IAEA member states. They will include activities for improving radiation protection, safety, and security infrastructures that contribute to establishing the appropriate framework within which radiation therapy can be safely and securely administered. The agency's dosimetry laboratory supports ongoing quality control and quality assurance programs for radiotherapy. The agency is involved to a lesser degree in other aspects of cancer control, including cancer prevention (environmental health and nutrition) and cancer screening and diagnosis by radiological imaging, nuclear medicine, and molecular biology. NN