Educational Applications on Particle Accelerators

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Abstract

The Brazilian production of radiopharmaceuticals and radioisotopes for medical usage dates back to the 50's, since the beginning up to 2006; it was a monopoly of the government owned corporations. After the market was open for the private enterprise, the quantity of small particle accelerators is increasing. The difficulties are many, from industry installation to the hard time on finding qualified personnel. The lack of investment on this area brought few trained people and the trained ones keep working in the government laboratories. Facing this issue, a strong program was started on training and educating people on universities, businesses enterprises and at hospitals in order to increase the human resources capabilities in the country. Activities such as laboratory research and lectures are being made as well in order to adapt Brazil to the renascence of the nuclear technology and increase the knowledge in the field of particle accelerators. These investments on education are preparing professionals in several areas, such as: physics, engineering, pharmacy, medicine, administration, among others. It started on the universities not only with lectures and workshops, but also with research partnerships on the stand-by time of the particle accelerators. At clinics and hospitals the efforts are focused in the improvement and training of the particle accelerator product applications. One of the private enterprise corporations has trained more than 30 people from five different states and established partnership with five different universities, qualifying people on installation, operation, maintenance and administration of the whole process of implementation of a particle accelerator site. It's also collaborating with the universities and researchers in the development of new techniques: the irradiation of other material targets or the use of non-usual particle beams, allowing the study of the nuclear activation of the concrete walls of the particle accelerator's bunker and the radionuclide capture on the filters of the air conditioning system in the factories.

Introduction

A great change in the national panorama of nuclear technologies has happened in Brazil since the adoption of the Constitution Amendment number 49 which ended the Union monopoly of the production, distribution and usage of radionuclides with short half-lives for medical, agricultural and industrial purposes, and enabled the private enterprise to join this market in regime of concession.

The monopoly has lasted for fifty years, up to 2006, and during this period all the production and distribution of short half-life radionuclides for medical usage (the central focus of this study) were only possible through the Government Organizations or Institutes as CNEN (Comissão Nacional de Energia Nuclear) mainly in two research centers IPEN – "Instituto de Pesquisas Energéticas e Nucleares" and IEN – "Instituto de Engenharia Nuclear".

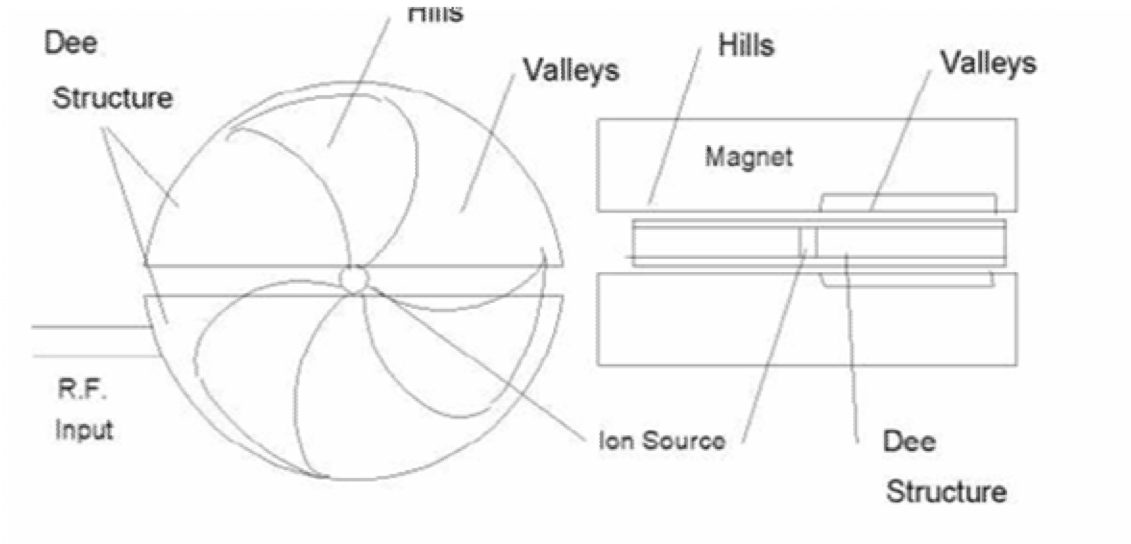
As the use of radionuclides for medical purposes grew, governmental organizations found impossible to keep the supply chain. After increments of the demand, throughout the years, it was impossible for them to supply the whole country. In the other hand, the development of nuclear technologies was really harmed once it was not well updated and the most peripheral places could not access neither the radionuclides due to the uncertainty of CNENs production and the short half life of the elements nor to improve equipments and techniques in the most different areas. Efficient transport systems, as required for short-lives radioisotopes, also contributed to the deficiency of the distribution.

Monopoly ended, after the Amendment 49, it became possible to install small accelerators cyclotrons and produce radionuclides with short half lives, having 18-Fluorine as the most relevant one for instance. In less than three years the national scenario changed from 2 cyclotrons operating at full scale to 11 ones.

About cyclotrons

"Cyclotrons are the most commonly used devices for the acceleration of particles to energies sufficient for bringing about the required nuclear reactions. It was the remarkable idea of Ernest O. Lawrence to bend the path of the particles in a linear accelerator into a circle and therefore use the same electrode system over and over again to accelerate the particles. This idea is the basis of all modern cyclotrons and has made the cyclotron the most widely used type of particle accelerator. The first model was built in 1930 with proof of particle acceleration being provided by M. S. Livingston in 1931 (1)."

"According to the theory of electrodynamics, the rotational frequency of a charged particle traveling in a magnetic field is independent of the radius of its orbit. The energy of the particle increases as the velocity of the particle increases. The cyclotron utilizes this fact to produce particles of reasonably high energy in a relative confined space. The acceleration chamber of the cyclotron is placed between the poles of a homogeneous magnetic field as shown in the source at the center of the machine and accelerated out from the center.



The ions are accelerated with a high frequency electric field through two or more hollow electrodes called 'dees'. The ions are accelerated as they pass from one dee to the next through a gap between the dees. Since the rotational frequency of the particles remains constant, as the energy of the particles increases, the diameter of the orbit increases until the particle can be extracted from the outer edge of the machine. The limit on the energy of a particle is determined on a practical basis by the diameter of the magnet pole face. Some very large, high energy cyclotrons have been built, but for the most part, the proton energy is less than about 70 MeV." (1)

Most of the recently installed cyclotrons are 11MeV, 18MeV and 30 MeV and are able to irradiate targets in order to produce ^{11}C, ^{13}N, ^{15}O and ^{18}F. At the IPEN, there is continuous production of ^{67}Ga through ^{68}Zi irradiation, ^{123}I through ^{124}Xe irradiation, ^{18}F through $H_2{}^{18}O$ irradiation, and ^{201}Ta (IPEN).

The medical area was the first to benefit from the new scenario. The radionuclides produced in cyclotrons are of particularly interest used in Nuclear Medicine, and can propitiate diagnosis exams as Positron Emission Tomography (PET) combined with Computerized Tomography (CT) or Magnetic Resonance (MR), that are now being spread to more territories.

Besides de Fluorine-18, it became possible to irradiate different targets in cyclotrons and produce ^{11}C, ^{13}N and ^{15}O which was not possible before due to the short half-life of the radionuclides altogether with the transit time to get to the patients. It is an advantage on cyclotrons located in hospitals that benefit patients and researchers.

Radionuclide	t ½ minutes	Decay Mode	Reaction	Energy (MeV)
^{11}C	20.3	β^+	$^{14}N(p,\alpha)$	11-17
^{13}N	9.97	β^+	$^{16}O(p,\alpha)$ $^{13}C(p,n)$	19 11
^{15}O	2.03	β^+	$^{15}N(p,n)$ $^{14}N(d,2n)$ $^{16}O(p,pn)$	11 6 >26
^{18}F	110	β^+	$^{18}O(p,n)$ $^{nat}Ne(d,\alpha)$	11-17 8-14

Table 1 – Radionuclides and their half lives (1)

"Positron emission tomography (PET) is a nuclear medicine imaging technique which produces a three-dimensional image or picture of functional processes in the body. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer), which is introduced into the body on a biologically active molecule. Images of tracer concentration in 3-dimensional space within the body are then reconstructed by computer analysis. In modern scanners, this reconstruction is often accomplished with the aid of a CT X-ray scan performed on the patient during the same session, in the same machine.

If the biologically active molecule chosen for PET is FDG, an analogue of glucose, the concentrations of tracer imaged then give tissue metabolic activity, in terms of regional glucose uptake. Although use of this tracer results in the most common type of PET scan, other tracer molecules are used in PET to image the tissue concentration of many other types of molecules of interest." (2)

The handling of radionuclides being allowed, Centralized Radiopharmacies, mainly with Technetium manipulation, became another possibility of the Amendment 49.

The existent radiopharmacies most of the times have structural problems, as the lack professionals (there is not a pharmacist involved directly in the production, manipulation and quality control of radiopharmaceuticals) and the impossibility of establishing Good Manufacturing Practices.

Centralized radiopharmacies arise specialized in tracers' production, bringing a multidisciplinary crew fully dedicated to the Good Manufacturing Practices. It is an economical alternative once the implementation of Radiopharmacies in each Center of Nuclear Medicine becomes unnecessary and with the single dose distribution, the quantity of residual waste diminishes.

Although all kinds of improvements on different areas are happening, the decades of monopoly had left a terrible heritage. The lack of investment in the educational centers to train specialists is the most concerning issue for instance.

Additionally, there were neither specific regulations concerning accelerators nor the licensing process and the civil responsibility is still not well based. (3)

As the most concerning issue, the lack of qualified professionals became not only a difficulty but a restrictive factor for the whole process: although most of the private installations were designed by the handlers of the cyclotrons that gathered expertise in many installations all over the world (as companies like GE Heath Care, Ion Beam Applications and Siemens), to adapt to the national statutes, the physicists, engineers and pharmacists were fully involved in the projects (since the drawings of the site plant, all the equipments to be bought up to the production), trained for several weeks abroad in existent manufacturers cyclotron sites. Once those trainings were not enough for national statutes, those professionals had to be trained by specialists on National Centers of Research.

Considering it was a new challenge for the National Commissions, to have so many sites being licensed at once, all the norms and statutes had to be revised and new requisitions appeared during the installation of the site. For example, it was demanded at least two Radioprotection Supervisors, one specialized in Nuclear Medicine and the other in Cyclotron Accelerators, in order to change the prior norm that established only one supervisor with any specialty.

It was also formed a commission of government specialists to license, supervise and inspect the future installations. Although all the persons of the group were specialists in Nuclear Medicine, Radiotherapy or Civil Engineering, none of them were specialized in cyclotron particularly, they had to put their skills together in order to oversee the many aspects of this kind of business. They were also trained in existent cyclotron facilities abroad to analyze the licensing procedures and statutes wide.

All these changes of during the site installation brought some gaps mainly in sanitary laws. There was not any specific health norm for radiopharmaceuticals up to the change of the Constitution. (4) Existent statutes became available for suggestions and are being revised. Many official actions that will take place are already understood but any regulation is written. It is a huge step for the health agencies once all the rules applied to radioactive material were only CNENs obligation but the difficulties will come at regional levels once this kinds of norms vary at each state of the country.

Then again, the specialists had to be taken national trainings and be tested by the National Commission of Nuclear Energy to be nominated Radioprotection Supervisors, specialists on cyclotrons and nuclear medicine. Once the specialists were trained and legally suitable, it was time to train the rest of the crew. It was necessary for everyone to know how the facility works.

The human resources in all areas of study, was beyond expectations. Another relevant issue is that the most of experienced professionals in these field is retired or in process of retiring. Even the governmental agencies of health and nuclear applications lack of qualified personnel and the salaries of the specialists of the government with the many beneficiations were far ahead what an initial project with future distribution could pay.

Studying a company called R2 with the ambitious project of installing three cyclotron sites concurrently, the need of teaching the technical and the administrative teams was clear. The efforts were many, although for the technical team there was chosen only the ones with college degree, the lack of specific knowledge was shown really fast. The pharmacists never studied radiopharmacy before, the physicists and the engineers never had to understand the special details of this kind of accelerator, and the many peculiarities of the project impose training of the administrative staff as well. All the areas as Procurement, Management, Nuclear Law and Information Technology had to understand how a cyclotron site works. And then it became a net of learning.

The barriers that the perception of risk due to the nuclear energy usage imposes, allied with the common sense of danger, with the many accidents and military purpose usage wide, are another heritage that the decades of the monopoly left, with no programs of consciousness-raising of its benefits.

The different levels of the government had to understand and accept what were the benefits of an accelerator facility located in their jurisdiction area. From environmental licenses to population consciousness-raising, it was only the beginning of the hard work.

With this open of the market it is clear that uranium enrichment will be the next step. Some doubts still remain.

Method

Internal

Facing the many issues the lack of knowledge would represent R2, initiated a comprehensive program on training people from different businesses throughout the country together with universities, companies, hospitals and the government and achieved amazing results. Now, there are more than 30 people trained and capable to run the cyclotron operation in its many faces at this company.

The investments on education inside the companies increased significantly the costs and the amount of time spent on the installation of the facility. R2 project of installing three cyclotrons concurrently needed to be delayed in six months for each site and the initial project of R$ 5 million turned out to be increased in 25%.

A simple study, based on the first business plan written, was demanded by the investors (on the top of the company hierarchy), included the raise and discussion of all the aspects that increased the final costs of the project, most of them showed education deficiencies in different levels: all national and abroad trainings; project redesign due to changes on statutes and norms; the licensing process in Nuclear, Health and Regional areas (that were made several times, took many extra hours and could not reach the perfect understanding of the national authorities); trips of the administrative staff to be able to understand regional peculiarities of laws, statutes and the training of their own collaborators; the hiring of specialized offices; the search for national and international loans and benefits; the unavailability of national equipments due to the lack of market; the project of new national equipments due to the impossibility of importing; the many changes on suppliers and constructors due to the difficulty on performing the facility on schedule; the congresses that demanded participation with learning and exposing; many extra hours; specific softwares that had to be designed; difficulty of the investors to understand the project, its needs and postponed some important steps.

The main conclusions showed that the constant redesign of projects and delays on the schedule were the most increasing factors for the first facility. The following projects gathered great expertise from the first one and from the plant to the staff, the savings were almost 45%.

The search and design for specific systems of data control integration and interlock security inside the plant required a lot of customization and partnership with national companies that at first were hard to find and then had to be taught carefully all the processes in order to synchronize them.

The import laws did not change with the Amendment, although this technology is not built in Brazil, to receive benefits and diminish high taxes it was necessary to prove at the regional levels of the government the huge step it was to improve the local nuclear medicine, research centers and universities, therefore presentations were made.

The attorneys in order to make these contracts needed to understand all the processes of the company in order to estipulate the minimum obligations and risks for exposed ones. The commercial and financial times of the company in order to make the business plan to happen, had to study the whole market and travel all around the country to understand how the sells were going to look like.

Procurement people had to understand the peculiarity of the products, mainly radioactive material and the technology of the machine to buy the certain products at the right time.

Facing these many issues, it turned to be necessary to train the whole crew to face the different aspects that the simple Amendment did not cover.

Even the technicians inside the companies had to have specific trainings abroad and inside the country, to understand the specificity of the health and radiological statements in order to write the internal procedures.

Many training programs were written in order to qualify the whole crew, the technical staff spent 120 hours in cyclotron facilities abroad and another 120 hours in national sites, including managers, physicists, engineers and pharmacists. Inside hospitals and nuclear medicine clinics, the same group spent 200 hours. They had practice and theory trainings.

All the staff spent 60 hours on software trainings and at least one day a week and at Saturdays, there were diverse topic presentations (importation, fiscal flow, information technology, commercialization issues, scheduling, procurement flow…), all these were theoretical trainings.

Some offices were hired to train specific subjects, mainly financial and controlling issues, and in these cases, the crew traveled in order to have practical trainings.

All the suppliers of equipments, consumables or services had to understand the project, and were trained according to the service. The brokers and constructors had extensive trainings to master details of the project.

Now, training procedures system qualifies all future members of the project.

The increments of money and time improved the following projects as well as built partnerships for installation and production inside other companies, due to the expertise brought for minimal details. It did not start as a program of knowledge but once the crew faced all the trainings and difficulties this kind of installation could bring, they could start many other projects together with partnerships and teach third ones how to do this job.

Dissemination

At universities this program of education first started with short presentations followed by question and answer during the year and at regional congresses. It got many students and researchers attention and it was the first step in order to establish partnerships.

Some trainees were chosen to adapt to the dynamics of a company. This specific production that involves short half lives, all the processes have to be synchronized in order the cyclotron to run perfectly and the patients who will receive the radioactive medicine are scheduled according it, therefore mistakes can cause huge losses.

Partnerships were then established to knowledge management. The first one to happen was in the southern state of "Rio Grande do Sul" where the first site of R2 is located with trainees of the University PUC. As the facility is starting its commissioning, there are already four projects of research involving the specialists of the site, professors of the campus and many graduation students.

The first project that started at the concreting of the bunker door, during the building of the facility was the irradiation of concrete walls. Five cylindrical samples with the same concrete of the bunker walls were made. All of them are located inside the bunker to receive the same irradiation scattering of the walls. Each year the activation of them will be measured. This way it will be possible to know how is the wall activation in the first stage of the concrete after five years of irradiation.

At Sao Paulo University there is also a partnership involving students as trainees, some of them are already hired to work at the central offices in Sao Paulo city.

Those students did not master the many aspects of an accelerator facility so they had to study, the university brought specialists to train the private enterprise crew and in exchange the facility could be used for research of the university during the stand-by time of the accelerator.

This partnership brought only positive results for both parties, the technicians became even more specialized and the researches brought good results for the universities together with the training and interest of much more people once there is a market being established.

Another project taking place is the Active Carbon Filters, where each change of air filters the activity of the radioisotopes captured will be measured and the results will be compared with the irradiation time used, this way the estimate the activation of the bunker air can be estimated.

At clinics and hospitals the efforts were focused on improving the applications of the radiopharmaceuticals, the products of the accelerator, mainly with the centralized radiopharmacies.

Conclusion

Breaking down a monopoly is not enough to enable a country to get free from importation of radiopharmaceuticals. It seems to be necessary taking advanced steps to fulfill market with qualified human resources.

The government, through national agencies, should take the initiative – as recommend by the IAEA – to discharge their responsibilities in contributing for the establishment of a clear regulatory regime and for the formation necessary expertise.

Industry should be able to start developing its own expertise while pushing/encouraging governmental agencies and educational centers to accomplish their attributed tasks.

Cooperation at regional and international levels may be a way forward in minimizing the barriers for the establishment of an independence in the field of radioactive material for medical purposes.

The experience and lessons learned in the field of radiopharmaceuticals production may be used to avoid similar problems in the uranium mining/milling when the state monopoly finally ends.

In the other hand, the knowledge exchange through partnerships with universities, research centers and hospitals and researches in the state of art technology through the new centers of radionuclide and radiopharmaceutical production are working for the increase of national knowledge and the benefits for the underdog, now that these technologies are more spread and through the national health insurance it is possible for the ones with low money.

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