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Review

The Radiopharmaceuticals Production and Research Centre at the Heavy Ion Laboratory of the University of Warsaw

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Abstract

The planning, history of construction, description of the equipment and the expected activity program of the University of Warsaw Radiopharmaceuticals Production and Research Centre are presented.
Key words: medical radioisotopes, radiopharmaceuticals, nuclear medicine imaging, positron emission tomography.

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Introduction

At the beginning of this century, after more than six years successful operation of the U-200P heavy ion cyclotron and after the installation of the home–made ECR ion source, the Heavy Ion Laboratory (HIL) management decided that a new direction in the development of the Laboratory was necessary in order to maintain its vitality and place at the forefront of the Polish research infrastructure.

After profound internal discussions followed by the approval of the Laboratory Scientific Council the decision was taken that from a number of options considered the most appropriate would be the installation on the premises of HIL of a new, commercial cyclotron for the production of medical radioisotopes, with special emphasis on those used for Positron Emission Tomography (PET).

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At that time PET techniques had not yet been introduced in Poland. The motivation of the decision taken was mainly based on two arguments. First, the Laboratory team had long experience and expertise unique in Poland in cyclotron operation, so the installation of a second machine of this type at HIL should not give major running problems. Another argument was the vicinity of the Nuclear Medicine Department of the (at that time) Warsaw Academy of Medicine where the installation of a PET scanner was seriously considered.

Two major events occurred at the beginning of 2003. In February the first PET Centre in Poland was inaugurated at the Oncology Centre of the Prof. Lukaszczyk Memorial Hospital in Bydgoszcz with a 10 MeV proton cyclotron and PET/CT scanner. This pioneering initiative financed by Hospital funds had an enormous impact on the promotion of this branch of nuclear medicine in Poland. Similar funding was not imaginable in the case of the HIL project. Instead, a Warsaw Consortium for PET Collaboration was organized by HIL together with the Nuclear Medicine Department with the objective of obtaining the necessary funding to create a production centre for PET radiopharmaceuticals in Warsaw. Soon twenty Warsaw scientific and diagnostic centres had adhered to the Consortium.

In the second half of the same year a proposal was submitted to the International Atomic Energy Agency (IAEA) for support of the project within the Technical Cooperation Program aiming at the installation at HIL of a commercial cyclotron for the production of PET radioisotopes. This proposal was strongly supported by the Minister of Sciences and the Minister of Health, with declarations to contribute substantially to the cost of this project.

A crucial step was the final decision by the Minister of Sciences, taken at the end of 2004, to allocate to this project a grant of 10 Mzł for the adaptation of the building and purchase of equipment, shortly followed by a second grant allocated by the IAEA of the order of 1 MUS$ for the purchase of the cyclotron. In the following years consecutive grants from the Ministry of Health and European Structural Funds allowed almost all the necessary funds to be collected and eventually completed, during the final construction phase, by the University of Warsaw.

The participation of the IAEA in the project was not limited to the purchase of equipment; its whole realization was aided by the Agency's expertise in the planning of the site design, tender

preparation and launching, and by its contribution to the training of the Laboratory team during a number of years before completion of the project.

Project implementation

After many months of preparation, in February 2006 the Agency launched a turn-key tender for the complete execution of the Radiopharmaceuticals Production and Research Centre (RPRC — present name) at the premises of the Heavy Ion Laboratory. The tender included the adaptation of the building, the cyclotron and the equipment for the FDG (fluoro-deoxy-glucose) production line. At the end of the same year the General Electric Medical Systems Company was declared as the successful bidder. The above mentioned successive grants allowed a more extended (in comparison with the tender terms) completion of the Centre project, described in more detail below.

The very fact that all the funds collected for the construction of the Centre were not available at the moment of the tender launch substantially delayed the completion of the project. A number of unexpected events also contributed to the accumulated delays. Fortunately, during the first half of this year all building adaptation and equipment installation work was completed and on May 15, 2012 the Centre was officially inaugurated by the Rector Elect of the University of Warsaw [1].

Description of the centre

Project rationale

From the very beginning it was assumed that, based on the produced short lived radioisotopes, both commercial and research activities would be conducted at the RPRC. To this end chemical equipment allowing the production, distribution and quality control of various radiopharmaceuticals would have to be installed. The area for the everyday production of the most popular commercial PET radiopharmaceutical — fluoro-deoxy-glucose (FDG) — would be separated from the research one. It would also be useful for separate quality control areas to be arranged for commercial and research activities. As described below, the available space for the installation of the Centre and the available funds allowed the implementation of these objectives.

The site project also allows the construction of an external beam line for solid target irradiations producing longer lived species during the cyclotron spare time between the commercial FDG production cycles. The installation of underground capillary connections to the neighbouring (around 500 m) Nuclear Medicine Department PET/CT scanner for ^{15}O transportation for perfusion diagnostics will also be possible when the appropriate funds are available. Similarly, the animal micro-PET scanner, situated in the neighbouring Chemistry/Biology Faculties CENT III building, will also be connected with the ^{15}O production facility.

The Centre on the HIL Premises

In the HIL building about 500 sqm underground area was available and could be adapted to host the Centre. Figure 1 shows the ground floor of this building, where the large K = 160 heavy ion cyclotron, its experimental stations and the position of the RPRC are indicated.

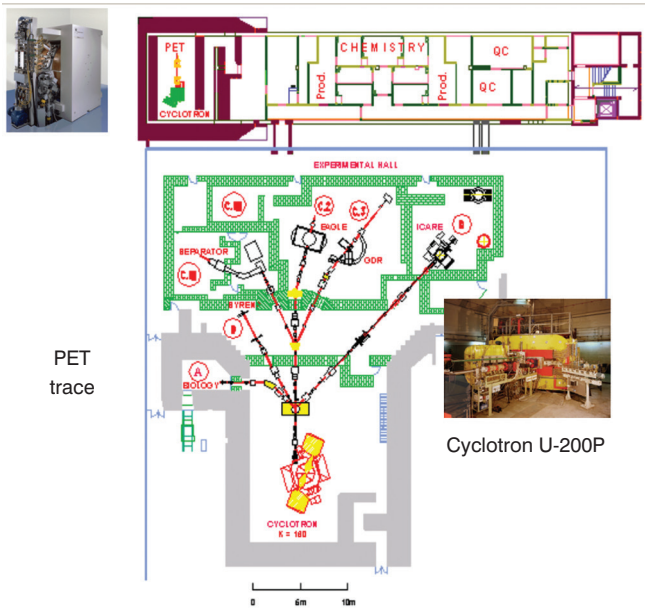

Figure 1. Layout of the ground floor of the HIL building. Lower part of the layout shows the heavy ion cyclotron, its beam lines and the nuclear physics experimental stations. Upper part shows the Radiopharmaceuticals Production and Research Centre, placed underground — 6 m) (adapted from ref. [2])

Centre layout and equipment

The layout of the Centre is displayed in Figures 2–4. The GE PETtrace cyclotron (Figure 5) is able to deliver up to 100 microamperes proton current of 16.5 MeV energy and up to 60 microamperes, 8.4 MeV energy deuterons. As indicated above, the chemistry area is composed of two parts: a so called area L1 for the everyday synthesis and dispensing of the most current radiopharmaceutical FDG, intended for the commercial activity of the Centre, and area L2 for the research activity. In area L1 two hot cells (single and double) host the FDG automatic synthesis and dispensing units. In area L2 two single and two double hot cells are available equipped with a universal ^{18}F synthesis unit (for FDG but also other ^{18}F-based radiopharmaceuticals) and a complete ^{11}C-based radiopharmaceuticals line with appropriate synthesis and dispensing units. A ^{15}O based water synthesis unit is also available there.

Expected centre activity

Besides the regular everyday production of the commercialized FDG radiopharmaceutical, syntheses of other known species are planned for preclinical research in collaboration with institutions belonging to the Warsaw Consortium for PET Collaboration or members of the Ochota Campus network. At the very beginning, depending on the expressed needs, the production of ^{18}F-FLT, ^{18}F-Choline or ^{18}F-Dopa may begin almost immediately. Two fully equipped ^{11}C radiopharmaceuticals synthesis lines can be used for e.g. ^{11}C-Choline, ^{11}C-Acetate or ^{11}C-Methionine production.

Another research area will be innovative radiopharmaceuticals for PET and combined imaging methods (PET-NMR). The research work and the application activity is focused mainly on new

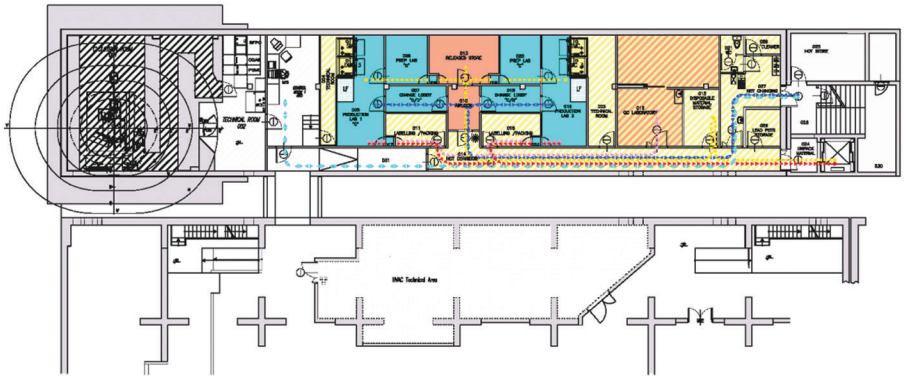

Figure 2. Layout of the RPRC. Proton/deuteron cyclotron and its control room is placed on the left part of the figure. Two independent production rooms are placed in the middle of the figure (the first one for the routine FDG production and the second one for other, also innovative, radiopharmaceuticals). The Quality Control room is placed in the right part of the figure (adapted from refs. [2, 4])

Figure 3. A 3D view of the RPRC represented in Figure 2 (courtesy of the M + W group, building adaptation designer and executor)

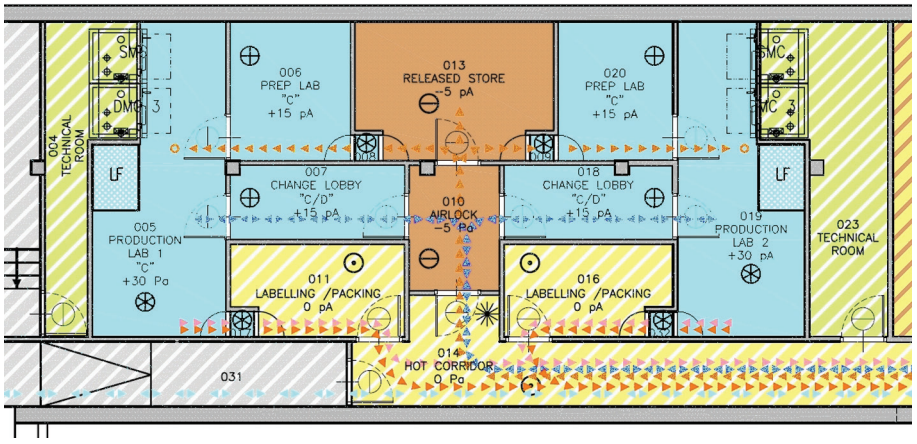

Figure 4. Enlarged view of the production rooms (adapted from ref. [3])

drugs applied in oncology, cardiology and neurology — significant fields of modern medicine.

The initial aim is to develop production technologies for substrates like ^{11}C-halogenes, ^{11}C-alcohols and $^{11}CO_2$, for studies of functioning and functional changes in the nervous system, to answer questions on the origin and course of Alzheimer's disease, Parkinson's disease or various forms of schizophrenia. The next task is to create the infrastructure for the production and application of ^{15}O marked water in advanced cardiologic and neurological diagnostics. The research program strongly supports the activities conducted by neighbouring institutions: the Medical University of Warsaw, which is interested in applying the above radiopharmaceuticals in clinical practice and the Institute of Experimental Biology, focused on ^{15}O application

Figure 5. The PETtrace p/d cyclotron

Figure 6. Hot cells in the research laboratory (photos Grzegorz Krzyżewski)

in the research of neurobiological processes and fundamental research on the mechanisms of mental illnesses.

An important example of cyclotron beam use for non-PET radiopharmaceuticals will be research into an alternative (via accelerators) way of producing the most popular isotope in nuclear medicine, ^{99m}Tc, presently obtained from the nuclear reactor produced ^{99}Mo generator.

Summary and conclusions

Supported by grants from the Ministry of Sciences, International Atomic Energy Agency, Ministry of Health, European Structural Funds and the University of Warsaw resources the Radiopharmaceuticals Production and Research Centre was created on the premises of the University of Warsaw Heavy Ion Laboratory. The main objective of the Centre will be the production of and research into Positron Emission Tomography radiopharmaceuticals. However, after the installation of the external beam line the available high intensity proton or deuteron beam will also be used for the production of other longer lived radioisotopes for life-sciences applications.

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