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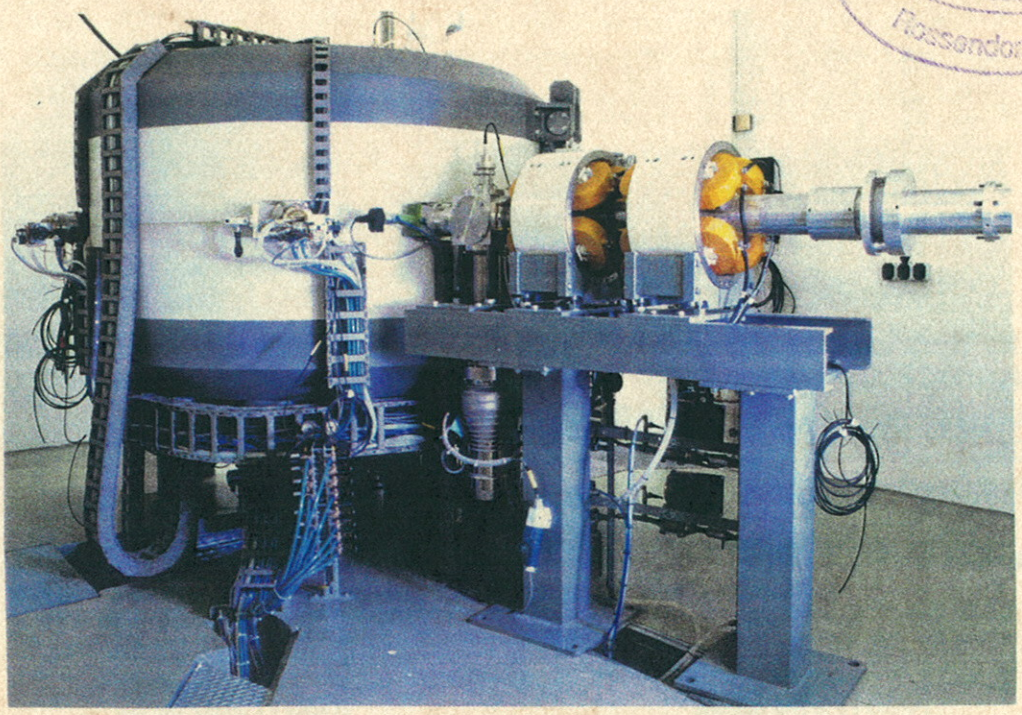
Institut für Bioanorganische und
Radiopharmazeutische Chemie

# CYCLONE 18/9 USER COMMUNITY

## First Workshop

Rossendorf, October 10/11 1996





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Cover picture:

The Rossendorf PET cyclotron "CYCLONE 18/9" with beam transport line.

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# CYCLONE 18/9 USER COMMUNITY

## First Workshop

**Rossendorf, October 10/11 1996**

Editor: B. Johannsen and St. Preusche

# Foreword

## An Idea Became Reality

*November 1994:*
Stephan Preusche, head of the Rossendorf PET cyclotron CYCLONE 18/9 stayed for two weeks at the medical cyclotron of the Montreal Neurological Institute. During his work at the MNI "CYCLONE 18/9" he felt that it would be necessary and very helpful to come in close contact to all other CYCLONE 18/9 users.
Stephan put forward his idea of the foundation of a world wide
CYCLONE 18/9 USER COMMUNITY
to his Canadian colleagues and he went down well.

The aims of the community should be:
- to come in contact with all other CYCLONE 18/9 users
- to have competent partners for discussion and
- to change experiences of operation and maintenance of the CYCLONE 18/9.

Back home Stephan elaborated and pursued the idea of establishing a forum for CYCLONE 18/9 users.

*October 1996:*
Two years later. Users of CYCLONE 18/9 facilities (existing and under planing) agreed with the idea, and our institute organizes the first workshop of the new community.

I am pleased and honoured to welcome the participants of the first workshop of the CYCLONE 18/9 USER COMMUNITY to Rossendorf. The participants are from **all** CYCLONE 18/9 facilities around the world and, of course, from IBA - the manufacturer of the PET cyclotron CYCLONE18/9. I wish all of them two busy, fruitful and pleasant days at Rossendorf/Dresden.

Prof. Bernd Johannsen
Director of the Institute of Bioinorganic
and Radiopharmaceutical Chemistry

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# I. REPORTS

# THE CYCLOTRON CYCLONE 18/9 IN BAD OEYNHAUSEN

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## 1. Introduction

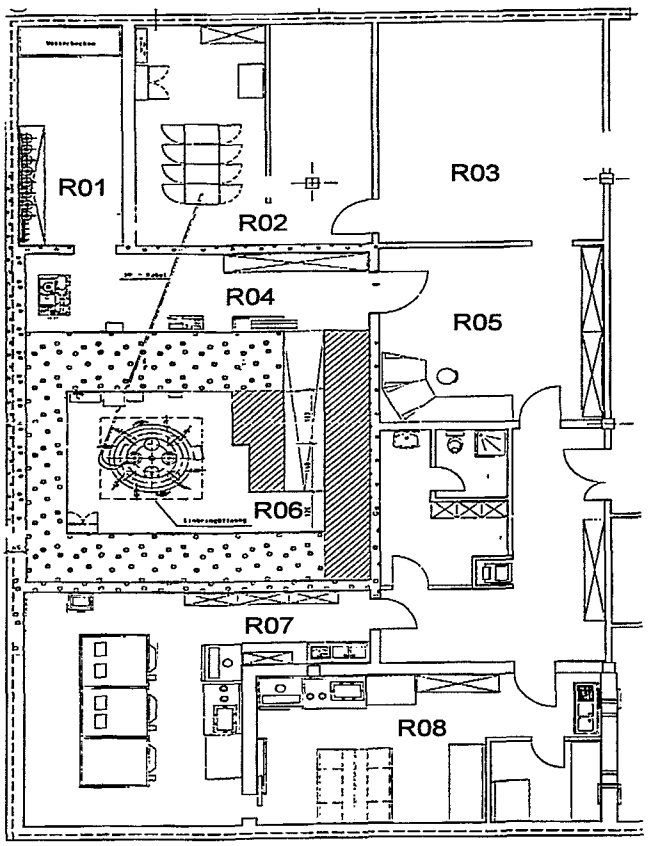
The *Herz-und Diabeteszentrum Nordrhein-Westfalen* is a hospital specialized in diagnostics and medical treatment of cardiovascular diseases and diabetes mellitus.
The PET - Center including cyclotron and radiochemistry is a part of the *Institut für molekulare Biophysik , Radiopharmazie und Nuklearmedizin* and completes the traditional nuclear medicine .
In May 1993 the PET camera ( Siemens ECAT 951/A ) started working with 2-FDG ordered by KFA Jülich. The installation of the cyclotron started in January 1994 with the cyclotron and the yields being accepted in May. After the installation of the complete exhaust air emission measuring system in August 1994 the license to run the cyclotron was granted. We started with the production of [F18] - fluorine and the synthesis of [F18] 2-FDG. In March 1995 the first patient could be examined with our own tracer. At the moment we have up to 6 patients a day ( tracers : [F18] 2 - FDG, [N13] - ammonia and [C11] - acetate, for the next future [C11] - methionine , [F18] - FTHA only scientific interest).

## 2. Building

### 2.1. Description

The PET camera, the cyclotron vault , the hotcells and the laboratories are located in the basement of a new part of the hospital.
The walls of the cyclotron vault are made of concrete including baryt. The door to the vault is filled with lead and paraffin and has a special sealing filled with compressed air when the door is closed. The doors to the laboratories and the scanner room are filled with lead.
The produced radioactivity is transported to the laboratory via polyethylene tubes for the liquids ( ID 0.5 mm for fluorine and ID 0.8 mm for ammonia ) and stainless steel tubes for the gases. Both sorts are lying in a lead tube ( ID 30 mm ) which is placed in the basement of the PET center. The distance between cyclotron and hot cells is about 20 m , between cyclotron and scanner is about 25 m, so that we can collect the produced radionuclides after about 30 sec.
A liquid waste system, a compressor system for waste gases and a part of the ventilation system is located in the cellar of the PET center .
The radiochemistry is equipped with 3 hotcells which have been installed by Van Gahlen, several fume hoods and HPLCs , GC , TLC, y-spectrometry, pH-meter and a LAL test for the quality control.

2.2. Layout




| | |
|---|---|
| R01 | Waste room, gas dristibution |
| R02 | Power supply room |
| R03 | Laboratory |
| R04 | Technical equipment |
| R05 | Control room |
| R06 | Vault |
| R07 | Hot Lab |
| R08 | Semi Hot Lab |

**3. Targets and modules**

At the moment 4 targets from IBA are installed which are not positioned for the dual beam mode.
The small $^{18}$ F - target deliver a sufficient amount of 2 - FDG to supply the PET for the whole day.
Ammonia is produced for each examination so that a good cooperation with the PET team is required.
Acetate is so far not applied routinely.

Targets:

| | |
|---|---|
| $^{18}$ F - Fluorine ( small volume 300µl ) | routinely 15 GBq EOB at 12 µA for 45 min.<br>max. 26 GBq EOB at 12 µA for 90 min. |
| $^{13}$ N - Nitrogen-Ammonia | routinely 5 GBq EOB at 12 µA for 10 min.<br>max. 9.5 GBq EOB at 15 µA for 20 min. |
| $^{11}$ C - Carbon | routinely 9.5 GBq EOB at 12 µA for 10 min.<br>max. 25 GBq EOB at 12 µA for 20 min. |
| $^{15}$ O - Oxygen | no experience, only acceptance test |

Table 1: Overview of the isotope production and the breakdowns in 1995 and 1996 (until may)

| | 1995 ( 2160h ) | | | 1996 ( until May 832 h ) | | |
|---|---|---|---|---|---|---|
| Target | hours beam | % | Activity [GBq] | hours beam | % | Activity [GBq] |
| $^{18}F^-$ | 125.6 | 5.8 | 1756 | 40.63 | 4.9 | 650 |
| $^{13}N$ | 7.5 | 0.3 | 169 | 29.9 | 3.6 | 682 |
| $^{11}C$ | 7.9 | 0.4 | 258 | 3.3 | 0.4 | 74 |
| | | | | | | |
| Maintenance/Installation | 160 | 7.4 | | 64 | 7.6 | |
| Failures | 152 | 7 | | 24 | 2.9 | |
| | | | | | | |

At the moment the radiochemistry is equipped with 5 modules

- 2- [18 F] - FDG
- [18 F] - FTHA
- [11 C] - acetate
- [11 C] - methionine
- [15 O] - water

The [15 O] - water module has been supplied by IBA, the others by Nuclear Interface. At the moment we use only the optimized FDG module ( about 200 FDG synthesis ) for routine production. Ammonia is produce directly in the target which makes production very easy. The anion exchange resin for the purification of ammonia is placed in the acetate module so that we can use one GM counter to determine the produced quantity. The first methionine synthesis tests are finished and we hope that we can use [11 C] - methionine soon for patient application.

| Yield (c.f.d): | | |
|---|---|---|
| | FDG | 45 % , 53 min. time of synthese |
| | FTHA | 15 % , 120 min. |
| | Acetate | 40 % , 12 min. |
| | Ammonia | 98 % , on line |

## 4. Safety and security mesurements , environmental care

### 4.1. Ventilation system general

The ventilation system is divided into different zones. In each zone there is a special low pressure, which is controlled and indicated. The cyclotron vault and the hotlab with the hotcells have the highest low pressure. ( cyclotron vault - 200 Pa , hotlab - 40 Pa )

### 4.2. Radiation protection instruments

In the cyclotron vault, the hot lab and the semi hot lab a Geiger Müller counter was installed for radiation surveillance. The mesurement system in the vault is used for the vault door interlock. If the value is too high, the door cannot be opened. The normal value is about 1 mSv/h, during the bombardment the value is about 9 mSv/h at fluorine production. The other systems in the radiochemistry are not used for interlock.

4.3 Liquid waste system

The liquid waste system is very simple due to the short half - lives of the produced radiopharmaceuticals.
Two tanks are available with a complete volume of 2000 l. Every two weeks we have to unload the tanks after controlling a sample of 20 l of the waste water.

4.4 Compressor system

The compressor system existing of two redundant systems is used for the waste gases produced by the synthesis. We are able to compress the gases into two tanks with a volume of together 400 l both at 6 bar.

4.5 Monitoring of radiation in ventilation

3 places for mesurement systems

- Cyclotron value too high: the ion source stops ( or can not be started ), the vault is closed by special valves in the ventilation system, and the air condition is stopped for the cyclotron vault and the room nearby
- Hotcells value too high: the valves of the ventilation of the hotcells are closed
- Chimney this place (near the end of the chimney ) was used only for the documentation of the values (german radiation protection prescription)

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# THE GENEVA PET PROJECT

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**Abstract**

The Geneva PET project started in the early 80s with the construction of a rotating PET camera made of two large area avalanche chambers. Then a prototype BGO-based rotating positron tomograph (PRT-1) became operational in 1991, followed in 1995 by the acquisition of the commercial ECAT ART system. The decision to develop a fully equipped PET centre in Geneva with a cyclotron and a radiopharmaceutical production unit was made in 1992. In this presentation we will cover the most important points that have motivated our choices for cyclotron and laboratory layout. An IBA Cyclone 18/9 has been ordered and manufactured. The construction of the vault will start at the end of this year and the equipment will be delivered within about one year from now.

## 1. Background of the Geneva PET project

The Geneva University Hospital played an important role with D. Townsend in the development of a new generation of cost-effective PET scanners. In 1983, D. Townsend et al. developed a rotating PET camera comprising two large area gas detectors: the HIDAC camera[1]. It has been extensively used until the late 80s for human thyroid studies with $^{124}I$. Very similar detectors developed in Rossendorf by Manfrass[2] et al. initiated the Rossendorf PET program as well.

Since the overall efficiency of such gas detectors for 511 keV is rather poor, D. Townsend et al., together with industry, started to develop a new type of rotating PET camera based on BGO detector blocks. As a result of this, a prototype rotating tomograph using standard CTI BGO detector blocks, the PRT-1 camera[3], became operational in 1991, and a second prototype also developed by D. Townsend et al., the PRT-2 camera[4], has been installed last year at the Paul Scherrer Institute (PSI) in Villigen. PRT-1 was used for clinical routine application with [$^{18}$F]fluorodeoxyglucose (FDG) shipped to Geneva from Lyon and PSI. Finally, late 1993 the Republic and Canton of Geneva voted a law to provide Geneva with a fully equipped PET centre comprising a cyclotron and a radiopharmaceutical production unit.

## 2. Guide lines for the Geneva PET project

### 2.1 General remarks

Based on a tradition of many years of research and development at the Geneva University Hospital, the future Geneva PET centre is designed to fulfil clinical routine and research missions. Clinical routine and research will rely on standard positron-emitting radio-pharmaceuticals, whereas more fundamental research on PET radiochemistry and instrumentation, as well as scientific training and teaching will be made possible. As an example, equipment setup will allow to think of operating production technologies for medium Z positron emitters. These requirements have clearly motivated the choice of the cyclotron which is going to be installed in Geneva, the IBA Cyclone 18/9, and have guided the design of the cyclotron vault that will allow to build an external beam line.

The guidelines listed below were taken into account to design the laboratory layout of the radio-pharmaceutical production unit.

i Radiation protection rules:
- radiation shielding,
- radiation dose monitoring,
- radiation interference limits with atmosphere and water;

ii Pharmaceutical production rules:
- pharma laws,
- good manufacturing practice (GMP) and good laboratory practice (GLP),
- quality insurance.

2.2 Radiation protection

Due to space constraints, the cyclotron vault will be equipped with a heavy concrete air-lifted French door. The thickness of the vault and of the door will be 2 m of 2.35 g/cm$^3$ concrete, so that dose rates outside the vault will stay below 100 µSv/h.

Interference limits in the exhaust air of 200 Bq/m$^3$ averaged over one year need to be met. To fulfil this limit, air change in the cyclotron vault will be diminished from 10 fold air change when there is no beam to less than 3 fold air change in presence of beam. Air will be continuously pumped out of the vault to monitor its dose rate. Incoming air will be stopped and the cyclotron turned off each time the measured dose rate exceeds a given threshold value.

About 10 to 20 fold air change will be maintained in the laboratories, following a recommendation for keeping a class D certification for clean room conditions. High attention is paid to the design of the hot cells, as for as interference and radiation protection are concerned. They must be tight and must continuously stay depressed. Moreover, they must be ventilated with a diagonal air flow, even when air change is drastically diminished. Cells will be run below 1 fold air change when synthesis is performed.

The whole radiopharmaceutical production unit, including the cyclotron vault and its related areas will represent a class B laboratory and be a single controlled area according to the Swiss regulation on radioprotection.

2.2 Radiopharmaceutical production

We expect that in the near future:
- short-lived radio-pharmaceuticals will have to be handled like pharmaceuticals,
- different persons will be responsible for production and for application,
- in-house delivering of an in-house produced radiopharmaceutical will have to comply with distribution rules to a third party.

Moreover, we will need special authorisations from:
- the Swiss authorities to operate the installation for producing short-lived PET radio-pharmaceuticals,
- the Republic and Canton of Geneva to exploit in-house produced PET radio-pharmaceuticals.

Laboratory layout must be designed to meet the requirements for pharmaceutical production as close as possible. This implies to fulfil at least D class clean room conditions where dust sources need to be avoided, providing that synthesis of pharmaceuticals will be carried out under aseptic conditions. Commercially available modules for routine production of PET radiopharmaceuticals, as well as equipment for quality control and quality insurance, will be selected according to the requirements mentioned above.

## 3. The Geneva PET laboratory

The PET radiopharmaceutical production unit will be located between the entrance of the hospital and the building where the division of nuclear medicine is located. Figure 1 shows the layout of the site. The cyclotron vault and the hot laboratory, as well as a technical room and a small workshop, will be located in a new building, whereas the chemistry and quality control laboratories, the control room and the entering sluice with its decontamination shower, as well as a meeting room out of the controlled area, will be three floors below the division of nuclear medicine, in the same building. For details, see Figure 1 and Table 1.

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Table 1: Technical specifications for the Geneva PET project

| | |
|---|---|
| *General aspects:* | |
| Cyclotron: | IBA Cyclone 18/9. |
| Cyclotron vault: | 2 m of 2.35 g/cm$^3$ concrete. |
| Access to cyclotron: | 2 m thick air-lifted French door. |
| *Classification:* | |
| Clean room conditions: | class D laboratory. |
| Radiation protection: | class B laboratory in a single controlled area,<br>entrance through a sluice with a chicane and a decontamination shower,<br>emergency exit not accessible from outside the controlled area. |
| *Laboratories lying inside the controlled area:* | |
| Control room: | 25 m$^2$, cyclotron and radiation control room, electronic workshop, passage to other rooms of the controlled area. |
| Hot laboratory: | 50 m$^2$, 3 hot cells and 6 mini-cells, 2 laboratory hoods for isotope work, dispensing unit, computer, other equipment. |
| Quality control laboratory: | 36 m$^2$, quality control equipment, other equipment. |
| Chemistry laboratory: | 24 m$^2$, 2 laboratory hoods, glass washing machine, sterile water producer, other standard laboratory equipment. |
| Technical room: | 20 m$^2$, RF and control electronics for the cyclotron. |
| Workshop: | 15 m$^2$, drill, milling-cutter, lathe. |
| Conditioning room: | 8 m$^2$, for packing and shipping. |
| Safety corridor: | access to the emergency exit, belongs to the hot laboratory. |
| Cyclotron corridor: | access to the cyclotron. |
| *Rooms lying outside the controlled area:* | |
| Technique: | 80 m$^2$, ventilation. |
| Gases: | 15 m$^2$, open air shelter for gas bottles. |
| Meeting room: | 25 m$^2$. |
| Toilette: | near entrance of the controlled area. |

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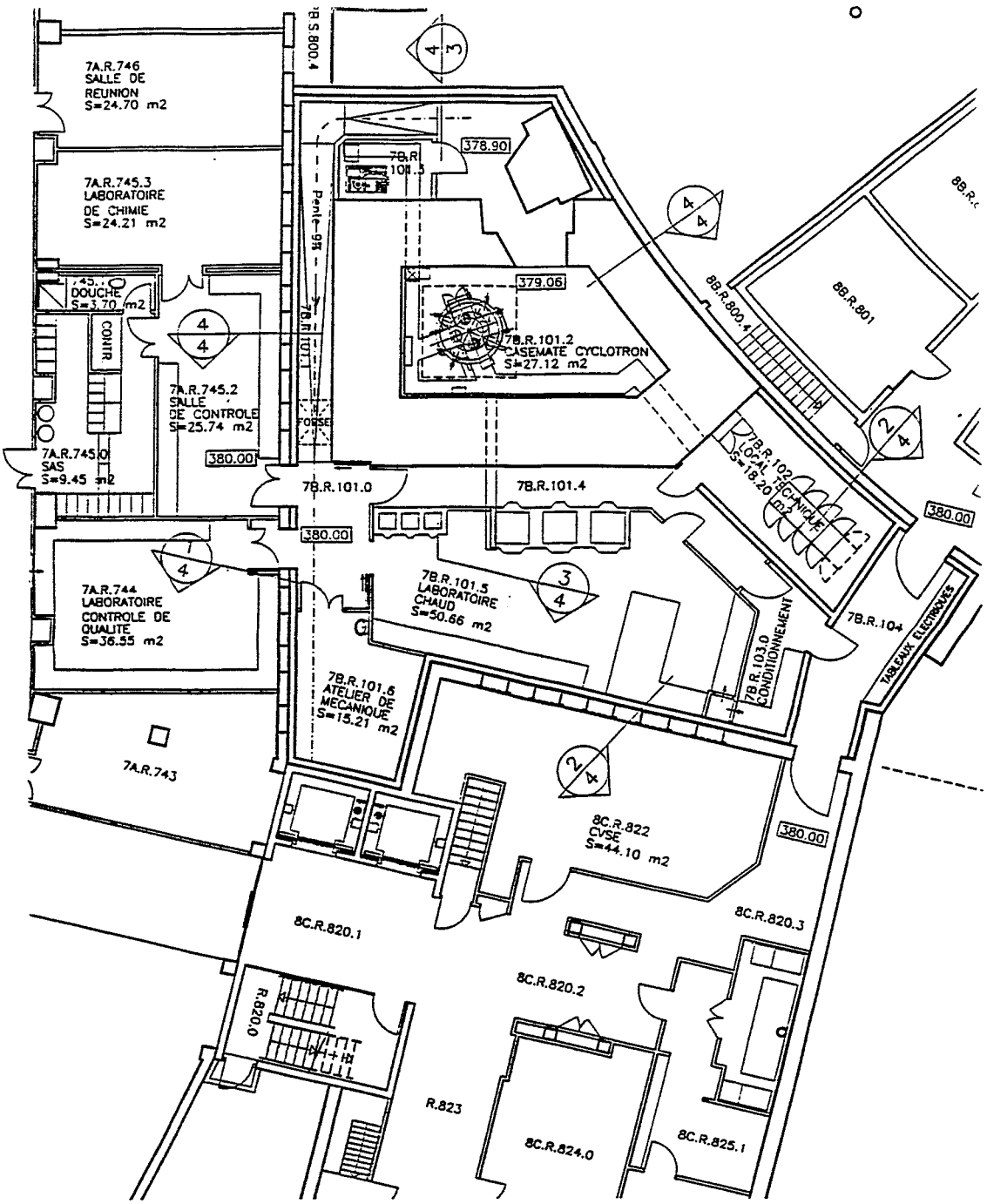


Figure 1: Layout of the radiopharmaceutical production unit of the Geneva PET project

# SHORT PRESENTATION OF IBA

Ion Beam Applications (IBA), a Belgian medium-sized company, is a spin-off of the Cyclotron Research Center of the University of Louvain (UCL) and of the National Institute for Radioelements (IRE), both leading institutions in particle accelerator development and operation. Founded in 1986, IBA employs now a personnel of 85 and has a yearly turnover of about 20 M USD.

IBA builds its success on innovative products. At the roots of its foundation lays the design and development of a new type of compact cyclotron, the CYCLONE 30. This revolutionary system, specifically designed for industrial-scale production of radioisotopes has rapidly made the company a recognized leader in particle accelerators for medicine and industry.

Applying the innovative principles of the CYCLONE 30 to smaller models, IBA has created, for hospital operation, a range of radioisotope production systems based on ultra-compact, low-energy, cyclotrons. These systems are dedicated to Positron Emission Tomography (PET), one of the most advanced techniques in medical imaging.

The experience gained from the design of the low and medium energy cyclotrons was carried over to the development of higher energy cyclotrons from 70 to 235 MeV for radioisotpe production and radiation therapy applications. In the field of proton therapy, IBA has developed a cyclotron-based in-hospital system equipped with isocentric gantries. The treatment capacity of such equipment is in the 20.000-30.000 sessions range per year. It allows a much larger number of cancer patients to benefit from the very high precision of proton beam therapy.

In the field of sterilisation and industrial ionisation, IBA manufactures and markets the RHODOTRON. It is a new breed of high power/high energy electron accelerators based on the beam recirculating principle. RHODOTRON produces, at low energy consumption, a continuous beam of up to 250 kW power and energy range from 3 to 10 MeV. Such performances allow controlled treatment of a large number of products at on-line production speed under non-sterile conditions.

IBA also develops customised systems such as the CYCLONE 18+, a compact cyclotron with beam intensity in the 1,5 mA range, replacing nuclear reactors for producing palladium-103, a radioisotope used in brachytherapy.

## Summary of manufactured accelerators

**CYCLONE 30**
Cyclotron acknowledged as the ideal equipment for industrial-scale production of most radioisotopes used in nuclear medicine. Accelerating negative ions, CYCLONE 30 produces reliable, high-intensity, extracted beam in the 350-700 microamps range with a level of productivity nearing 100%. Its energy conversion efficiency is over 15%: 15 kW of extracted beam for less than 100 kW power consumption The system allows simultaneous extraction of two beams. Fully automated, of straightforward design it allows for quick and easy maintenance. It is worth noticing that today, all industrial producers of radiopharmaceuticals operate one or two CYCLONE 30 cyclotrons.

**Compact PET-dedicated cyclotrons to cover all needs of PET radionuclide production:**

**Cyclone 18/9**
Accelerating protons up to 18 MeV and deuterons up to 9 MeV, CYCLONE 18/9 has been designed for large scale production of PET compounds. Having inherited the innovative features of CYLCONE 30, CYCLONE 18/9 accelerates negatively charged ions with an extraction efficiency nearing 100 %. Especially compact, considering its power and capacity, the system can be equipped with 8 targets and can simultaneously produce two radioisotopes. Because of its high level of productivity and its flexibility, Cyclone 18/9 is ideally matched to the requirements of PET distribution centres, large hospitals and research institutions.

**CYCLONE 10/5**
A small version of CYCLONE 18/9, CYCLONE 10/5 (10 MeV proton, 5 MeV deuterons) carries the innovative features of larger accelerators: acceleration of negative ions, 8 targets, simultaneous extraction of two radioisotopes, complete reliability and high production yields. It is the cost-effective solution for producing all PET radioisotopes. It can be installed with self-shielding.

**CYCLONE 3**
It is a $^{15}O$ generator providing a steady supply of 4 important radiolabelled compounds: $^{15}O_2$, $C^{15}O$, $C^{15}O_2$ and $H_2{}^{15}O$. Probably the smallest commercial cyclotron available, it is designed for easy installation at virtually any site. CYCLONE 3 is particularly useful for medical centres which specialise in diagnostic procedures employing $^{15}O$ or which collaborate with distribution centres producing F-18 compounds.

**PROTONTHERAPY**
Applying here again the innovative principles of CYCLONE 30, IBA was the first to put forward the concept of a marketable, turnkey, proton therapy centre designed for in-hospital operation.
*The IBA proton therapy system is based on a compact, high energy 235 MeV cyclotron providing beams to 4 treatment rooms allowing over 20,000 sessions per year. This corresponds to the full treatment of more than 1,000 patients.* Some treatment rooms are equipped with isocentric gantries which rotate around the patient allowing the tumour to be irradiated, with very high precision, from the most favourable angles. Other treatment rooms, equipped with stationary beam systems, vertical or horizontal, are reserved for specific cases and for research applications. Proton beam radiotherapy is a technologically advanced means of achieving precise radiation dose distribution.

**CYCLONE 18+**
At first, experts rated its exceptional performances as "impossible". Its beam current *of more than one milliampere* amounts to five times more than the current capability of a standard cyclotron. It allows production, in a cost-effective way, of palladium 103 by using rhodium, a commonplace metal. Until CYCLONE 18+ started operation, palladium 103 could only be produced by nuclear reactors. Palladium 103 is a radioisotope used by implants, in the treatment of certain type of cancer, especially prostate cancer. IBA's remarquable performance was accomplished in record time. From design of the new machine to start-up at customer's site, the whole project was carried out within the incredibly short period of 12 months.

**RODHOTRON**
The Rhodotron's innovative design is based on the beam recirculating principle where the electrons are recirculated throughout a single cavity by using several deflecting magnets. This unique design is a departure from classical electron beam techniques and limitations where electrons are accelerated through a succession of cavities along a linear path.
Marketed in several models with an energy range from 1 to 10 MeV combined with a power range from 35 kW to 250 kW, the Rhodotron family of accelerators provides a superior level of reliability, flexibility and operational economy. It can meet the most strenuous of industrial demands. Additional benefits include compactness and lower building costs as well as fast, easy maintenance.

## CYCLONE 18/9 IMPROVEMENTS

IBA has continuously up-graded its accelerator systems to improve their reliability and performance. This upgrade program includes:

**1. Redesign of the central region, the dee/cavity structure and the ion sources to maximize beam current stability and output.**

The Cyclone 18/9 has a "deep valley" magnet design. The sources, one producing $H^-$ ions the other producing $D^-$ ions, are located in two opposite valleys. Their insertion mode is radial. The dees are located in the valleys that do not contain a source. The dees are connected at the center and supported on one side by vertical copper stems.
On the three first CYCLONE 18/9 (Montreal, Shreveport and Rossendorf machines), these stems are fixed to the upper part of the yoke. Therefore, central region and source adjustments have to be carried out after each opening and closing of the cyclotron, by means of radial and azimutal movements.
From the fourth machine, the stems are fixed to the lower part of the yoke and then, the sources and the central region can be adjusted with the cyclotron opened. The source movements have been suppressed and the sources are now stabilized and set in their optimal position. This redesign avoids any tuning or uncertainty about the source position, and accidental burning of the source chimneys.

**2. A relocalization of the targets, improving beam transmission and target shielding.**

Targets are now directly mounted on the vacuum chamber, rather than on short external beam lines. Access to the targets is always possible without lifting the upper yoke.
This new location improves the beam extraction yield: as an illustration, the proton beam transmission yield is now about 80 to 100%, through a collimator of 10 mm in diameter, (instead of 50-60%, previously).
Better extraction efficiency allows to reduce accelerated beam intensity, providing several benefits:

- reduction of the source gas flow and then improvement of the internal beam transmission,
- reduction of loss in the machine and of the activation in the machine,
- increase of the lifetime of consumable such as cathodes and chimneys.

Table 1

| | Beam on Target | Beam on Stripper | Extract° Yield | Beam on Pop- Up | Transmiss° Yield | Source Gas Flow | Source Arc Intensity |
|---|---|---|---|---|---|---|---|
| New design | 15 µA | 17 µA | 90 % | 21 µA | 80 % | 2 cc/min | 0.1 A |
| Old design | 15 µA | 25 µA | 60 % | 35 µA | 70 % | 3 cc/min | 0.2 A |

The eight targets are located in the mid-plane all around the vacuum chamber and are partially shielded by the yoke. An operator working on any target is thus able to be at the maximum distance from other possibly activated targets.
Optional shielded doors can also be mounted in front of each target in order to reduce the radioactivity level. As an example, on one of our Cyclone 18/9 machines installed at the Herzzentrum Nordrhein-Westfalen in Bad Oeynhausen, each target is self-shielded with a steel door, 10 cm thick, reducing the radioactive dose rate by a factor 4.

### 3. Pneumatic gate valve on target.

In the case of internal target configuration (see point 2), pneumatic gate valves have been designed to be installed between the vacuum chamber and each target (implemented on Geneva and Hadassah machines). Maintenance on target, window holder and collimator can be performed without interrupting the vacuum in the cyclotron.

### 4. Pressure transducer inside the target.

The Cyclone 18/9 from Geneva is mounted with pressure transducers inside the targets, allowing the internal pressure to be measured and thus preventing window foil rupture. This is specifically helpful for the F2, C-11 and F-18 targets.

### 5. F-18 large volume target

For high F-18 production, IBA has designed a large volume target of 1.5 ml (installed on Pamplona machine). This target allows to produce more than 3 Ci of F-18 in two hours, with 18 MeV protons. More than 6 Ci of F-18 can be achieved in dual beam mode, in irradiating simultaneously two F-18 targets.

### 6. Source gas control

For an easier optimization of the beam transmission yield inside the machine, the source gas flowmeter could optionally be controlled from the control system.

### 7. The ongoing development of the software.

Software is continuously improved for better access to the main parameters and easier operation of the system. A logbook of cyclotron operation can be provided as well as a data log which records the main data of the system. These records can be easily transferred to a spreadsheet table for analysis. For example, the integrated beam current of each particle (protons or deuterons) is recorded to keep track of the lifetime of the cathodes of the ion sources. The same measurement is done for each stripper foil. These records are very useful for planning and scheduling preventive maintenance. The Programmable Logic Controller can accomodate signals coming from other equipment, such as flags from the stack monitors or area radiation monitors to be used as safety interlocks.
A new display representing vacuum level versus time is very helpful to detect a vacuum leak.

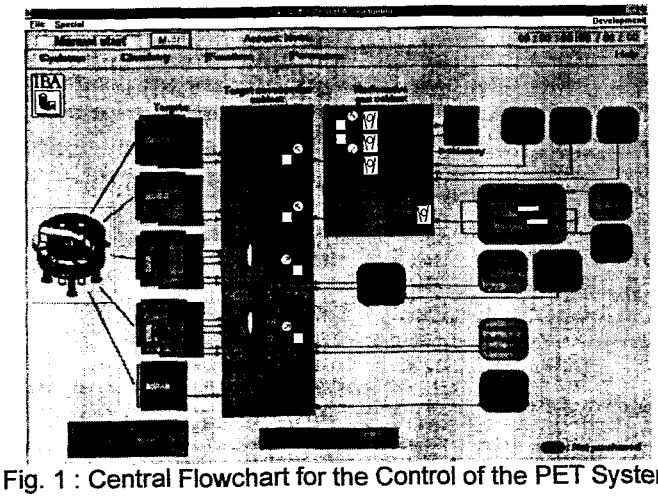

Fig. 1 : Central Flowchart for the Control of the PET System

## 8. Maintenance

For more efficient maintenance, a special effort has been made on providing quick release connections for water, electrical and gas tubing to allow an easy and rapid dismount of each part of the cyclotron sub-systems.

## 9. Customized system

An external beam transport line has been specially designed on the Cyclone 18/9 for Forschungszentrum Rossendorf, to enable it to be used for target development and education purposes. The transmission yields are higher than 50% through a collimator of 12 mm diameter. The beam spot diameter is approximately 15 mm, without hot spot. Beam current instabilities are less than 5%.

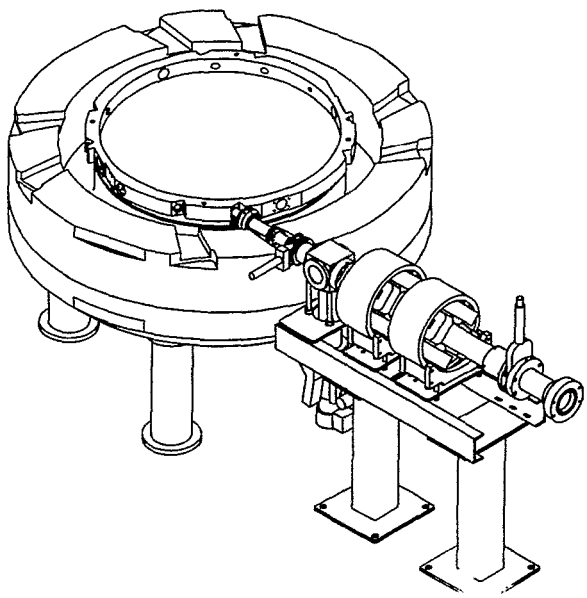

Fig. 2 : External transport beam line

## Conclusion:

The main aim of these improvements has been to *increase reliability and the radioisotopes production yields*, whilst, at the same time, reducing *the activation* in the machine and providing an *increase in the lifetime of consumable* such as source chimney and cathodes.

The table 2, hereafter, recapitulates the production yields obtained during the installation of the Cyclone 18/9 at Pamplona, the latest installed machine.

Table 2

| Isotopes | Chemical Form | Beam Current on Target | Irradiation Time | Recovered Activity |
|---|---|---|---|---|
| C-11 | $CO_2$ | 45 μA | 30 min | 4.058 mCi EOB |
| F-18 | $F^-$ | 22 μA | 120 min | 3.372 mCi EOB |
| F-18 | $F_2$ | 25 μA | 60 min | 370 mCi EOB |
| N-13 | $NH_3$ | 20 μA | 20 min | 500 mCi EOB |
| O-15 | $H_2O$ | 30 μA | 10 min | 980 mCi EOS |
| O-15 | $O_2$ | 20 μA | on line | 540 mCi/min |
| O-15 | CO | 20 μA | on line | 167 mCi/min |
| O-15 | $CO_2$ | 20 μA | on line | 544 mCi/min |

Target pressure transducers (item 4), source gas control (item 6), software modification (item 7) could easily be retrofitted on all the Cyclone 18/9 machines. Internal location of the targets (items 2 and 3) and the up grade of the RF system (item 1) i.e. to replace the dee stems in the lower yoke, would be a major retrofit requiring large modifications to the machine.

## THE IBA CUSTOMER SERVICE

The IBA Customer Service Section is part of the Technical Department, which is supervised by Mr. Jean-Louis Bol, Technical Director and Mr. Claude Dupont, Technical Department Deputy Manager.

Mrs Charline Englebert, the Administrative Assistant in the Customer Service, is the contact in the first instance for all follow up and day-to-day requests as information, quotations, orders, technical supports, urgent intervention...
She will forward the request/call to the most appropriate person/specialist.

Mr David Clark will answer all commercial matters and finalise all quotations.

Their contact telephone numbers are the following:

| | |
|---|---|
| *Mrs Charline Englebert*<br>Administrative Assistant Customer Service | 32 10 47 58 31 |
| *Mr David Clark*<br>Area Sales Manager | 32 10 47 59 52 |
| *IBA Reception Desk* | 32 10 47 58 11 |
| *IBA Fax Machine* | 32 10 47 58 10 |
| *Mrs Charline Englebert Fax Machine* | 32 10 47 59 18 |

# PET Compounds Production System - IBA Customer Reference List
## (sorted by locations)

| Customer | Address | Equipment | Contact | Telephone | Fax |
|---|---|---|---|---|---|
| **Asia & Oceania** | | | | | |
| Austin Hospital | Studley Road, Heidelberg Victoria, 3084, Australia | Cyclone 10/5 s-s + PET | Dr. H. Tochon-Danguy | 61-3-450.51.63 | 61-3-457.66.05 |
| ANSTO (Australian Nuclear Science & Technology Organization) | Lucas Heights Research Lab., New Illawarra Road, Menai, NSW 2234, Australia | Cyclone 30 + PET | Dr. C. Jamieson | 61-2-565.76.01 | 61-2-565.76.76 |
| Hadassah Hebrew University | Kiryat Hadassah, POB 12000, Jerusalem 91120, Israel | Cyclone 18/9 + PET | Prof. Y. Mahler | 972-2-77.66.30 | 972-2-43.44.34 |
| China Institute of Atomic Energy | PO Box 275(82), Beijing 102413, People's Republic of China | Cyclone 30 + FDG | Pr. Sun Zuxun | 86-1-935.70.08 | 86-1-935.71.95 |
| **Europe** | | | | | |
| Hammersmith Hospital | MRC Cyclotron Unit, Ducane Road, London W12 0HS, Great Britain | Cyclone 3 + PET | Dr. John Clark | 44-181-740.31.62 | 44-181-743.39.87 |
| Rudolf Virchow Hospital | Augustenburger Platz 1, 13353 Berlin, Germany | Cyclone 3 s-s + PET | Pr. D.L. Munz | 49-30-28.02.20.74 | 49-30-28.02.27.35 |
| Turku University | Central Hospital, Kiinamyllynkatu 4-8, 20520 Turku, Finland | Cyclone 3 + PET | Dr. H. Sipila | 358-21-61.18.49 | 358-21-31.81.91 |
| Nat. Hosp. for Neurology & Neurosurgery | The Functional Laboratory Imaging, 12 Queen Square, London WC1 N3BG, UK | Cyclone 3 + PET | Pr. Fracoviak | 44-1-740.31.66 | |
| University of Leuven (KUL) | UZ Gasthuisberg, Nucl. Geneeskunde, Herestraat 49, 3000 Leuven, Belgium | Cyclone 10/5 + PET | Pr. Mortelmans | 32-16-34.37.14 | 32-16-34.37.59 |
| University of Helsinki | Lab. of Radiochemistry, P.O. Box 55, 00014 Helsinki, Finland | Cyclone 10/5 | Pr. E. Karttunen | 358-0-191.40.133 | 358-0-191.40.121 |
| Forschungszentrum Rossendorf | Bautzner Landstrasse 128, 01474 Dresden, Germany | Cyclone 18/9 + PET | Dr. Steinbach | 49-351-260.21.70 | 49-351-260.32.32 |
| Herz- und Diabeteszentrum NRW | Georgstrasse 11, 32545 Bad Oeynhausen, Germany | Cyclone 18/9 + PET | Dr. G. Notohamiprodjo | 49-5731-97.18.65 | 49-5731-97.18.62 |
| Klinikum der Universität Ulm | Nuklearmedizin, Abteilung 3, Rober Koch Strasse 8, 89070 Ulm, Germany | Cyclone 18/9 + PET | Dr. Weller / Pr. Reske | 49-731-502.45.08 | 49-731-502.45.03 |
| Cantonal Univ. Hospital of Geneva | Rue Micheli-du-Crest 24, 1211 Geneva 14, Switzerland | Cyclone 18/9 + PET | Dr. Ch. Vachey | 41-22-372.60.22 | 41-22-372.60.20 |
| Clinica Universitaria de Navarra | Servicio de Medicina Nuclear, Avenida Pio XII, 36, 31080 Pamplona, Spain | Cyclone 18/9 + PET | Dr. J. Richter / Dr. J. Marti | 34-48-25.54.00 | 34-48-17.22.94 |
| Hôpital Erasme (ULB) | Route de Lennik 808, 1070 Brussels, Belgium | Cyclone 30 + PET | Dr. S. Lejeune | 32-2-568.31.11 | |
| University of Louvain (UCL) | CRC, Chemin du Cyclotron 2, 1348 Louvain-la-Neuve, Belgium | Cyclone 30 proto + PET | Dr. G. Ryckewaert | 32-10-47.32.37 | 32-10-47.24.31 |
| Forschungszentrum Karlsruhe | Hauptabteilung Zyklotron, Weberstrasse 5, 76133 Karlsruhe, Germany | F-18 Target - FDG | Dr. V. Bechtold | 49-7247-82.24.33 | 49-7247-82.31.56 |
| DKFZ (German Cancer Research Center) | Dept of Radiology, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany | FDG Module | Dr. G. Wolber | 49-6221-42.26.81 | 49-6621-41.13.07 |
| **North America** | | | | | |
| Biomedical Research Foundation | 5925 Line Avenue, Shreveport, Louisiana 71130, USA | Cyclone 18/9 + PET | Dr. L.F. Moore | 1-318-865.51.13 | 1-318-865.51.14 |
| Montreal Neurological Institute | McGill University, Dept of Neurology & Neurosurgery, 3801 University Street, Montreal H3A 2B4, Quebec, Canada | Cyclone 18/9 + PET | Pr. M. Diksic | 1-514-398.85.26 | 1-514-398.85.40 |
| VA-SUNY at Buffalo | 105 Parker Hall, 3435 Main Street, Buffalo, NY 14214, USA | Cyclone 30 + PET | Pr. R. Ackerhalt | 1-716-838.58.89 | 1-716-838.49.18 |
| **South America** | | | | | |
| CNEN/SP - IPEN | Travessa R, 400, Caixa Postal 11049, CEP 05422-970, Sao Paulo, Brasil | FDG Module | Dr. C. Pagano G. da Silva | 55-11-816.91.85 | 55-11-816.92.57 |

## IBA REFERENCES

### 1. EUROPE

| | | |
|---|---|---|
| Erasme Hospital (ULB) | Brussels, B | CYCLONE 30 + PET |
| Nordion Europe | Fleurus, B | CYCLONE 30<br>4 BEAM LINES |
| University of Louvain (UCL) | Louvain-la-Neuve, B | CYCLONE 30 + PET |
| CIS Bio International | Orsay, F | CYCLONE 30<br>2 SOLID TARGETS<br>BUILDING SAFETY |
| Mallinckrodt Diagnostica | Petten, NL | CYCLONE 30<br>4 BEAM LINES |
| Herz- und Diabeteszentrum NRW | Bad Oeynhausen, D | CYCLONE 18/9 + PET |
| Forschungszentrum Rossendorf | Dresden, D | CYCLONE 18/9 + PET<br>1 BEAM LINE |
| Klinikum der Universität Ulm | Ulm, D | CYCLONE 18/9 + PET |
| Cantonal University Hospital | Geneva, CH | CYCLONE 18/9 + PET |
| Clínica Universitaria de Navarra | Pamplona, E | CYCLONE 18/9 + PET |
| University of Leuven (KUL) | Leuven, B | CYCLONE 10/5 + PET |
| University of Helsinki | Helsinki, SF | CYCLONE 10/5 |
| Rudolf-Virchow Hospital | Berlin, D | CYCLONE 3 + PET |
| Turku University | Turku, SF | CYCLONE 3 + PET |
| Hammersmith Hospital | London, UK | CYCLONE 3 + PET |
| National Hospital for Neurology and Neurosurgery | London, UK | CYCLONE 3 + PET |
| D.K.F.Z.<br>(German Cancer Research Center) | Heidelberg, D | FDG MODULE |
| Forschungszentrum Karlsruhe (FZK) | Karlsruhe, D | F-18 PET Target<br>FDG MODULE |
| Studer, A.G | Däniken, CH | RHODOTRON TT200 |

| | | |
|---|---|---|
| Hospal Dasco S.p.A. | Medolla, I | RHODOTRON TT100 |
| ECI (Energy Center for Industrial Applications) | Mortsel, B | RHODOTRON TT200 |
| ENUSA | Madrid, E | RHODOTRON TT200 |

## 2. NORTH AMERICA

| | | |
|---|---|---|
| Massachusetts General. Hospital | MA, USA | PROTONTHERAPY SYST. |
| DuPont Merck Pharmaceutical | MA, USA | CYCLONE 30<br>3 BEAM LINES |
| Mallinckrodt Medical | MO, USA | CYCLONE 30<br>4 BEAM LINES |
| Medi-Physics Inc. | NJ, USA | CYCLONE 30 |
| VA - SUNY at Buffalo | NY, USA | CYCLONE 30 + PET |
| Biomedical Research Foundation | Shreveport, LA, USA | CYCLONE 18/9 + PET |
| McGill University, Neurological Inst. | Montreal, Canada | CYCLONE 18/9 + PET |
| Theragenics Corporation | GA, USA | CYCLONE $18^+$ (#1)<br>HIGH INTENSITY TARGET |
| Theragenics Corporation | GA, USA | CYCLONE $18^+$ (#2)<br>HIGH INTENSITY TARGET |
| Theragenics Corporation | GA, USA | CYCLONE $18^+$ (#3)<br>HIGH INTENSITY TARGET |
| *Theragenics Corporation* | GA, USA | CYCLONE $18^+$ (#4)<br>HIGH INTENSITY TARGET |

## 3. SOUTH AMERICA

| | | |
|---|---|---|
| IPEN (Instituto de Pesquisas Energéticas e Nucleares) | Sao Paulo, Brazil | F-18 PET Target<br>FDG MODULE |

## 4. ASIA - OCEANIA - MIDDLE EAST

| | | |
|---|---|---|
| Shanghai Inst. of Nuclear Research | Shanghai, China | CYCLONE 30<br>2 BEAM LINES<br>2 SOLID TARGETS |
| China Institute of Atomic Energy | Pekin, China | CYCLONE 30 + FDG |
| Daiichi Radioisotope Labs | Chiba, Japan | CYCLONE 30<br>4 BEAM LINES<br>2 SOLID TARGETS |
| Nihon Medi-Physics | Hyogo, Japan | CYCLONE 30 (#1)<br>4 BEAM LINES |
| Nihon Medi-Physics | Hyogo, Japan | CYCLONE 30 (#2)<br>4 BEAM LINES |
| Atomic Energy Organization | Tehran, Iran | CYCLONE 30 p,d<br>2 BEAM LINES<br>1 SOLID TARGET<br>CHEMISTRY GA, TL<br>LABOR. EQUIPMENT |
| Atomic Energy Organization | Tehran, Iran | RHODOTRON TT200 |
| Hadassah Medical Centers | Jerusalem, Israel | CYCLONE 18/9 + PET |
| ANSTO<br>(Australian National Science &<br>Technology Organization) | Sydney, Australia | CYCLONE 30 + PET<br>1 BEAM LINE<br>1 SOLID TARGET |
| Austin Hospital | Melbourne, Australia | CYCLONE 10/5 + PET |
| Badan Tenaga Atom Nasional | Jakarta, Indonesia | Cyclotron Conversion |

# THE PET/CYCLOTRON CENTER OF THE HUMAN BIOLOGY RESEARCH CENTER (HBRC) AT HADASSAH HEBREW UNIVERSITY HOSPITAL (JERUSALEM, ISRAEL)

ROLAND CHISIN, MD, YONA MAHLER, Ph.D., NAHUM LIFSHITZ, Eng.

**A PET/Cyclotron Center** (as part of the HBRC) is erected on the Ein Kerem campus of Hadassah Hebrew University Hospital in Jerusalem (Israel). The current PET camera is a Posicam HZL imager from Positron Corporation (Houston, Texas) and will be exchanged for a "G.E." Advance system in spring of next year (1997). This center is operated by the Department of Medical Biophysics and Nuclear Medicine and the Department of Medical Engineering and Instrumentation Division. This PET Laboratory is devoted to research, including clinical research. Up to the end of August 1996, 280 PET heart scans have been performed using Rubidium generators imported from the U.S. The cyclotron should be operational in February 1997 and FDG-PET scans done in a first stage.

**The PET suite** located in Nuclear Medicine is composed of 2 rooms for PET imagers, a hot laboratory used in particular for blood sample radioactivity counting, an ancillary cold laboratory and an evaluation room with workstations networked with the PET camera and the SPECT machines of the Department of Nuclear Medicine.

**The Cyclotron** is housed in a three-level building located in an excavation site. One level is occupied by the cyclotron, the hot and cold radiochemistry laboratories, one level below contains mainly the various pipes and one level above houses the air conditioning system.

**The targets** which will be used are: F-18, C-11, N-13, O-15 and 18-F-2 targets.

**The ordered modules** comprise an "IBA" FDG automated system and a [11C]-methylation "Nuclear Interface" system as well as other IBA modules housed in 6 "Comecer" cabinets. In addition, there will be two big hot cells for research works.

We have hired the services of the Rotem Company (Nahal Soreq, Israel) which has designed and sold us a **safety network of detectors** placed along the air conditioning system, drainage routes and all over the cyclotron area.

Director of PET/Cyclotron Center:
Roland Chisin, MD
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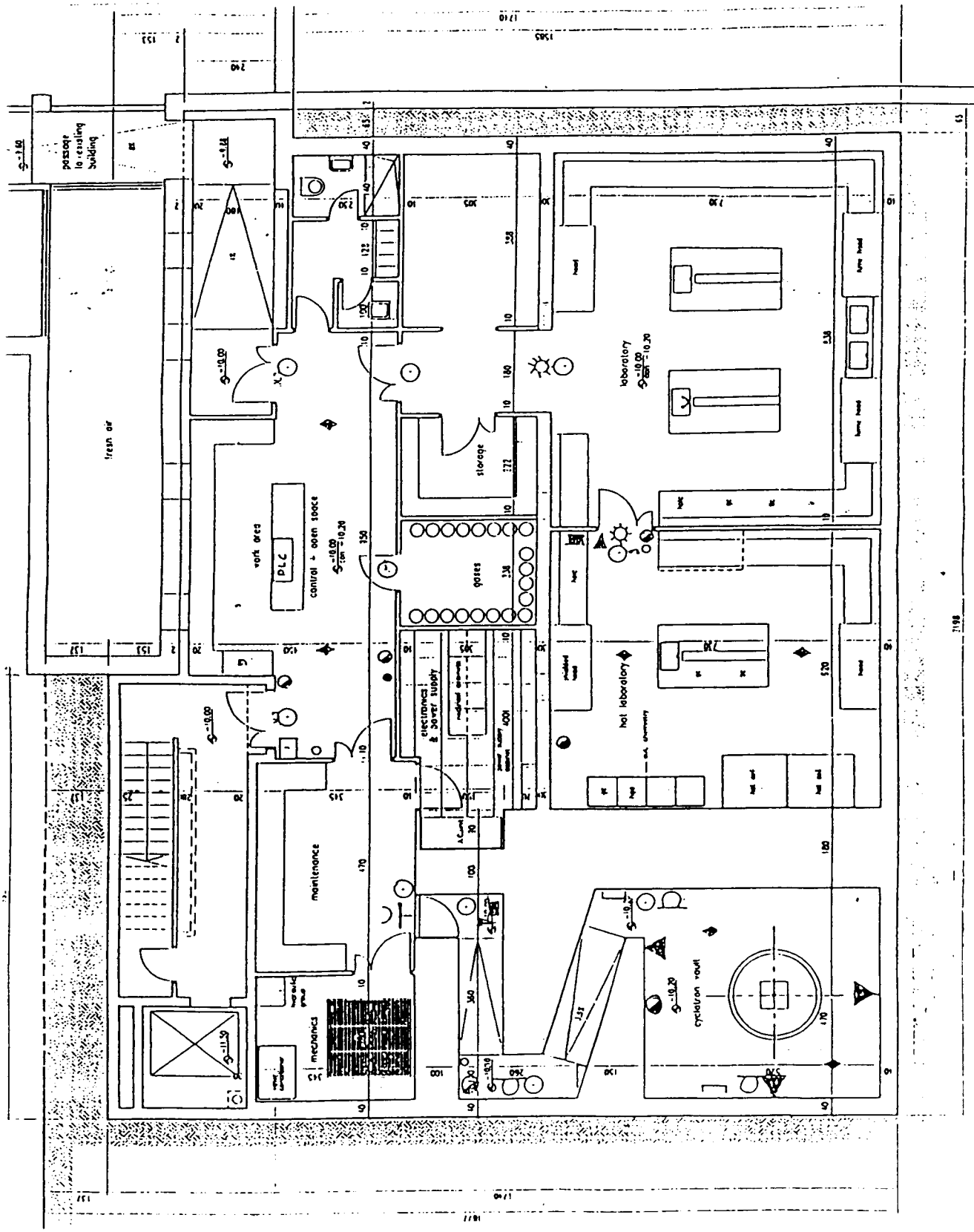
fax: 972-2-6421203

Cyclotron Engineer:
Nahum Lifshits
Tel: 972-2-6777058

Radiochemist:
Dr. Eyal Mishani (see R. Chisin)


passage to existing building
fresh air
work area
PLC
control + open space
storage
gases
laboratory
hot laboratory
electrical & power supply
maintenance
mechanics
cyclotron vault

# The CYCLONE 18/9 at MNI

Dean Jolly

## Introduction

The radiochemistry - cyclotron unit is a "service provider" developing and producing tracers, mainly on a collaborative basis, for the scientists at MNI.

At the present time, the following tracers are available :

$^{15}O$ - gases
$^{15}O\ H_2O$

$^{11}C$ - alphamethyl tryptophan
$^{11}C$ - Benztropine
$^{11}C$ - Deprenyl
$^{11}C$ - Flumazenyl
$^{11}C$ - PK 11195
$^{11}C$ - Raclopride
$^{11}C$ - SCH 23390

$^{18}F$ - FDG
$^{18}F$ - FDOPA
$^{18}F$- 3 Omethyl FDOPA

## Layout of the facility

The cyclotron arrived in Montreal in August of 1992 and after many months of work it became operational.

It was installed in a pre-existing setup comprising of a vault, to house the cyclotron, one hot lab, one cold lab, a power supply room and a control room.

The facility is undergoing renovations to increase the work space by building two new offices, a larger chemical stock room and two new labs.

## Description of the cyclotron

The CYCLONE 18/9 at MNI was one of the first of its kind built.
This means that the DEES are suspended with pillars from the top yoke and the ion sources are fully adjustable from outside the vacuum chamber.

Five of the eight exits are being used , three for $H^+$ and two for $D^+$.

**Targetry**

Because of the wide scope of interests at MNI there are targets to produce all the common PET isotopes.

table 1 : Cyclotron targets

| EXIT # | TARGET | MANUFACTURER |
|---|---|---|
| 1 | $^{18}F$-$F_2$ ( $^{18}O$- $O_2$ gas ) | CTI |
| 2 | $^{18}F$-$F_2$ ( $F_2$ / Ne ) | IBA |
| 3 | $^{18}F$- $F^-$ ( $^{18}O$ - $H_2O$ ) | IBA |
| 4 | not used | |
| 5 | not used | |
| 6 | $^{15}O$ gases | IBA |
| 7 | not used | |
| 8 | $^{11}C$ gases | IBA |

Depending on the study and isotope, varying beam intensities are used. They range from 2 to 12 uA for $D^-$ and 10 to 20 uA for $H^-$.

table 2 : Isotope production

| Isotope | Mode | Beam uA | Bombardment time min | Yield mCi |
|---|---|---|---|---|
| $^{15}O$- $H_2O$ | batch | 3 | 10 | 55 - 60 |
| $^{11}C$ -$CO_2$ | batch | 20 | 60 | 2000 |
| $^{18}F$- $F_2$ ( $F_2$/Ne ) | batch | 12 | 60 | 150 |
| $^{18}$ F- $F^-$ | batch | 14 | 60 | 150 |

Cyclotron Operation and Maintenance

The cyclotron operates reasonably well, with a heavy demand ( three days out of six; eight to twelve hours/ day ) for $^{15}O$ - $H_2O$.

Because of this, the $D^-$ source requires maintenance every six to eight weeks ( new cathodes every second maintenance and two to three chimneys a year ).
On the other hand, the $H^-$ source is only cleaned every six months.

The other major problem is that after using a silver target 12 to 15 times, it starts releasing silver and thus causes poor yields of FDG due to metal poisoning of the kryptofix potassium complex.

table 3 : Typical Operating parameters

| Parameter | Isotope | | | |
|---|---|---|---|---|
| | $^{18}F$-$F_2$ | $^{18}F$-$F^-$ | $^{15}O$ | $^{11}C$ |
| Base Vacuum | 5.9 - 7 | 3.6 - 7 | 4.2 - 7 | 3.7 - 7 |
| I.S. gas on | 9.3 - 6 | 3.8 - 6 | 6.3 - 6 | 3.8 - 6 |
| Port | 2 | 3 | 6 | 8 |
| Particle | $D^-$ | $H^-$ | $D^-$ | $D^-$ |
| Magnet voltage | 109.3 | 120 | 113.5 | 107.4 |
| current | 178.5 | 194.6 | 178.1 | 194.1 |
| RF Voltage | 34.2 | 30.5 | 29.2 | 32.2 |
| incident power | 7300 | 6600 | 5800 | 7000 |
| refelcted power | 135 | 90 | 130 | 130 |
| Ion Source Voltage | 240 | 570 | 400 | 600 |
| Current | 0.44 | 0.17 | 0.20 | 0.15 |
| Stripper position | -3664 | -4392 | -9512 | -8792 |
| Beam Currents | | | | |
| - Stripper | 20.2 | 39.8 | 9.4 | 32.2 |
| - Collimator | 10.9 | 25.6 | 5.1 | 9.6 |
| - Target | 11.3 | 13.8 | 4.6 | 22.7 |
| -% Tgt/Str | 56 | 35 | 49 | 71 |

Chemistry Modules

There are three commercially available chemistry modules on site and one designed and built at MNI.

A $^{11}C$ - $CH_3I$ black box from Scanditronix producing routinely over 1 Ci of $CH_3I$, and from CTI two CPCUs, one for FDG ( 50 % yield ) and one for FDOPA ( still testing ).

The module designed and built at MNI is a simple module utilizing a low cost robot that does all the $^{11}C$ syntheses. It has undergone several months of testing, without a single downtime since its construction in June 1996.

At present it is used to make , on a routine basis, Benztropine,Deprenyl, PK 11195 and SCH 23390.

**Address**

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Montreal Neurological Institute
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Canada
H3 2B4

**Telephone**

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fax : 514 398 - 8195

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Cyclotron operator : Edward Errington

Chemist / Cyclotron operator : Dean Jolly
EMail - DEANJ@BIC.MNI.MCGILL.CA

Chemist : Donald Porter
EMail - Don@BIC.MNI.MCGILL.CA

Research Associate : Dr Shadrek Mzengeza
EMail - SHADRECK@BIC.MNI.MCGILL.CA

# PET-CUN CENTER
# University Hospital of Navarra School of Medicine
# Pamplona. Spain

JM Martí-Climent, I Peñuelas, JA Richter

## 1. Aims of the institute

The University Clinic is a General Hospital with interest in the clinical and research applications of PET: neurology, cardiology and oncology.
Only ten months were elapsed from the signature of the contract until the end of the acceptance tests for the cyclotron. The final approval of the installation from the Nuclear Security Council was received in July 1996.

## 2. PET center

The PET CUN center is constituted by a Cyclone 18/9 cyclotron, a high resolution PET scanner (ECAT EXACT HR+, Siemens) and a radiochemistry laboratory. The layout of the center is shown in figure 1. The total surface of the PET facility is around 400 $m^2$.

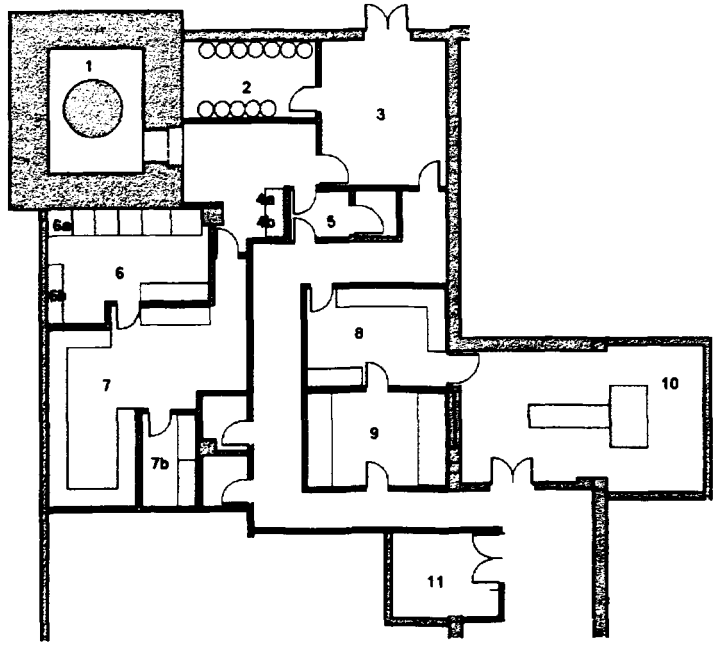


**Figure 1:** General representation of the PET CUN center facilities. The numbers indicate the following areas: 1) Cyclotron vault. 2) Technical room (gas supply cabinets, cooling system...) 3) Technical room (power supply, electronics...) 4) Control room (ventilation system and cyclotron) 5) Decontamination area. 6) Hot laboratory —6a. hot cells for automatic synthesis modules, 6b. hot cells for dose preparation and shielded laminar flow hood—. 7) Quality control laboratory. 8) Blood laboratory. 9) PET scanner control room. 10) PET scanner room. 11) Patient preparation area.

### 2.1 Targetry

The cyclotron is equipped with five targets, for the production of, $^{11}C$, $^{13}N$, $^{15}O$, $^{18}F_2$ and $^{18}F^-$ (large volume). The location of the targets in the cyclotron is shown in table 1. Result of the acceptance tests are shown in table 2.

**Table 1:** Targetry

| target | port # |
|---|---|
| $^{18}F_2$ | 1 |
| $^{18}F^-$ | 2 |
| $^{11}C$ | 3 |
| $^{15}O$ | 5 |
| $^{13}N$ | 6 |

**Table 2:** Cyclotron production: Acceptance test results

| target | Time (min) | μA | GBq | mCi |
|---|---|---|---|---|
| $^{18}F_2$ | 60 | 22 | 10 | 270 |
| $^{18}F^-$ | 120 | 22 | 125 | 3372 |
| $^{11}CO_2$ | 30 | 35 | 115 | 3126 |
| $^{15}O_2$ | – | 20 | 20/min | 540/min |
| $H_2{}^{15}O_2$ | 10 | 30 | 37 | 980 |
| $C^{15}O_2$ | – | 20 | 20/min | 544/min |
| $C^{15}O$ | – | 20 | 6 | 167/min |
| $^{13}NH_4$ | 20 | 20 | 19 | 502 |

**2.2 Chemistry modules**

The PET CUN center facility is equipped with a very complete radiochemistry (table 3).

**Table 3:** Radiochemistry modules

| Module | Supplier | Status |
|---|---|---|
| FDG-1 | Nuclear Interface | Operating daily |
| FDG-2 with water recovery unit | IBA | Installed |
| H2O module | IBA | Operating |
| Methylation unit | Nuclear Interface | Installed |
| Nucleophilic and electrophilic subsitution unit | Nuclear Interface | Not installed yet |
| Gas module | IBA | Installed |

Only the FDG module from Nuclear Interface is fully operative, and more than 50 FDG synthesis have been carried out with it, with very good yields. The FDG module from IBA has only been used three times until now.

The amonia stand and the water module have been used several times, mainly for experiments and not for patients, with quite good production rates (table 4). Nonetheless, five $H_2{}^{15}O$ studies have already been carried out.

**Table 4:** Saturation yields for the different compounds

| Compound | GBq/μA | mCi/μA |
|---|---|---|
| $^{18}F^-$ | 8.9 | 240 |
| $^{13}NH_4$ | 1.3 | 36 |
| $H_2{}^{15}O$ | 1 | 28 |

### 2.3 Time of operation

The cyclotron is operated daily, from monday to friday, an average time of 1 hour per day for the production of $^{18}F^-$ in the morning and some days it is also operated for the production of $^{15}O_2$, $^{13}NH_3$ or $^{11}CO_2$. The $^{18}F_2$ target has only been used in the acceptance tests. The operating conditions for each one of the targets, along with the obtained yields are summarised in table 5.

**Table 5:** Operational conditions of the cyclotron

| Target/compound | Time of irradiation (min) | Current (μA) | Production GBq (mCi) |
|---|---|---|---|
| $^{18}F^-$ | 60 | 17 | 48.1 (1300) |
| $^{13}NH_4$ | 10 | 10 | 6.7 (180) |
| $H_2{}^{15}O$ | 10 | 10 | 10 (270) |

### 2.4 Safety and security measures

Several safety interlocks have been installed for the safeguarded operation of the cyclotron and to avoid any kind of accident when transferring the activity from the target to the hot cells.

The signals arriving to the cyclotron are the following:

1. Emergency stop signals coming from the hot lab, inside the vault, the technical rooms and the control room
2. The irradiation is allowed only if the following conditions are satisfied: the cyclotron vault door is closed, there is no emergency signal in the cyclotron vault door, the ventilation system is OK, and there is no fire signal
3. The radiation levels inside the vault are below 200 μSv/h
4. The hot cells are closed. This is used when transferring materials from the cyclotron.
5. Unable to send gases to the PET scanner room unless it is authorised from the PET area
6. Unable to send target content to synthesis modules unless a ready signal comes from the module (only used with the Nuclear Interface modules)

The output signals from the cyclotron are:

1. The magnetic field is on. A light is turned on in the cyclotron control zone
2. The beam is on. Light signals are turned on in the cyclotron vault room, hot laboratory, and technical rooms
3. Cyclotron vault door opening is not allowed:
    - During irradiation
    - During 5 minutes after the end of the irradiation
    - if the radiation inside the vault is greater than 200 μSv/h

The cyclotron vault door has an emergency opening, acoustic and light signals when moving, and gets a signal from the cyclotron not allowing it to be opened.

Different lead containers are used to reduce the radiation levels when handling radioactive materials.

The radiation detectors used in the PET center are:

- Gamma area monitor in the cyclotron vault, with the display in the control zone
- Neutron area monitor outside the cyclotron vault
- Gamma area monitor in the hot laboratory
- Portable survey gamma meter (ion chamber)
- Portable contamination detector (pancake Geiger counter)
- Hands, feet and clothe contamination detector
- Personal dosimeters: Whole body and ring thermoluminescence detectors, and direct reading dosimeters with acoustic alarm

### 2.5 Environmental care

A special ventilation system for the cyclotron vault, hot laboratory, hot cells and PET scanner room is used (figure 2):

- It provides 10 air renovations per hour in each zone and 10 PA of underpressure.
- A gamma detector (1"x1" NaI(Tl)) is placed in each smokestack in order to detect any release from its zone. If the release is over an authorised limit, it turns on a dilution system (from 2200 to 22000 $m^3/h$).
- Another detector (2"x2" NaI(Tl)) is in the general smokestack to detect if the final concentration (after dilution) is below the operational limit (2.5 μSv/h). When the release is not allowed, it closes the floodgate of the contaminated zone.
- Display of each detector is placed in the corresponding area in order to show to the people working there the radiation levels of their area. The radiation levels are also controlled through a personal computer, where it is possible to follow the reading of each detector. An alarm signal is send to the ventilation system when the release is higher than the authorised levels.

A thermoluminescence detector is installed in the general smokestack to integrate the dose released per month.

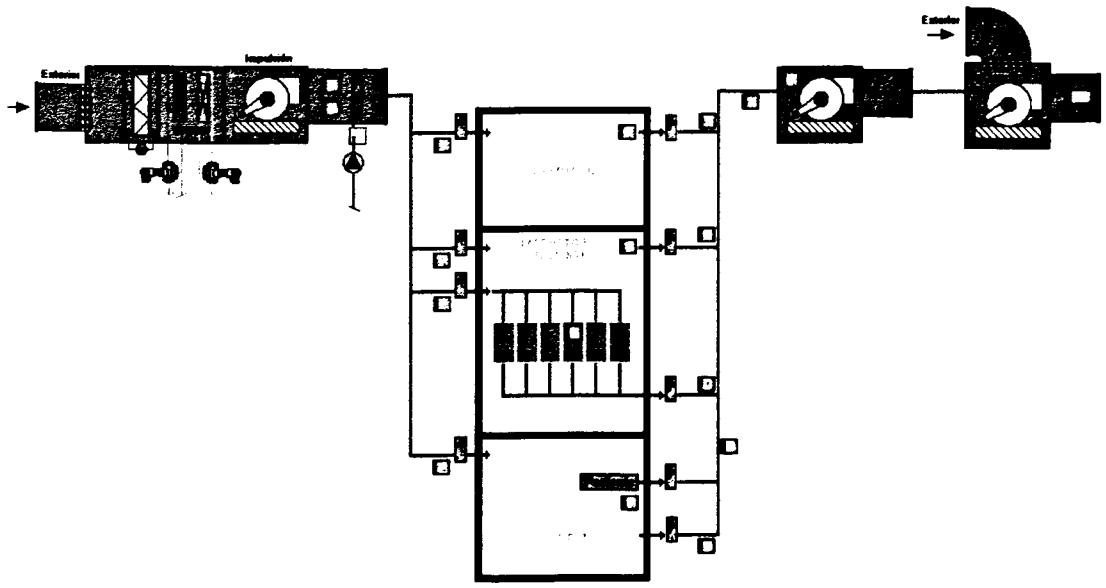

**Figure 2:** Ventilation system. D: 1"x1"NaI(Tl) detector, D2: 2"x2"NaI(Tl) detector. P: Input and output pressure reading of each zone.

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# THE ROSSENDORF PET CYCLOTRON "CYCLONE 18/9" FACILITY

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## 1. Introduction

In the Rossendorf PET Center cooperate the Research Center Rossendorf Inc. and Dresden's University Hospital. It`s scientific programme is dedicated to fundamental radiochemical, radiopharmaceutical, biomedical research and clinical application.
Our PET Center is equiped with the PET cyclotron "CYCLONE 18/9" inclusive an external beam transport line, radiochemical laboratories for research purposes and production of radiopharmaceuticals according to GMP rules (Good Manufacturing Practice) and the Siemens PET camera ECAT EXACT HR (+).
On grounds of local conditions the existing U-120 cyclotron building is also used for the CYCLONE 18/9. The 500 m distance to the radiopharmaceutical laboratories is bridged by our own developed radionuclide transport system.
Present status: All acceptance tests of the cyclotron and chemistry modules were fulfilled sucessfully at the end of February 1996 and the final check of the cyclotron facility by the TÜV organisation (TÜV = Association for Technical Inspection) were also done in that month. We anticipate the granting of the licence for routine operation of our PET cyclotron at the beginning of October 1996.

## 2. Building

The layout of the rooms is shown in Fig. 1. All of the rooms are located at cellar level. Wall thickness of the vault: 1.40 m - outer walls, 1.90 m - sealing, 2.35 m - wall to control room. The hot lab (R001d) with box 0 (= hot cell) is the cyclotron-end terminal of the pneumatic post system between cyclotron and radiochemistry building.
During operation of the cyclotron the vault is closed with 2 doors. The door to room R001b is a sliding door filled with interlaced polyethylene bricks (thickness 16 cm). The rear is covered with cadmium sheet metal. The door will be sealed airtight by an inflatable rubber tube which has to be filled with compressed air (low pressure inside the vault: - 50 Pa). The door to room R001c is filled with polyethylene plates (thickness 3 cm) and the rear is covered with 0.6 cm lead[1,2].
There are three ventilation systems for ventilation of active/nonactive rooms and hot cell 0 and additional one for venting the ($N_2$ + 0.5 % $F_2$) gas valve and two systems for removing flue gases in case of fire.
All necessary gas bottles are placed inside closed racks outside the building. Compressed air (max. 6 bar) is available in each room.

## 3. Cyclotron, Targetry, Beam Transport Line and Chemistry

The cyclotron/chemistry modules can be controlled both with terminal 1 (cyclotron building) and terminal 2 (radiochemistry building). Each of the terminals can be either the master or the slave. Only the master terminal has the control of the cyclotron but all information is given on both screens. There is a special procedure for handing the control to the other terminal.
At our cyclotron five IBA targets and a beam transport line (BTL) are installed. We use the large volume target (1.5 ml) for [$^{18}$F]F$^-$. The results of beam and yield acceptance tests are summarized in Table 1.
The Rossendorf chemistry modules ([$^{18}$F]6-Fluoro-DOPA, [$^{11}$C]Methyliodide), the Nuclear Interface chemistry module ([$^{18}$F]FDG) and the IBA chemistry modules ([$^{15}$O]$H_2O$, [$^{15}$O]/[$^{11}$C] gas processing, [$^{11}$C]HCN) are placed inside the hot cells 1 - 3 of the radiochemistry building (Fig. 2).

The 2 m long BTL at exit 2 is a special IBA development for Rossendorf. Target development and use for PET in Rossendorf began in 1983. A vertical target changing device for 8 targets was built in 1990 and is used now at the U-120 cyclotron for [$^{11}$C]$CO_2$, [$^{18}$F]$F_2$, [$^{18}$F]F$^-$ and [$^{15}$O]$O_2$ production and for solid targets. In 1997 we want to connect BTL and the vertical target changing device (then equiped with PLC control too). BTL is necessary for improvement of the reliability and availability of the targetry, future target development, production of other radionuclides and for training of technicians and radiochemists. To accept the BTL parameters only beam tests were carried out but with both particle types (Table 1).

Table 1: Results of beam and chemistry tests

| Exit | 1 | 2 / BTL | | 3 | 4 | 5 | 7 |
|---|---|---|---|---|---|---|---|
| Target for | $^{11}C$ | FZR targets | | $[^{18}F]F_2$ | $[^{13}N]NH_3$ | $[^{18}F]F^-$ | $^{15}O$ |
| Particle | $H^-$ | $H^-$ | $D^-$ | $D^-$ | $H^-$ | $H^-$ | $D^-$ |
| *Beam test* | | | | | | | |
| Beam on - Stripper / µA | 80 | 37 | 29 | 40 | 83 | 81 | 42 |
| - Collimator / µA | 25 | 12 | 13 | 13 | 63 | 35 | 20 |
| - Target / µA | 55 | 25 | 15 | 27 | 20 | 46 | 23 |
| *Chemistry test* | | | | | | | |
| Activity at EOB / GBq | > 74 | ---- | ---- | > 11 | > 15 | > 74 | > 9 |
| - irradiation time / min | 30 | | | 120 | 20 | 120 | 10 |
| - beam on target / µA | 34 | | | 20 | 20 | 23 | 20 |

The measured instabilities of all beam currents on targets during irradiation times were less than ± 5 % and fulfilled our requirements of beam stability on target for production of radionuclides. The diameters of the beam spot on a quartz at the end of BTL both for protons and deuterons were approximatly 15 mm and confirmed the IBA calculations. If required, it is possible to reach higher beam currents at exit 2. Dual beams are possible at the exits 1/5 and 3/7. The results are given in Table 2.

Table 2: Results of dual beams

| Particle | $H^-$ | | $D^-$ | |
|---|---|---|---|---|
| Dual beam at exit | 1 | 5 | 3 | 7 |
| Beam on - Stripper / µA | 32.8 | 39.2 | 10.8 | 22.3 |
| - Collimator / µA | 14.5 | 21.0 | 1.0 | 11.7 |
| - Target / µA | 18.3 | 18.2 | 9.8 | 10.6 |

Our radiochemistry/radiopharmaceutical laboratories are equiped with nine hot cells (FZR, Waelischmiller), several fume hoods, HPLC, GC, MC, TLC (BAS 2000), γ-spectrometry, pH-meter and a LAL test for reseach purposes and production of radiopharmaceuticals including the quality control.

## 4. Radionuclide Transport System (RATS)

The 500 m long RATS (Fig. 2) was designed to transport small volumes of the irradiated liquids $[^{18}O]H_2O/[^{18}F]F^-$ and $H_2O/[^{13}N]NH_3$ with a pneumatic post system and the radioactive gases within copper capillaries (ID: 1.5 mm) from the cyclotron to the radiochemistry laboratories. In the final layout of activity distribution the radiopharmaceutical laboratories of the nuclear medicine building will also be connected to the existing system (Fig. 3). The pneumatic post box system consists of two polyethylene tubes (ID: 33 mm, wall thickness: 8.4 mm). The pneumatic post box (length: 110 mm) contains a vial. We use the same type of polyethylene tubes as second containment to protect the copper capillaries. Outside the cyclotron and radiochemistry building all polyethylene tubes lay 80 cm below ground level.
The loading time of a pneumatic post box is approximatly 2 minutes and the transfer time for the 500 m 1:30 minutes (with 4 - 5 bar of compressed air). In more than 300 runs of pneumatic post boxes the reliability of RATS was demonstrated. For $^{11}C$ transport (EOB ==> BOS) we reached 4:30 minutes with 26 bar of push gas.
RATS is also controlled by 2 terminals using the same master-slave principle as in the control of the cyclotron. Both control systems are coupled. Several interlock signals prevent the unloading process of a target if cyclotron or RATS is not ready for unloading[3].

## 5. Safety Aspects and Radiation Protection

Cyclotron: For personnel safety we installed an external interlock system that switches off or disables the beam, if one of the four components is not in OK status:

- emergency stop buttons in all rooms
- ST1/ST2 door security circuit (Fig.1)
- sensors of the fire-alarm system in all rooms
- pressure conditions in the vault: (-50 ± 20) Pa.

The radiation protection areas of the PET cyclotron are:

| | without beam | with beam |
|---|---|---|
| controlled area: | R001b, R001c, R001d | R001d |
| prohibited area: | none | R001b, R001c. |

An exhaust air emission measuring facility (Berthold) was installed for both the new PET cyclotron and the U-120 cyclotron to fulfil the demands of our authority. It contains of four main parts: a gas monitor for continuous monitoring of radioactive gases with short half-life, a continuous aerosol collector with a constant flow of air, a transportable gas collector unit and an electronic system with switches for thresholds and a lot of possibilities for presentation of the measured values. A stationary dose rate meter (Berthold) with a GM tube and an ionisation chamber is installed inside the vault. The measured values are displayd in the control room, so that we have the knowledge of the radiation level inside the vault at any time. Both systems are not involved into the interlock system.

RATS: Additional to the interlock system the loading unit of the pneumatic post system is equiped with a LASER sensor to detect the right postion of the vial. The running time of the pneumatic post box is monitored too.
Estimations of the possible exposure to radiation during transport of activity gave an additional dose/year of < 1µSv (= 0.04 % of natural dose) for normal operation and 74 µSv for worst case operation (pneumatic post box with 94 GBq of $[^{18}F]F^-$ stay inside the transportation tube).

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2. Preusche, St. et al., The New Cyclotron Of The Rossendorf PET Center, Poster at the 14. Int. Conf. On Cyclotrons And Their Applications, Cape Town, South Africa, 08.-13.10.1995
3. Preusche, St. et al., The Radionuclide Transport System of the Rossendorf PET Center, Poster at the XXX European Cyclotron Progress Meeting, Catania, Italy, 04.- 06.09.1996


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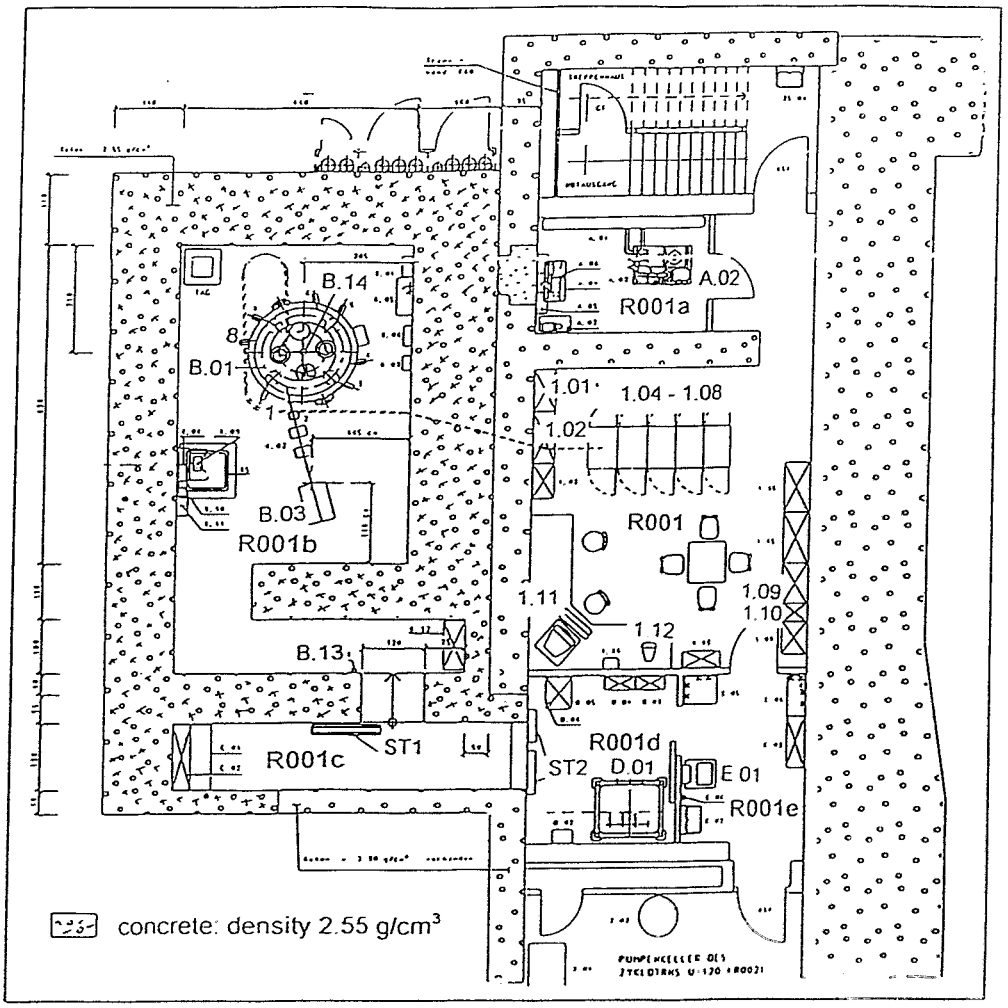


Figure 1: Layout of the cyclotron facility

**R001a - Room for Technical Equipment**

| | |
|---|---|
| A.02 | heat exchanger |

**R001b - Cyclotron Vault**

| | |
|---|---|
| B.01 | CYCLONE 18/9 |
| 1 - 8 | ports for targets |
| B.03 | target changing device |
| B.13 | GM tube |
| B.14 | ionisation chamber |

**R001c - Entry Room**

| | |
|---|---|
| ST1 | radiation protection door |

**R001d - Hot Lab**

| | |
|---|---|
| ST2 | radiation protection door |
| D.01 | Box 0 (= hot cell): cyclotron`s terminal of the radionuclide transport system |

**R001e - Personnel Air Lock**

| | |
|---|---|
| E.01 | contamination monitor |

**R001 - Control Room**

| | |
|---|---|
| 1.01/1.02 | power distribution cabinets |
| 1.04 - 1.08 | power supply racks/PLC |
| 1.09/1.10 | emergency power supply |
| 1.11 | PC for control |
| 1.12 | monitor of the exhaust air measurement device |

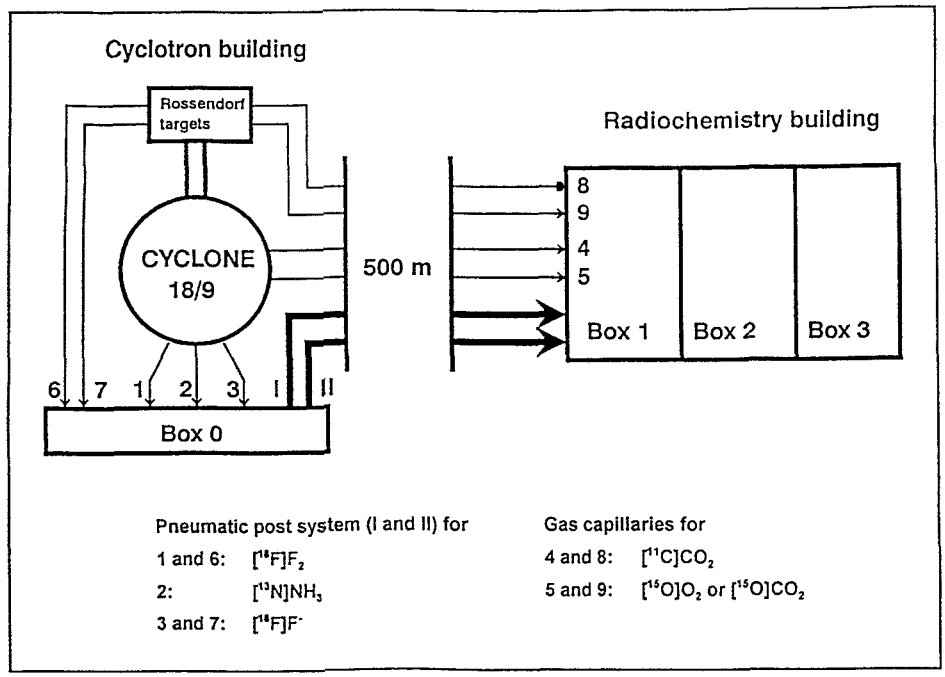


Figure 2: General layout of the radionuclide transport system

The hot cells 0 and 1contain the loading/unloading units of the pneumatic post system and the distribution units for transfer of the radionuclides into the hot cells 2 - 5 and 11 -14 (final stage)

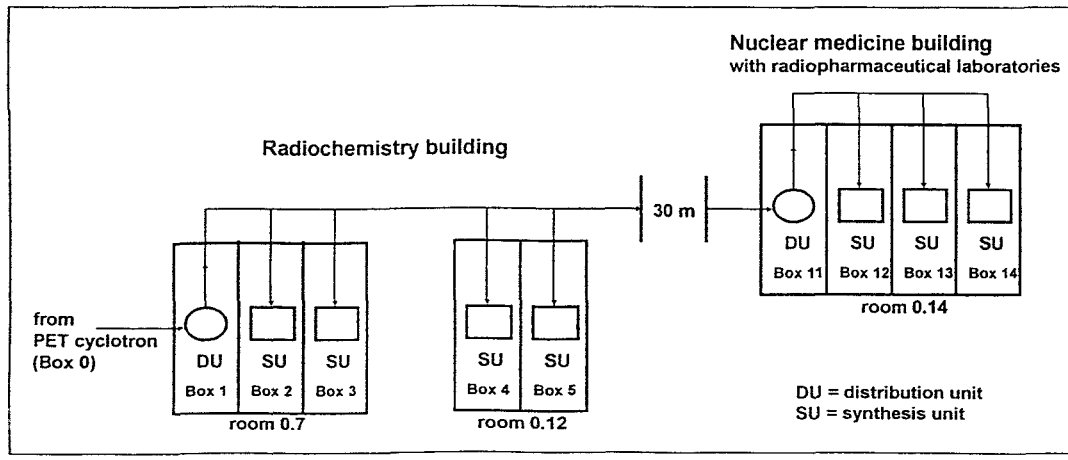


Figure 3: Final layout of radionuclide distribution (under construction)

| | |
|---|---|
| hot cells 1 - 3: | special radiotracer |
| hot cells 4, 5: | development of radiotracers with high activity level |
| hot cells 11 - 14: | routine production of radiopharmaceuticals |

## BIOMEDICAL RESEARCH FOUNDATION
## PET IMAGING CENTER

JOHN SUNDERLAND, JERRY BIDA, MIKE FULCHER, SUSAN GOEBEL

**Description:**
The Biomedical Research Institute is a business oriented research facility, combining traditional academic research and private-sector initiatives for the development and commercialization of new discoveries. The Biomedical Research Foundation opened its first research Facility, the Biomedical Research Institute (BRI), in February of 1994. The BRI is a 10 story, 160,000 square foot facility with 56 laboratories. The Louisiana State University School of Medicine in Shreveport occupies 48 of these laboratories to conduct biomedical research. These floors contain core research laboratories for monoclonal antibody production, oligonucleotide and peptide synthesis, gene cloning, DNA sequencing, high performance liquid chromatography, tissue culture, magnetic resonance spectroscopy, and electron microscopy. The ninth floor houses the animal care facilities. The anchor technology for the BRI is Positron Emission Tomography. Located on the bottom floor of the BRI, the PET Imaging Center has the capacity to operate two PET scanners and supply positron emitting isotopes for its own use, and that of other imaging sites in the region. The cyclotron is an IBA 18/9 dual particle machine, while the existing PET scanner is a GE Advance.

The BRF recently received a grant from the United States Department of Energy to establish The Center for Biomedical Technology Innovation (CBTI). It will focus on the development of instrumentation for minimally invasive procedures, including advanced imaging technologies for individual self-care, telemedicine and medical robotics.

Also, BRF scientists are involved in a Department of Energy grant with Fermi National Laboratory, University of Washington (Seattle) and Science Application International Corporation to develop a more cost-effective way to produce radioisotopes for use in Positron Emission Tomography. The effort centers around the use of a Helium-3 radio-frequency quadrupole (RFQ) accelerator presently housed at Fermi, soon to be transferred to the BRI.

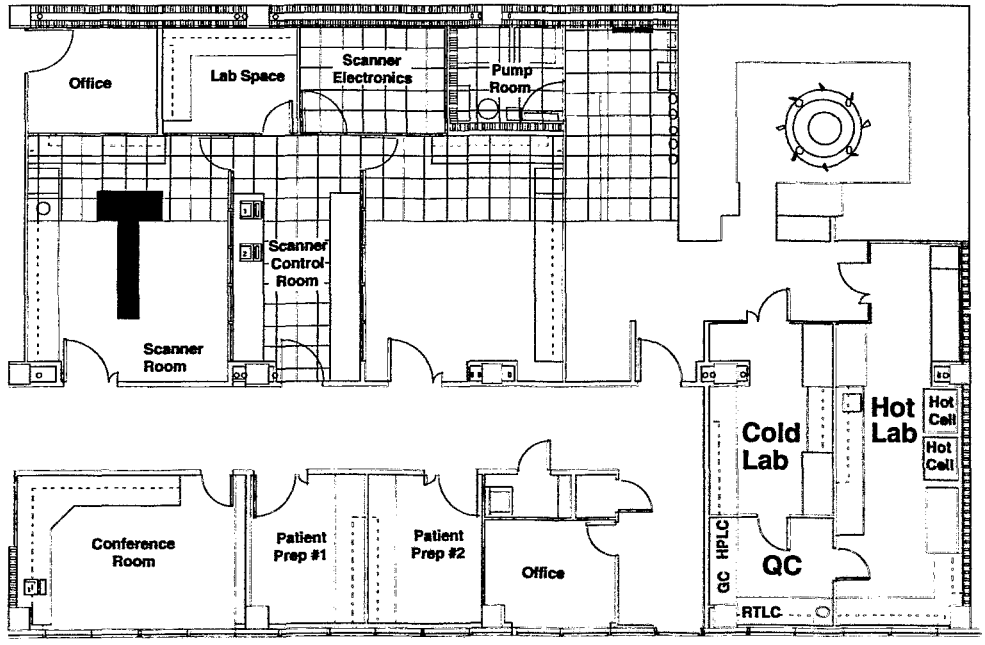


Figure 1.

The PET Imaging Center has been imaging patients for less than a year. A schematic of the ground floor facility can be seen in figure 1.

**Targetry**
Targetry is all IBA standard issue, with all targets external to the yoke. We have modified the [O-18]Water Targets minimally by adding a fixed volume target compression stack to the target vent line. We have also added pressure transducers to all targets and interfaced transducer output to the computer for real time display. Typical transmissions on each of the beam ports can be found in Table 1.

Table 1

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| Target | C-11 | F-18 | F-18 | O-15 | N-13 | N-13 | C-11 | O-15 |
| Tgt/Str | 91% | 30% | 40% | 58% | 70% | 63% | 60% | 60% |
| Collimator | 16 mm | 10 mm | 10 mm | 16 mm | 10 mm | 10 mm | 16 mm | 16 mm |

**Chemistry Modules**
We are using Siemens CPCU's for FDG production. Otherwise IBA modules are in use. Radiopharmaceuticals and yields are displayed in Table 2. We are not yet licensed to produce O-15 because some shielding issues are yet to be resolved to the satisfaction of State regulatory bodies.

Table 2

| Radiopharm | Runs | Sat Yield (mCi/μA) | I (μA) | t (min) | mCi | % Yield |
|---|---|---|---|---|---|---|
| [F-18]FDG | 18 | 232 ± 28 | 12 | 90 | 455 ± 35 | 54 ± 5 %* |
| [C-11]$CO_2$ | 10 | 115 ± 14 | 35 | 30 | 2290 ± 300 | |
| [C-11]CO | 10 | | 35 | 30 | 1211 ± 166** | |
| [C-11]HCN | 10 | | 35 | 20 | 1516 ± 100 | |
| [C-11]Acetate | 8 | 111 ± 12 | 35 | 30 | 458 ± 54 | 38 ± 5% |
| [N-13]$NH_3$ | 5 | | 30 | 15 | 465 ± 60 | |

* % Calculated from F-18 Delivered from Target. % Yield calculated from activity left in vials etc = 61%
** 17% N-13 content from p,pn reaction was subtracted to correct for contamination.

**Areas of Focus**
Clinical operation of our PET facility is our first priority at the moment. From the cyclotron operation standpoint, this means supplying a reliable stream of [F-18]FDG and [N-13]Ammonia to our clinical co-workers. We hope to branch into research applications and [F-18]FDG distribution in the near future (within 12 months).

Our present efforts have therefore focused on reliable synthesis of obscene quantities of [F-18]FDG while simultaneously attempting to meet the intensely stringent and stifling new FDA (Food and Drug Administration) regulations on the production of PET radiopharmaceuticals. Small target modifications have made an incredible difference to reliable F-18 production and [F-18]FDG synthesis. First we added pressure transducers to the target so that we could observe target dynamics during irradiation. In controlled experiments we found dramatic variations in target pressures during irradiations depending upon the volume loaded of [O-18]$H_2O$. Target yields correlated directly with the operating pressure. High pressure (>200 psi) resulted in high yields, low pressure (<100 psi) resulted in low yields and problematic target delivery. Initial stretching of the target foil following rebuild significantly affected target volume, and therefore target performance. Inconsistent loading volumes also plagued reliable production. Our present solution requires careful monitoring of target pressures. We have found optimal results running at about 12 μA and at an operating pressure between 300-500 psi. We have also modified the target vent line so as to provide a reproducible compressible air space between the target and Rheodyne valve. This is shown schematically in figure 2. This modification allows us to "overfill" the target with the syringe, yet still maintain a compressible air space outside of the beamstrike area to keep target pressures under control.

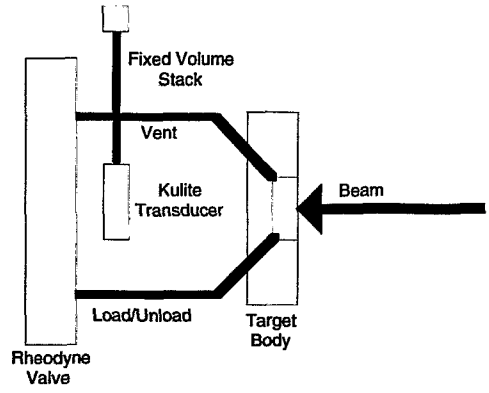


Figure 2. F-18 Target Modification

We are also beginning to concentrate on [N-13]ammonia production. We have two problems which we are attempting to overcome. The first is pyrogenicity. Testing of our [N-13]ammonia product has resulted in unacceptably high levels of pyrogens in some of our runs. We expect to solve this problem by flushing the target and delivery lines thoroughly prior to bombardment, but we need to validate this. We also have detected some long lived Scandium isotopes ($^{44,47}$Sc from p,$\alpha$ on $^{47,50}$Ti apparently leaching from the Titanium window. We are looking into further energy degradation of the proton beam to 11-12 MeV in the hopes of dropping below activation energies for these reactions. We would be interested in anyone's solutions to these problems.

**Safety and Security Measures**

There are a number of safety interlocks wired into the cyclotron system both to protect the equipment and the personnel. For Radiation Safety purposes there are 4 "Scram" buttons placed all over the cyclotron laboratory and within the vault. Pressing any of the buttons shuts down and disables cyclotron power supplies. Two NaI stack monitors record any activity released to the atmosphere through the stack. Should the count rate at either of the two detectors exceed 2 x $10^5$ cpm, the cyclotron is shut down. A radiation monitoring system continually monitors dose rates in each of the rooms in the cyclotron, scanner, and patient prep areas. Levels are logged automatically onto a computer every 15 seconds. The door to the cyclotron vault is both software and hardware interlocked.

Primary water flow, primary water temperature and compressed air all have software interlocks built in (water temperature must be less than 58° F, and air compressor must be > 100 psi). Room temperature and relative humidity are also monitored. If the level reaches 80% relative humidity or room temperature reaches 85° F the cyclotron shuts down. There is a newly installed helium flow interlock which prevents beam running on target if there is insufficient flow.

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# THE CYCLOTRON AND RADIOCHEMISTRY FACILITIES IN ULM

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## 1. Introduction

The University Hospital Ulm has a capacity of 1053 beds and consists of 45 departments. 37.398 in-patients were treated in the year 1995. The share of the Department of Nuclear Medicine was 0.64 % (238 patients). In total 10.834 in- and outpatient nuclear medical diagnostics were performed. About 40 medical, scientific and technical employees are working in the Department of Nucl. Med. at this time. The number of scientists amounts to 7 (2 chemists, 1 pharmacist, 1 biologist, 2 physicists and 1 engineer). Since 1995 we are provided with a cyclotron and radiopharmaceutical laboratories. The medical section has two PET scanners (Siemens-CTI ECAT 931-08-12 and Siemens-CTI Exact HR$^+$). Furthermore we are equipped with 5 different gamma cameras (partly SPECT). The main research area is cancer diagnosis besides cardiac and neurological questions. On this scope the development of new reactions for the labeling of anticancer drugs with PET nuclides is an important intention. Another point of interest lays in the investigation of molecular biological fundamentals for the metabolism of clinically used radiopharmaceuticals. In this connection we analyze the expression of distinct glucose transporter genes in different cancer tissues which are responsible for the elevated uptake of [$^{18}$F]-FDG. Another molecular biological project deals with the labeling of DNA and RNA oligonucleotide antisense molecules with radioactive isotopes (mainly with PET nuclides).
As we were able to start working with the cyclotron and radiochemistry facilities not before autumn 1995 and because of unexpected problems with the exhausted activity using gaseous radioactive compounds (see below) we still are busy establishing and expanding the range of routinely produced radiopharmaceuticals.

## 2. Radiopharmaceutical laboratories

In Ulm the radiopharmaceutical area is clearly separated from the medical section. The gamma cameras and the PET scanners are located at the second floor, the cold and hot laboratories are at the first floor, and the cyclotron is at level 0. Therefore the radioactive compounds have to cover considerable distances. Transfer from the target to the hot lab is realized through 1/16" teflon tubes by helium pressure. The hot lab is connected with the scanner room by a pneumatic dispatch to transport the radiopharmaceuticals after quality control to the PET scanner. The radiopharmaceutical facilities are divided into three radiation protection areas (Fig.2):

- non controlled area: corridor, common room, bathroom
- controlled area: office, control room, technical room, hot lab, quality control room, cold lab, workshop, cyclotron vault (without beam)
- prohibited area: cyclotron vault (with beam)

## 3. Cyclone 18/9

At the moment 5 target positions of the cyclotron are installed, 3 are free (Tab. 1).

Tab.1: Targetry and radiochemical yields of Cyclone 18/9 in Ulm

| Exit | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| Nuclide | $^{18}F^-$ | $^{15}O$ | --- | --- | --- | $^{18}F_2$ | $^{13}N$ | $^{11}C$ |
| Particle | $H^-$ | $D^-$ | --- | --- | --- | $D^-$ | $H^-$ | $H^-$ |
| Beam test: current on stripper [µA] | 88 | 36 | --- | --- | --- | 45 | 85 | 85 |
| Chemistry test: activity [mCi] | 732 ($F^-$) | 237 ($O_2$) | --- | --- | --- | 333 ($F_2$) | 478 ($NH_4^+$) | 2110 ($CO_2$) |

Dual beam at the exits 2 and 6 is possible. All targets are from IBA.

Cyclone 18/9 is normally running from Tuesday till Friday, Monday we try to save for servicing and repairs. Beam time is usually in the morning (dependent on medical demand).

**4. Chemistry modules**

We are equipped with the following chemistry modules from IBA:

- $^{18}$F-FDG module
- $^{13}$N-$NH_3$ module
- $^{11}$C-acetate module
- $^{11}$C-HCN module
- $^{15}$O-water module
- $^{15}$O and $^{11}$C $CO/CO_2$ gas module

In addition we have a second $^{18}$F-FDG module from the KFA Jülich and a $^{11}$C methylation module from Nuclear Interface. The chemistry modules are placed in 7 hot cells (Van Gahlen).

As mentioned above, at the moment we have problems with the exhausted activity using volatile radioactive compounds because of unforeseen leakages of the hot cells. This is the reason why we are not yet allowed to produce and handle radioactive gases. In September 1996 a system will be installed to deposit the aspirated radioactive gases from the hot cell temporarily in gas cylinders before being let off into the ventilation system. So we can not give a report on our own experiences handling $^{11}$C and $^{15}$O at this time.

For almost one year we routinely produce $^{18}F^-$, $^{18}$F-FDG (4-5 days per week) and $^{13}$N-ammonia (2-3 days per week). The (not decay corrected) radiochemical yield of the FDG production with the module from KFA Jülich is illustrated in Fig.1. Producing FDG with the IBA-$^{18}$F-FDG module leads to much lower yields (<35 %), thats why we do not use this module for routine production.

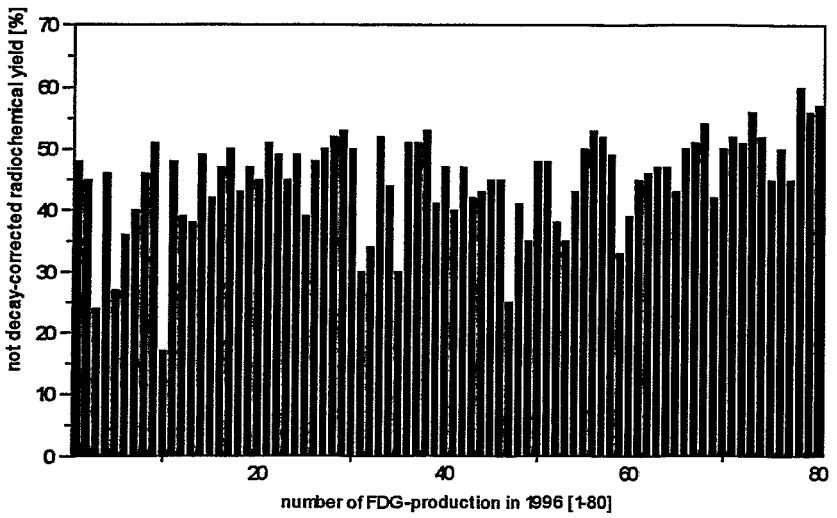


Fig.1: Radiochemical yield of $^{18}$F-FDG (not decay corrected) in 1996

**5. Radiation protection, safety measures, environmental care**

The cyclotron vault is shielded by approx. 2 metres of a special $BaSO_4$/concrete. Starting of the beam is integrated in an external interlock system consisting of different components:

- Emergency stop buttons in all rooms.
- Minimum pressure difference between cyclotron vault and technical room (20 Pa).
- Monitoring of the seal-pressure in the cyclotron door.
- Hot cell doors have to be closed for purging the target.

All rooms of the controlled area and each of the 7 hot cells are radiation monitored which can be displayed in the control room. The entire waste air is also monitored continuously and must not exceed 200 Bq/cbm in the annual average. The waste water is separately collected and may not be drained off until falling below certain activity limits.

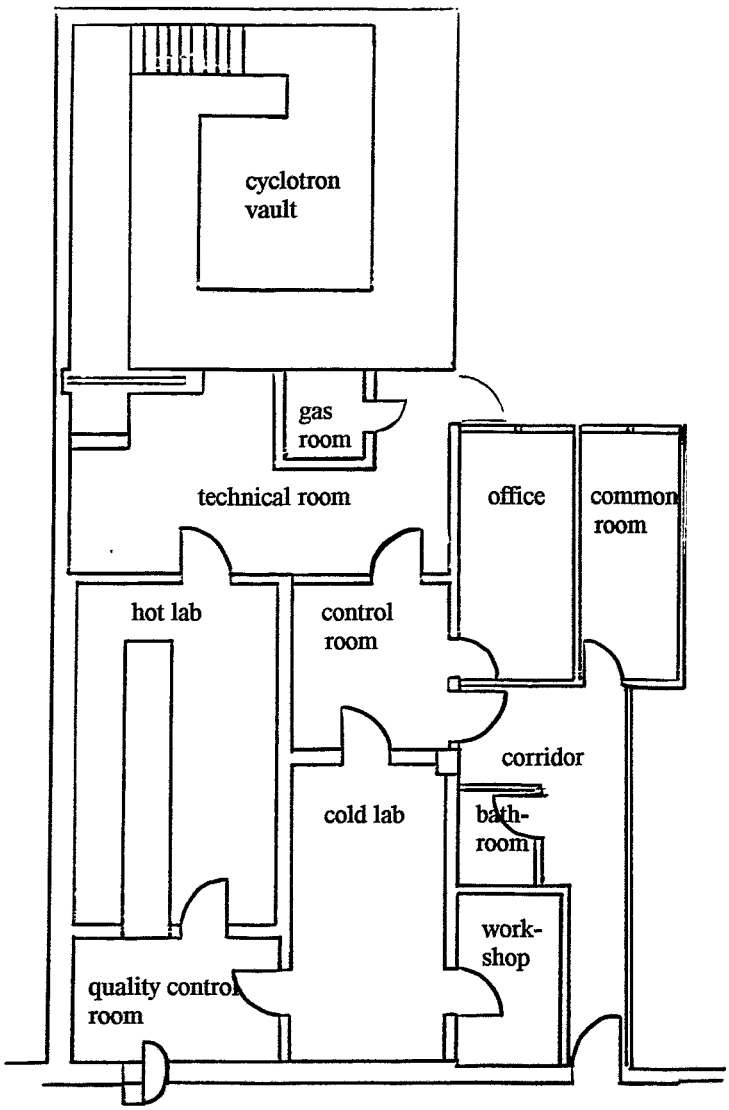


Fig.2: Layout of the radiopharmaceutical laboratories in Ulm

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# List of Participants

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