SIEMENS

Eclipse Cyclotrons

Eclipse Cyclotron Systems Technical Description

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Answers for Life

Introduction

Eclipse™ Cyclotron provides a low-cost, automated, efficient and easy-to-operate system for the production of PET isotopes (^{18}F, ^{11}C, ^{13}N, ^{64}Cu, and ^{15}O) and radiochemicals.

It does so using the following characteristics:

- 11 MeV cyclotron
- Negative hydrogen ion source
- Deep valley magnet design
- Self-shielding
- Small system footprint
- The most complete line of targetry and automated chemistry in the industry
- Innovative single beam port with two versions of rotating carousels that can hold four or eight targets
- Graphical user interface (GUI) running on a dedicated PC
- Dual bombardment capability

Deep Valley
Eclipse is a deep valley design cyclotron. The term "deep valley" refers to gaps between the hills and valleys of the magnetic system. The ratio between the hills and valleys is on the order of 27:1. This high ratio enables better axial beam focusing.

Targetry and Chemistry
[^{18}F]F^- target is standard, as is the Explora FDG_4 module. Optional target equipment includes targets that produce [^{11}C]CO_2, [^{18}F]F_2, [^{15}O]O_2, [^{64}Cu]Copper, and [^{13}N]Ammonium ion. Optional chemical processing modules include the Gas Processing Unit, the [^{15}O]water module, and a large selection of ^{18}F and ^{11}C chemistry synthesis modules.

This document describes the major components and subsystems of the cyclotron.

Magnet System

The main components of the magnet are the upper and lower pole, return yoke, coil, and vacuum tank. The field excitation of the magnet is provided by a single magnet coil, as opposed to a pair of coils. The magnet coil[1] is wound from a single, continuous strip of copper. Because of the low resistivity of this design, the coil power consumption is very low. The heat generated in the coil is removed by cooling water traces. To excite the magnet, the system uses a low voltage, high current, switching-type power supply located in the adjacent equipment cabinet.

The accelerating region of the magnet has four sectors with narrow gaps. These sectors are called hills. Between each pair of neighboring hills is a valley. The system has a total of four valleys, which are distinguished by larger gaps than the hills. The ratio of valley-to-hill gap is approximately 27:1. Consequently, the magnetic field in the hill is much stronger than the field in the valleys. The steep field gradient at the boundary of a hill-valley provides strong vertical focusing to confine the accelerating particles to the median plane. The concept of the deep valley is to produce this steep field gradient by using a large valley-to-hill gap ratio.

Eclipse Design Parameters

Hill angle	56 degrees
Hill gap	1.5 cm
Valley gap	40 cm (nominal)
Pole diameter	90 cm
Extraction radius	40 cm (11 MeV)
Peak hill field	1.9 Tesla
Excitation	51,000 Ampere turns

RF System

The negative ions produced by the ion source are accelerated by a resonant structure consisting of four dees, each 30 degrees wide and supported by a grounded, water-cooled stem. The dees are electrically connected at the center of the machine and, consequently, oscillate in phase. The system is designed so that the high voltage required for dee operation is contained inside the vacuum chamber.

Ion path gyro frequency	approx. 18 MHz
Cavity resonant frequency	approx. 72 MHz
Nominal dee voltage	approx. 30 kV peak
Energy gain per turn	approx. 140 keV

RF power is supplied via a 10kW RF amplifier, located in the adjacent equipment rack. The amplifier is linked with 50 ohm coaxial cable to the resonant cavity using a gamma match connection. The gamma match is adjusted so that the impedance of the resonator matches the characteristic impedance of the cable.

Slow thermal drifts in the natural frequency of the resonator are tracked and compensated for using a circuit that measures the phase relationship between RF current and RF voltage in the transmission line. The oscillator frequency is then adjusted to maintain a resonant load condition. The output voltage of the RF amplifier is low, due to the high gain resonant cavity.

Protection against load faults due to sparking of the resonator is provided by a high speed transmission line VSWR detector, which shuts off the RF drive until the fault can clear.

The frequency of the RF system is set by a digitally-controlled synthesizer. No tuning or adjustment of the amplifier is required by the operator.

1: U.S. Patent number 5,463,291

Ion Source

Eclipse uses a modified Penning type ion source. The arc is initiated by the ion source power supply, which can provide up to 3 kV across the anode and two cathodes to start the hydrogen gas breakdown. The voltage for maintaining the arc depends on the arc current, and for normal operation is below 1 kV. The pressure inside the source is optimized for maximum production of negative hydrogen ions by controlling the gas flow rate. The source is electrically isolated from ground. To extract the negative hydrogen ions, the source is biased approximately 15 kV with respect to ground. The optics (the geometrical shape of the anode puller, etc.) has been designed to minimize dispersion and maximize brightness for the extracted beam.

The source is mounted vertically from the top of the cyclotron and it can be taken out for maintenance without opening the tank. The gas load from the source is taken up primarily by a dedicated diffusion pump. Only a fraction of the source gas enters the main chamber, maintaining low negative ion gas stripping losses, while preserving the inherent operational simplicity on an internal ion source.

Maximum arc current is approximately 2 Amps. Operating current is typically much less than 1 Amp.

Vacuum System

The vacuum system is designed to have a low stripping loss of the accelerating particles, as well as a short pump-down interval to reach operating pressure. The system uses three 160 mm diffusion pumps (rated at 1495 l/sec H_2) and a mechanical forepump located beneath the cyclotron.

Standby vacuum	typically 5 x 10^{-7} Torr.
Operating vacuum	typically below 5 x 10^{-6} Torr.

Beam Extraction

The negative ions are accelerated to the extraction radius, where they pass through a thin carbon stripper foil and the electrons are removed, producing a proton beam.

The trajectory of the particles traveling in the strong axial magnetic field of the cyclotron changes curvature from inward to outward and the proton beam exits the accelerator through an adjacent beam port. Extraction efficiency of the foils is approximately 99%.

A maximum of three foils are located on a vertically mounted extractor. The average foil is expected to last approximately 10,000 µA-hr. A new foil easily can be selected (using the control system) if the existing one is damaged or worn out.

Beam collimators clip the edges of the Gaussian-shaped beam just before it enters the target. A single ring collimator transmits approximately 80% of the beam to the target in a beamline approximately 10 mm in diameter.

Targetry

Eclipse includes targets for production of the commonly used PET isotopes. There are three basic target types – gas, liquid and solid. No fluid-bed (e.g., "slurry") targets are included with Eclipse.

There are two target carousel formats available on Eclipse – Eclipse HP and Eclipse RD. Eclipse HP is a four-position target carousel capable of running 60 µA. Eclipse RD is an eight-position target carousel capable of running 40 µA. Eclipse HP has no vacuum windows, and therefore no helium recirculation system. Eclipse RD does have a single vacuum window and therefore does have a helium recirculation system. Furthermore, Eclipse RD can not be outfitted with solid targets or $[^{18}F]F^-$ target bodies made of tantalum.

Each operational target (already plumbed and ready to operate) is connected to its associated Target Support Unit (TSU), which is mounted in an adjacent equipment cabinet. The TSUs provide integrated system control functions, plumbing and control of target material loading and unloading.

This section contains detailed descriptions of:

- Target carousel and TSUs
- Collimator, target and vacuum windows
- Targetry specifications
- Radioactivity transport

Target Carousel and TSUs

The modular Eclipse targets are mounted in a 4 or 8 position rotating carousel, 20 cm in diameter, which is nested in the steel return-yoke of the cyclotron magnet.

This innovative design enables the installation of multiple targets, in any combination, on a single beamline. Any position not occupied by a target is occupied by a Faraday cup or beam stop.

All of the targets in the carousel are cooled by one set of water lines, thereby reducing the complexity of the system and the likelihood of leaks. The water flows through passages in the carousel, eliminating plumbing connections to the targets.

The operator can move a target into the beamline automatically from outside the shield, in less than 30 seconds, without breaking or making any vacuum, water, helium (in the case of Eclipse RD) or product connections. Any target can be removed or installed in less than one minute without breaking or reconnecting water or helium lines or breaking vacuum.

Eclipse HP target changer operates without helium window cooling or vacuum windows. This is made possible by a differently pumped faceseal plenum. The face of the target under bombardment is at machine vacuum. Two other target faces are at plenum pressure, which is "rough" vacuum (10^{-2} torr). One target face is in the pump-out position, which can go from plenum to atmosphere without affecting machine vacuum. Rotation in this state is prevented by a gauge lockout.

Either type of target changer can be adjusted for proper mechanical alignment with the proton beam. If subsequent removal for service is necessary, the adjustment remains on the cyclotron, and the target changer may be reinstalled without further alignment.

The entire target carousel assembly is electrically insulated from ground, so that beam current on target may be monitored by the computer.

Target support units (TSUs) also are modular in nature. The system can accept up to 12 TSUs (6 per beamline) in any combination. The only limitation is that no more than 2 [^{18}F]F^- TSUs may be installed on any one beamline. Field installation of additional target systems requires no more than the TSU, target, and up to three cables.

Collimator and Windows

Collimator

The entrance aperture to the target is defined by a beamline collimator made of graphite.

Windows

Each target has its own high-pressure target window. These are made of 0.001" Arnavar or titanium. The windows are designed to be operated at pressures up to 1000 psi under full beam conditions and have been burst-tested to 1200 psi.

Window cooling on Eclipse HP is provided by hexagonal support grids, cooled by recirculating water at the edges. No helium cooling is necessary. The grid pattern passes ~90% of the extracted beam.

Window cooling on Eclipse RD is provided by recirculating cool helium gas.

Targetry Specifications

This section gives physical specifications for these targets:
Note: For isotope production specifications, see the Eclipse Data Sheet.

- [^{18}F] F^- Fluoride Target
- [^{13}N] Ammonia Target
- [^{11}C] Target
- [^{15}O] Target
- [^{18}F] F_2 Target
- [^{64}Cu] Copper Target

Additional target bodies may be purchased as spares and installed in a carousel – but not necessarily connected – in order to:

- Provide additional back-up and redundancy
- Allow for scheduled cool-down period to minimize radiation exposure during maintenance and repair of targets
- Minimize unscheduled down-time for target maintenance or extend the period between maintenance interventions

	HP	RD
[^{18}F]F^- Target (standard)		
Chemical form	Aqueous fluoride ion	
Irradiated volume	2100 µl	800 µl
Total target volume	2300 µl	1400 µl
Target body material	Silver or tantalum	Silver only
Target material	^{18}O enriched water	
Window material	Arnavar	
Window thickness	.001"	
Loading pressure	Ambient	
Operating target pressure	350 psi	650 psi
Nuclear reaction	$^{18}O(p,n)^{18}F$	

	HP	RD
[^{13}N]Ammonia Target (optional)		
Chemical form	Aqueous ammonium ion	
Irradiated volume	~3 ml	
Target body material	Aluminum	
Target material	5 mmol EtOH/water solution	
Window material	Titanium	
Window thickness	.001"	
Loading pressure	400 psi	
Operating target pressure	400 psi	
Nuclear reaction	$^{16}O(p,\alpha)^{13}N$	

	HP	RD
[^{11}C] Target (optional)		
Chemical form	Carbon dioxide gas	
Irradiated volume	9.8 ml	6.7 ml
Total target volume	~10 ml	~7 ml
Target body material	Aluminum	
Target material	Natural N_2 + 2.5% O_2	
Window material	Arnavar	
Window thickness	.001"	
Loading pressure	320 psi	300 psi
Nuclear reaction	$^{14}N(p,\alpha)\ ^{11}C$	

	HP	RD
[^{15}O] Target (optional)		
Chemical form	Oxygen gas	
Irradiated volume	9.8 ml	6.7 ml
Total target volume	~10 ml	~7 ml
Target body material	Aluminum	
Target material	^{15}N enriched N_2 with 2.5% O_2	
Window material	Arnavar	
Window thickness	.001"	
Loading pressure	270 psi	300 psi
Nuclear reaction	$^{15}N(p,n)\ ^{15}O$	

	HP	RD
F_2 Target (optional)		
Chemical form	Electrophilic fluorine gas	
Irradiated volume	9.8 ml	6.7 ml
Total target volume	~10 ml	~7 ml
Target body material	Aluminum	
Target material	^{18}O enriched oxygen gas - F_2/Ar gas mix	
Window material	Arnavar	
Window thickness	.001"	
Loading pressure	270 psi	300 psi
Nuclear reaction	$^{18}O(p,n)\ ^{18}F$	

	HP	RD
Solid Target (optional)		Not Available
Chemical form	Solid	
Target puck material	Gold	
Target material	^{64}Ni	
Window material	Windowless	
Nuclear reaction	$^{64}Ni(p,n)^{64}Cu$	

Radioactivity Transport
Gaseous products and aqueous fluoride ion are transferred using gas pressure from inside the main shield to the chemistry laboratory or to the dispensing apparatus through small-bore tubing threaded through conduits buried in the concrete floor.

Irradiated target material from the ammonia target, in aqueous liquid form, is transferred by fluid pressure from inside the main shield to the processing and dispensing apparatus also by means of small-bore tubing – threaded through the same conduits as above.

Routing and installation of these conduits is required as part of the initial site planning. The concrete pad is poured around the conduits to provide an attenuation factor for 511 keV gamma rays equivalent to 1" of solid lead.

Maximum line length from end-to-end for fluid transfer is 100 ft in a standard site installation. Greater distances – 500 ft and more – may be accommodated by means of an alternative design.

Chemistry

Standard Chemistry
The standard chemistry module included with Eclipse is Explora™ FDG_4.

Explora FDG_4
The FDG module is a valve and tubing unit that is programmed to affect a variety of processes remotely and automatically under computer control. The system contains hardware components that perform reagent addition, transfer, heating, cooling, reflux, evaporation and purification steps by means of timed and adaptive operations. Control commands are transmitted through a control interface separate from that on the cyclotron.

Explora FDG_4 is designed to perform four syntheses back to back without user intervention. There is an automated clean procedure between each synthesis and after the fourth synthesis. Explora FDG_4 offers patented[2] recipe builder software that affords the end user an easy to use method of process development in a manner that simulates standard chemical synthesis reactions. The module also provides user feedback that is useful in both service procedures and process development. The module supports the recovery of [^{18}O]H_2O.

Explora FDG_4 has demonstrated flexibility in effecting a variety of different nucleophilic fluorinations, including that required to produce FDG.

2: U.S. Patent #7,369,913

In Target Chemistry

^{13}N Ammonia

[^{13}N]Ammonia is made in the target. Further processing is required to remove [^{13}N]NO_x impurities.

^{64}Cu Copper

The gold target puck is electroplated with a few milligrams of ^{64}Ni. The target puck is then loaded into the solid target position on the target carousel. The target puck is rotated into the bombardment position and the ^{64}Ni is directly irradiated producing ^{64}Cu from the ^{64}Ni(p,n)^{64}Cu nuclear reaction. At the end of bombardment, the target puck is removed from the target carousel and the ^{64}Cu is separated from the ^{64}Ni via ion exchange. The ^{64}Ni is recovered and made available for future replating.

Optional Chemistry

Optional chemistry modules include:

Explora GN

Explora GN takes advantage of proven technologies and incorporates the flexibility of back-to-back synthesis of various PET biomarkers. Explora GN offers flexible recipe builder software that affords the end user an easy-to-use method of process development in a manner that simulates standard chemical synthesis reactions. Explora GN is compatible with most nucleophilic solvents.

Explora LC

Explora LC is a semi-preparative HPLC module that can be used as a general separation unit in the radiochemistry facility. The module is supplied with solvent handling, two semi-prep C-18 columns, column switching valve, solvent degasser, fraction collection valve, radiation detector, UV detector and control software.

Explora FM

Explora FM module is a fully automated solid phase extraction (SPE) module. The module can be used to carry out various SPE routines to provide a specific formulation of a PET radiochemical. The module offers flexible software to allow the end user the ability to design custom routines. The module is useful in the production of [^{18}F]NaF.

System Control

Routine operation of Eclipse, including cold start-up and conditioning, is entirely automatic. To ensure optimum operation efficiency, the system must be correctly maintained and operated within these specifications:

- Environmental limits, such as room temperature and humidity, must be observed
- Consumables such as ion source cathodes, extractor foils, etc., must be maintained and replaced on schedule
- System vacuum must be within the prescribed range.
- Liquid and gaseous raw materials and reagents must be correctly plumbed and leak-tight
- Manual valves and regulators must be correctly set
- Chemical processing modules must be properly set up

Distributed Control

Eclipse makes use of distributed processing and control wherever possible. The cyclotron itself is controlled by a standalone VME processor and related interface cards. VME card I/O channels have enough current capacity to drive most devices without relays. Where possible, subsystems operate autonomously to minimize effects of a single failure on adjacent subsystems.

Easy Installation

The control system configuration enables all necessary communication to take place over a network that is installed during facility construction. Installing a system (or adding one at a later date) entails plugging it into an AC power outlet and into the network. Installation is complete after these steps. Subsequent chemistry and other systems may easily be added to the existing system.

Record Keeping

The control system architecture enables information to be recorded and automatically archived in a manner that is easily accessible and requires little manual intervention.

System Maintenance

Eclipse maintenance is facilitated by a manual mode which is used to monitor, modify and control pertinent operational parameters in real-time. Commands are entered through a keyboard/terminal located near the main equipment rack. Manual mode is to be used only by trained and specifically-qualified personnel who are well-versed in the underlying physics, chemistry and engineering principles.

Summary

In summary, the control system for Eclipse has the following features:

- Communication between the Eclipse cyclotron and other entities uses a modern industry standard protocol
- The system provides a local terminal connection to facilitate system integration, testing, monitoring, maintenance and local operation
- Operational and safety interlocks are integral to the system, thus ensuring machine and personnel safety
- The system design allows for easy addition of control/view workstations at other locations (e.g., at the scanner, laboratory or at the radiopharmaceutical distribution point)
- Five password protected levels of security that can be configured by the user or administrator for different levels of personnel

Note: Please refer to chemistry module data sheets for chemical reactions and specifications.

- System hard copy device (printer) will be located on the network with the control computer
- Data and operational parameters are accessible for logging and report generation

Radiation Issues

Note: What follows is a quick summary of radiation issues for the Eclipse cyclotron. For a full description see "Radiation Safety Aspects of the Eclipse Cyclotron."

Radiation Protection
It is the user's responsibility to obtain the required license to operate a radiation-producing particle accelerator, and to produce, possess, use and distribute (as appropriate) radioactive materials.

It is also the user's responsibility to establish a comprehensive in-house radiation-protection program and to ensure and maintain compliance with applicable local, state and federal regulations.

Accelerator-Related Radiation
Prompt, penetrating radiation is produced during normal cyclotron operation. Radiation from the accelerator due to collisions is minimized by two factors:

- Beam loss due to stripping is minimized by exploiting the improved background pressure inherent with the isolated ion source and large-capacity vacuum pumping system
- Proper choice of materials (e.g., tantalum or graphite) for components lying in the path of energetic particles minimizes activation radiation

Target Radiation
Prompt neutron and gamma radiation is an unavoidable byproduct of the target nuclear reactions which are used to produce the desired radioactive isotopes.

Shielding
Radiation produced in the targets and in the accelerator is attenuated by means of a unique surface shield, which is built around – and is integral to – the system. The shielding is designed so that radiation exposure rates for persons occupying the room while the accelerator is in operation are consistent with guidelines established for monitored personnel. Monitored personnel are operators and technicians working in a controlled-access environment where radioactive materials are prepared and dispensed – i.e., radiation workers.

The shield is effective against various forms of radiation – fast neutrons, prompt and induced high-energy gamma radiation, etc. To ensure minimal radiation levels, the system must be operated and maintained within defined and prescribed procedures and protocols.

The shield comprises two main functional components; an inner, 30 cm thick, high-density core cast out of a mixture of lead, epoxy, and boron carbide. This layer degrades the energy of neutrons above 1–2 MeV, absorbs most of the prompt gamma radiation from the target reactions, and absorbs the thermalized neutrons produced by collisions in the inner shield core.

Beyond the inner core is a 70 cm thick outer shield layer made of polyethylene and boron carbide loaded concrete. The primary function of the outer shield layer is to moderate neutrons through elastic collisions with the hydrogen atoms in its water and polyethylene constituents, slowing them to thermal energies. Secondary radiation due to neutron capture in hydrogen (or in the heavy elements that make up the cyclotron, such as iron or copper) is minimized as the shield absorbs the neutrons in boron.

Service and maintenance personnel can move the shield to work on the cyclotron and its targets by using the electrically-driven roller mechanism.

Activation
Residual radiation due to direct charged-particle bombardment of cyclotron components, such as collimators, is rendered negligible due to proper choice of materials lying in the beam path.

Residual neutron-induced radiation in the accelerator and in the shield itself is manifest as a diffuse, low-level background which is held to a minimum by absorbing most thermal neutrons in the heavily borated inner layer of shielding.

Residual radiation due to direct proton irradiation of target components, foils, etc., may, on the other hand, be hazardous. Only trained and authorized service and maintenance personnel may be permitted to work on those parts.

In addition, provision must be made by the customer for secure, shielded storage and ultimate safe disposal of irradiated target components.

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