An Autosynthesizer for 2-[Fluorine-18]Fluoro-2-deoxy-D-glucose

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Introduction

[^{18}F]2-FDG as an important reagent for PET users is produced successfully in various apparatus all over the world. However most of these automated synthesizers are delicate, high-tech scientific machines with features that are not absolutely necessary for routine production of [^{18}F]2-FDG.

Thus, the goal of our development project was to create a reliable, simple to operate and low cost autosynthesizer which requires a minimum of maintenance. In this context, some new and unconventional units must be developed to reduce mechanical movement and eliminate the need to handle the liquids for heating and cooling, or periodic manual cleaning steps.

Concept of the Autosynthesizer

The [^{18}F]2-FDG is produced by the HAMACHER method [1] with some modifications [2]. The apparatus uses interchangeable, standard Reacti-Vials(TM) as reaction vessels. Each vial is placed in the two special DANATEC® heating/cooling reactors. The reactors are mounted directly under a movable bridge that holds teflon heads with fitted connections for the reactors. On the bridge are also fourteen plugs for special solenoid valves. These can be interchanged between different positions and can be freely oriented in the plugs.

The whole bridge can easily be exchanged with another one, *e.g.* for a totally different synthesis.

The reagents for synthesis and rinse operations contained in glass vials sealed with a septum are placed in a casket inside of the hot cell. An automated servo-driven unit connects the reagent flasks through hollow needles and a motorized multi-way teflon valve to the apparatus and a nitrogen pressure source.

The units in the hot cell are absolutely free of electronic devices.

Outside of the hot cell, a compact, separated, microprocessor-driven controller manages the synthesis in a fully automated way.

It comments the momentary operation with a message on its LCD-screen. The controller is fully solid state and contains no fans, disc- or harddisc-drives. Because the controller operates sequentially, the number of devices, like servo-valves, solenoids, temperature controllers, printers, pumps, sensors *etc.* is not limited.

DANATEC®-Heating/Cooling Reactor

This unit eliminates the need to move the sample from hot bath or metallic block to a cold bath or fan. It operates with a fast flow of air, running in a closed loop. No warm-up effects in the hot cell and a very fast heat-up time are two of the advantages of these technology. The full heat-power is used to warm up the reactor and the reaction vessel only. Both of them have a low caloric content (glass, teflon). The fast PID-Temperature Controller is easily able to set exact temperatures at the reaction vessel, due to its high dynamic heat transfer rate.

The reactor is equipped with a magnetic stirrer. The stirrer rotates around the side wall of the Reacti-Vial(TM) so that the teflon tube can reach the conical center of the vial. There is no remaining dead volume after liquid transfer outside of the vial. The input teflon tube is mounted tangentially in the teflon head, so that a complete rinsing of the Reacti-Vial's(TM) inner walls is achieved.

References

[1] K. Hamacher, H.H. Coenen and G. Stöcklin, Efficient stereospecific synthesis of no-carrier-added 2-[^{18}F]-fluoro-2-deoxy-D-glucose using aminopolyether supported nucleophilic substitution. J. Nucl. Med. 27, 235-238 (1986).

[2] M. Argentini, T. Mäder, L. Wyer and R. Weinreich, Improvements in quality assurance of 2-[Fluorine-18]Fluoro-2-deoxy-D-glucose. These proceedings.

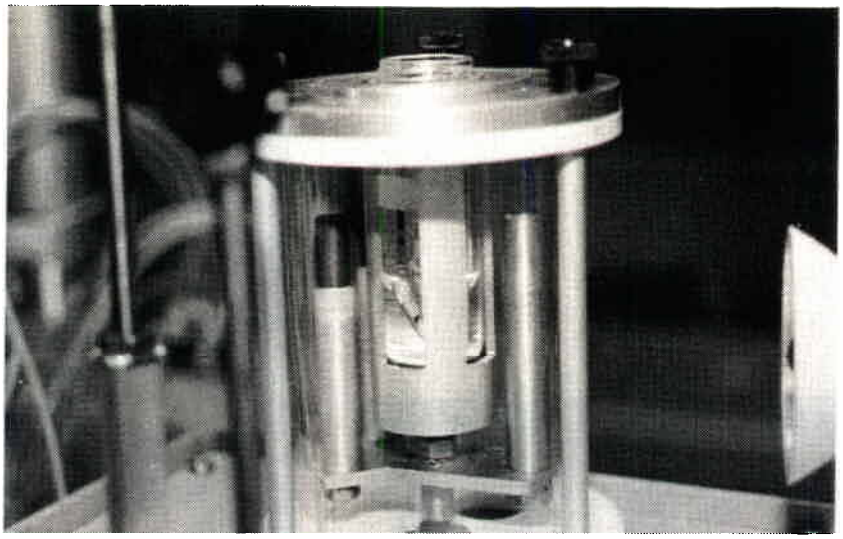
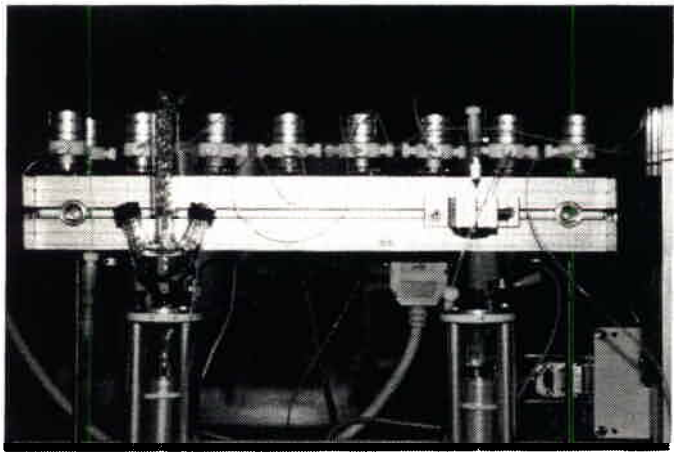


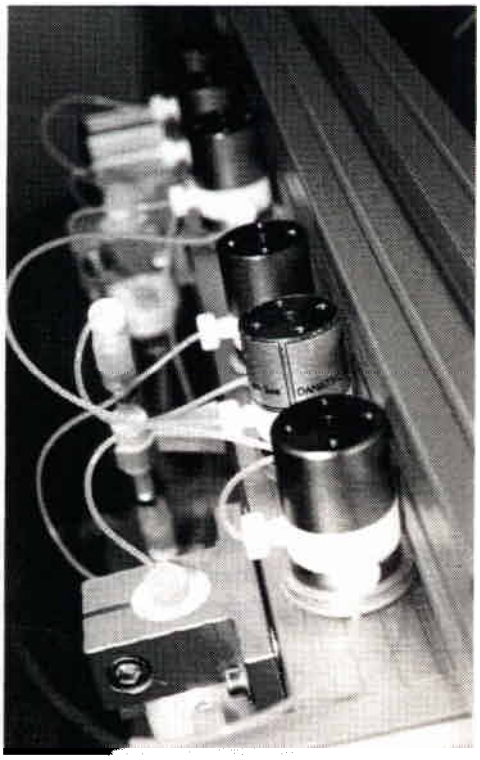
Figure 1: DANATEC® - Heating/Cooling Reactor

- Clear view in the reaction vessel (kind of boiling, liquid and gas dosage, change in color *etc.*)
- Adjustable, magnetic stirring, the PTFE spin bar runs around the walls of the vessel
- Interchangeable vessel inserts (standard: 10 ml Reacti-Vial(TM))
- Heating up over circulated air with high velocity, halogen-burner heater
- Cooling over compressed air (option: compressed air / whirl-tube at -20°C or cold gas LN_2).

Figure 2: Computer Controller

- Customer guide over a alpha-numeric display
- „Solid state" technology, no moving parts (like harddiscs, relays, fans, discdrives *etc.*)
- The program is directly interchangeable without any additional tools
- Interfaces to an IBM-PC, to a graphic display or to a modem *etc.* are available
- Simple programming in BASIC with extended commands
- Connections for printers and radioactivity monitors are provided.





Figures 3a and b: Solenoid Valves Movable Bridge

- The bridge is equipped with two servo-motors to move up and down
- The use of two motors is necessary to control the seal-force for both reactor vessels
- The moving of the bridge can be used to close and seal the reaction vessels with a special PTFE connection head, or to Pierce needles in septum-sealed vessels
- On the top of the bridge are 14 plugs for solenoid valves
- For change to a different synthesis normally only the change of software is required, however for complete different synthesis the whole bridge is easily interchangeable.

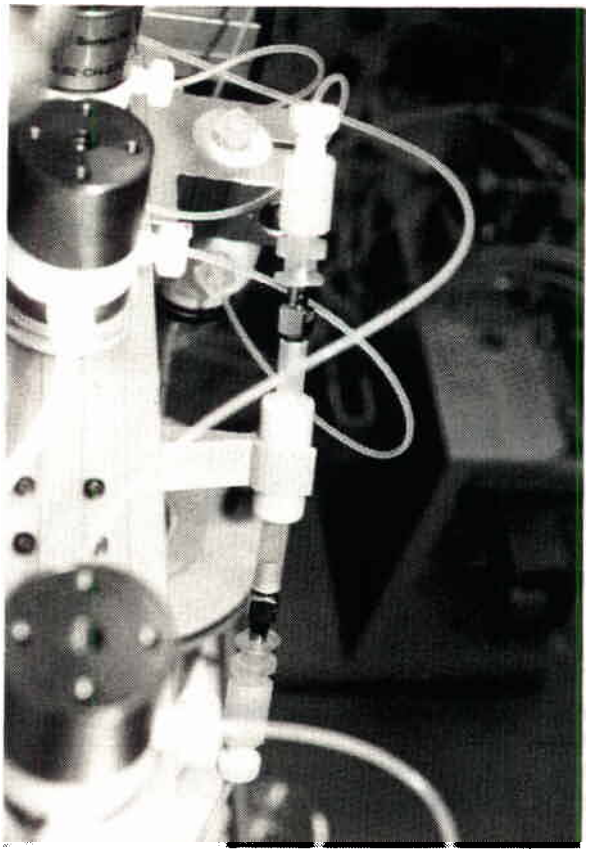


Figure 4: PTFE Solenoid Valve

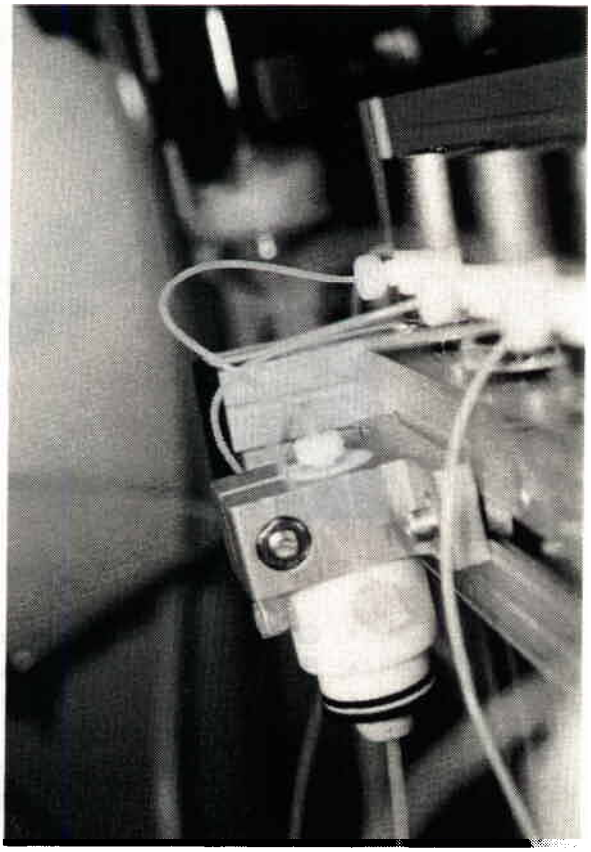


Figure 5: PTFE Connection Head

- All wet parts are made of PTFE; dead volume zero; inner diameter 1.5 mm
- Is capable to bear 2 bar overpressure against vacuum on all ports and in all directions
- Two-way or three-way models are available, 1/4" 28 UNF port
- Built in light indicator
- The solenoid valve can be oriented freely in the plugs.

- Is mounted at the movable bridge; closes the reaction vessel and connects it to the system
- PTFE/silicone seal; the quality of sealing would be tested by the program before the reaction starts. Nitrogen with 2 bar pressure is used for that purpose.
- Three ports are provided: one in the middle of the head with a tube to remove liquid outside of the reaction vessel; one port on the side comes tangential in and is used for dosage of liquids, gases and especially rinsing the reaction vessel; the third port on the side goes in the center of the head and is used to take gases and steams away from the vessel.

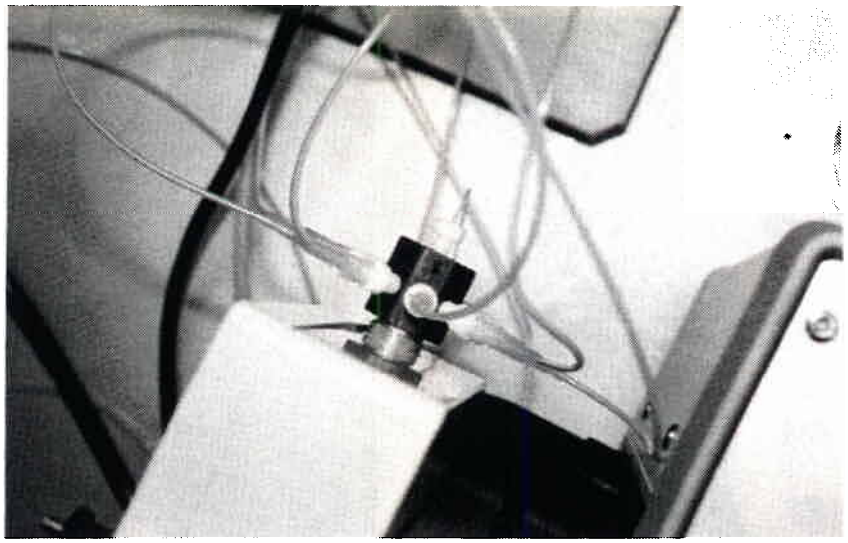


Figure 6: Servo-Motor Valve

- Computer-controlled, with record of momentary position
- PTFE/PCFT made; eight ports; small dead volume
- It is possible to set the valve to any desired position, for example also between two ports to keep the system closed
- The computer controls the dosage steps in such a way that no interactions are possible between two different reagents.

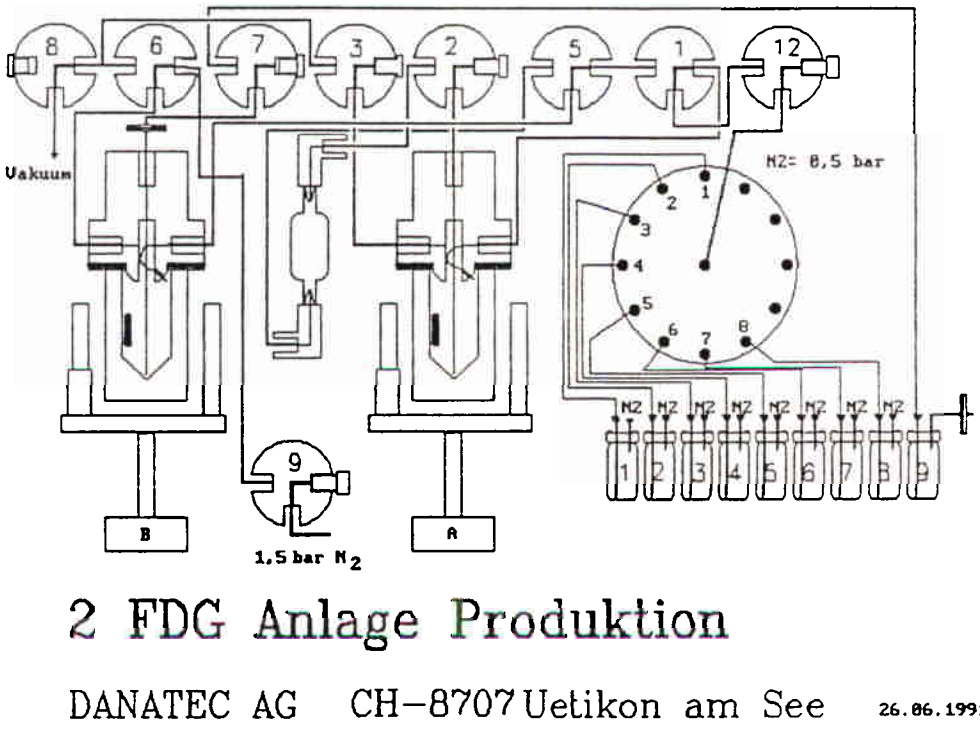


Figure 7: Valve Connections

- All connections are made of 1/16" PTFE tubes, except these for the vacuum (1/8")
- Special DANATEC® spacers against the cold-deforming effect of PTFE
- All connections are testable by the program; 2 bar nitrogen test-pressure
- The distillation of the [^{18}O]water is normally provided but in the described application not desired.

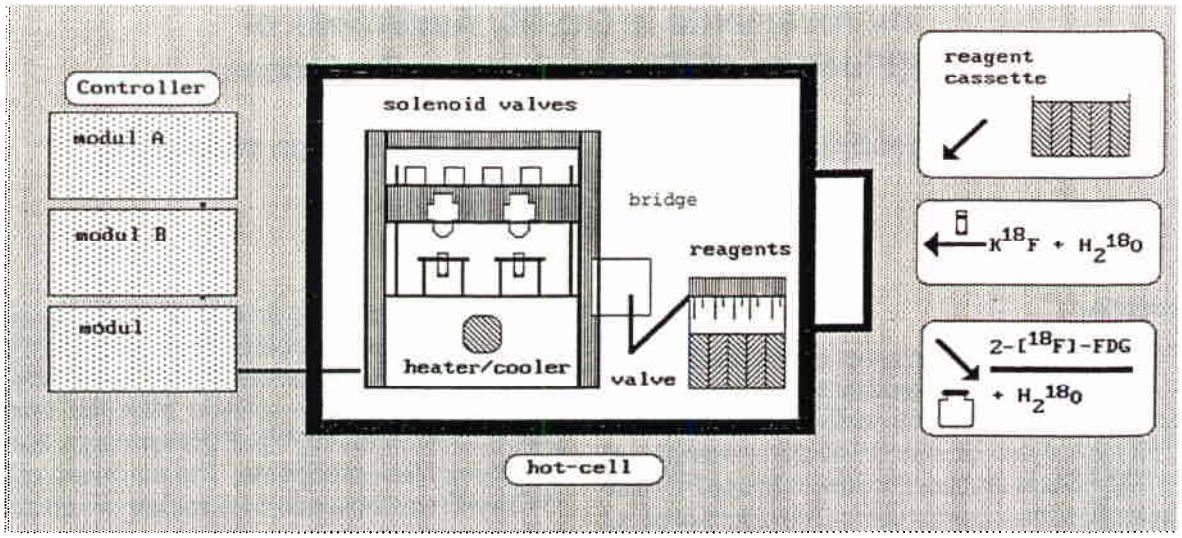


Figure 8: Arrangement of the [^{18}F]2-FDG autosynthesizer inside and outside the hot cell. Note that the autosynthesizer is constructed in such a compact way that it can be installed into a small shielded chamber. Then, an expensive hot cell is not necessary.