REPORTS FROM LABS : CERMEP, LYON, FRANCE

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The CERMEP, "Centre d'Explorations et de Recherches Médicales par Emission de Positons" is the third French PET centre, after the long experienced SHFJ in Orsay and our twin Centre, CYCERON in Caen (Normandy), six months older with the same equipment.

Although the building was finished in September '87, the CERMEP is only now (June '89) ready for PET examinations. The cyclotron was installed in January '88, the PET camera in February '89 and due to typical administrative problems we had to wait for the official opening authorization until now.

EQUIPMENT

The CERMEP is equipped with a CGR-MeV 325 Cyclotron, placed in a concrete vault in the basement of the two-storey building. The machine can produce typically 50 μA of 16 MeV Protons or 8 MeV Deutrons, with the possibility of a future extension to Helium 3. Basic productions in eight different targets (rotating target holder) are:

Oxygen 15:	$^{14}N(d,n)^{15}O$ O_2, CO_2, CO
Carbone 11:	$^{14}N(p\alpha)^{11}C$ CO_2, CO, CH_4
Nitrogen 13:	$^{16}O(p\alpha)^{13}N$ NH_3
	$^{12}C(d,n)^{13}N$ N_2
Fluorine 18:	$^{20}Ne(d\alpha)^{18}F$ F_2
	$^{18}O(p,n)^{18}F$ F-/H_2O (Ti target developed on site)

From these precursors, purified if necessary in a "hot chemistry Unit" placed in the vault, more complex ones are built (H_2O, HCN, CH_3COOF,...) in dedicated automatic units in four hot-cells situated just above the Cyclotron, in two hot labs.

All these productions are under the control of two interconnected industrial Programable Logic Controller, one for the monitoring of cyclotron status and parameters and one for the production lines, with a menu driven color CRT interface. After choosing for each precursor, electrovalves, flowmeters, furnaces can be individually or automatically controlled.

The system is simple, very effective, providing a lot of useful information and safeguards (eg. beam on/helium cooling, beam on/internal target pressure...) without being too much authoritative.

The starting clinical program will request first clinical gases and FDG, so our efforts were mainly devoted to these subjects; development of ligands and synthesis of various radiopharmaceuticals will come later with progress in the staffing of the Cyclotron/Radiochemistry Section.

Among things that we think may be of interest for the 3rd Targetry Workshop are the development in Lyon of a regulation system for the delivery of clinical gases and the use of magnesium instead of zinc for the reduction of $^{11}CO2$ to ^{11}CO.

REDUCTION OF $^{11}CO2$ TO ^{11}CO WITH MAGNESIUM

S. Iida in Groningen last July,[1] proposed replacement of the well established zinc reduction with magnesium reduction.

We tried this approach in Lyon and found it indeed very effective: ^{11}CO is produced easily in greater amounts and with a higher flow rate. The Merck Index states that Magnesium metal is a strong reducer, converting CO_2 AND CO to carbon; the reaction conditions are not too critical however, so it is relatively easy to stop the reduction at the CO stage. We use a column of only three

centimeters long x 1 cm in diameter of magnesium (fine turnings for grignard synthesis), at a temperature of 535-550° C. With a nitrogen flow rate of 200 ml/min through the system (target, furnace, traps) and a 10 μA proton beam the production is around 12 mCi/min of pure ^{11}CO (in the hot cell, 10 meters from the cyclotron).

This compares very favorably with the Zinc reduction we used before (1 to 2 mCi/min at only 80 ml/min maximum) and the data given by our Bible,[2] 8.4 mCi/min at 80 ml/min with 40 μA on target.

Other temperatures and flows may work equally well depending on the magnesium column.

A Radio gas chromatography showed the excellent purity of the ^{11}CO, only 3 to 8% $^{11}CO_2$ are produced, easily removed with a soda lime trap. We did not check the production of totally reduced ^{11}C on the column; at 570° C, we had a small diminution of the overall output yield probably due to the overreduction of CO to C. Nitrogen 13 from the $^{14}N(p,pn)^{13}N$ reaction is kept low (<8%) by a 500 μm aluminium degrader before the 50 μm Ti window, degrading the beam from 16 MeV to ~ 12 Mev.

We did not experience any trouble with magnesium itself (fires!); the magnesium used is not in a finely divided state, and anyway works under neutral atmosphere (nitrogen target and carrier). The magnesium is replaced after 10 hours of ^{11}CO production.

CLINICAL GASES REGULATION

To meet the requirements of the PET clinicians, we had to develop a regulation system for the production of radioactive clinical gases such as $^{15}O_2$, $C^{15}O$, $C^{15}O_2$, ^{11}CO. The aim was to obtain a constant radioactive output at a determined flow rate, in the PET camera room located 30 m from the cyclotron.

The beam intensity on target of the CGR 325 cyclotron is stable, as shown by a long duration bombardment (best than 5% over 1 hour). Even at low beams, a need for a dilution (5 to 10 fold) arises.

The small PLC we chose for this job is a Siemens SIMATIC 100, providing interesting possibilities of adding different interfaces; we use:

one module x 2 analog inputs
one module x 4 analog outputs
one module x 8 digital inputs
one module x 8 digital outputs

The input radioactivity signal is provided by a small finger ionisation chamber (40 x 10 mm) located inside a 10 ml loop of the final diluted gas; two analog outputs are controlling two regulating flowmeter Brooks TR 5850 (0-100 ml/min for activity, 0-500 ml/min for air dilution). The digital input are connected to the cyclotron PLC, accessing the information such as nature of gas, beam on, terminal electrovalve open, and to the control panel in the PET camera room. Digital outputs control the switching valves (patient/reject) and the lamps in the control panel (see Scheme 1).

Programming is done easily by simple instructions such as loading, transferring registers; instructions are grouped in functional blocks and the resulting program (< 100 instructions) is stored in the system EEPROM.

The regulation algorithm we use for the moment is the simplest one, i.e. direct control of the activity input flowmeter by comparison of the radioactivity after dilution to the required flow rate to the preset radioactivity level. The system regulates $^{15}O_2$ to 20 μCi/ml and $C^{15}O_2$ to 10 μCi/ml, at a constant flow rate of 500 ml/min; the stabilities at the output (PET Camera) are better than 3 %. These levels are easily modified by a new program. The system authorizes commutation of the radioactive flow to the patient only when regulation is achieved.

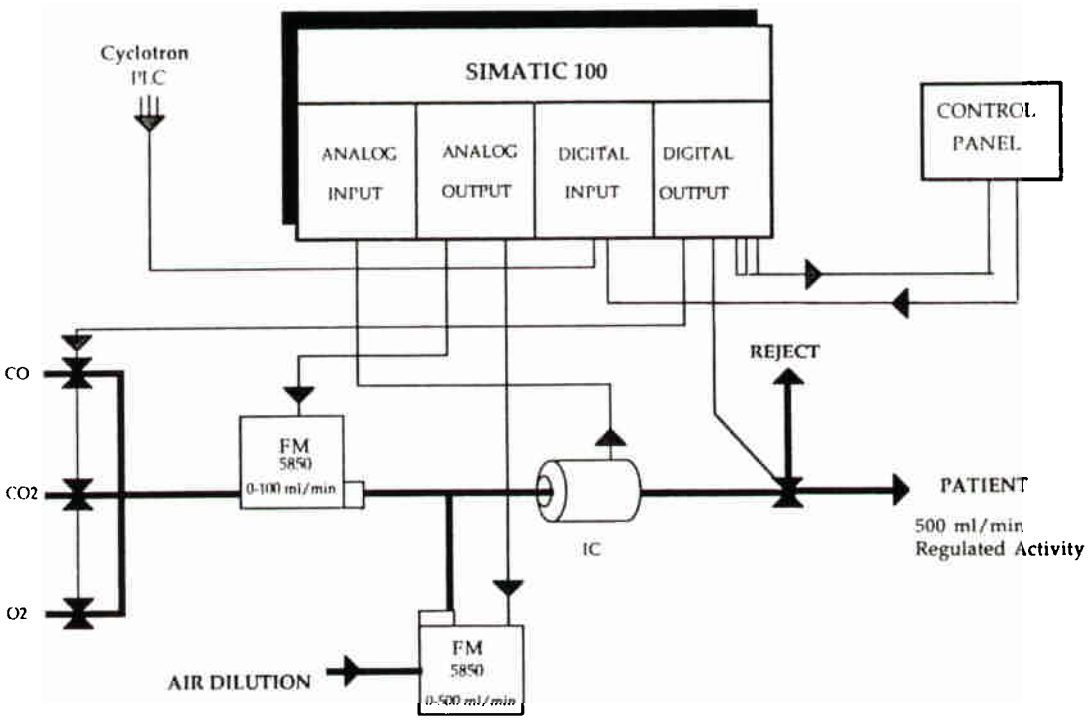
The trickiest programming problem was to realise a division by 5 in order to control the set point of the diluting flowmeter; the basic SIMATIC does not use direct division, we have only addition, substraction, and x or / by powers of 2 (shift of registers). The result of this brain-teaser is:

$$X/5 = X/4 - X/16 + X/64 - X/256 + X/1024 - X/2048 ...!!!$$

(this approach can be used for X/3 too; it is probably basic programming).

Radioactive clinical gases are controlled prior to administration by GC/Radiochromatography using a dual channel integrator, and a trace of the activity output / electrovalve position is recorded.

This regulation system allows a wide variation in the beam current on target; a very short interruption of bombardment can even pass unnoticed for the terminal user, as the active valve will open more to correct for the diminution of activity.



SCHEME I

CONCLUSION

We tried to develop some points of the basic radiochemistry system provided with the CGR-MeV cyclotron; maybe this information can be helpful for others and we hope to continue to develop systems and to contribute again to the next Targetry Workshop.

REFERENCES

1. S. Iida, J.Lab.Comp.Radiopharm., 1989, XXVI, 155-156.
2. J.C.Clark, P.D.Buckingham, Short-lived Radioactive Gases for Clinical Use, London, Butterworths, 1975.