PRODUCTION OF RADIONUCLIDES AT THE NAC CYCLOTRON FACILITY

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This report presents the status of the routine production of radionuclides, which was started seven years ago at the NAC. Various specially-designed and built facilities and specially-developed production procedures were successfully put into service during this period. A neutron therapy programme based on a 66 MeV proton beam dictates, for logistic reasons, the utilization of this beam (either directly or degraded) for the bombardment of production targets. A variety of radiopharmaceuticals, such as ^{18}F-FDG, ^{67}Ga-citrate, ^{81}Rb/^{81m}Kr-generators, ^{111}In-chloride, ^{123}I-sodium iodide and ^{123}I-labelled compounds as well as ^{210}Tl-chloride, are prepared for use by more than 30 hospitals, clinics and research institutions in South Africa. As part of a programme to optimize the beam utilization, the production of longer-lived radionuclides, such as ^{22}Na, ^{55}Fe and ^{133}Ba, was also started recently.

1 Introduction

From the outset, the National Accelerator Centre (NAC), with its variable-energy multi-particle separated-sector cyclotron (E_p = 200 MeV), was motivated, planned and established as a national facility for basic and applied research, the treatment of cancer and other patients with neutrons and protons, and the production of radionuclides. Joint projects with scientists from other countries were also envisaged. The cyclotron and its auxiliary facilities had to satisfy the stringent and diverse needs of the various user groups. It was designed and built by NAC staff and has been in routine operation since February 1987.

Accelerator radionuclides have been manufactured in South Africa since 1965 at the low-energy CSIR cyclotron in Pretoria. After its closure in 1988, the radioisotope production programme there was continued at the NAC. This programme is based on the utilization of a 66 MeV proton beam, which is shared, for logistic reasons, with the neutron therapy programme during part of the week.

The main emphasis is on the production of short-lived radionuclides and radiopharmaceuticals, which are supplied to more than 30 hospitals, clinics and institutions in South Africa for diagnostic nuclear medicine and research applications. To optimize the beam utilization and viability of the production programme, some long-lived radioisotopes are also produced. The current status of the production programme is discussed below and readers are also referred to previous overviews[1,2].

2 Facilities and procedures

The much higher proton energy available at the new facility has opened up new production possibilities, such as ^{18}F from natural Ne gas, ^{81}Rb/^{81m}Kr from natural Kr gas and ^{123}I from NaI targets via the indirect route ^{127}I(p,5n)^{123}Xe $\rightarrow$ ^{123}I. Consequently, new production routes had to be explored, necessitating a programme to determine excitation functions[3-11], and special production procedures as well as facilities had to be developed and established.

Targetry and Target Handling Facilities

Solid targets, in disc form (max ∅ : 2 mm), are either cut from metal rods or prepared from metal powders and salts, using compressing or melting and casting procedures, depending on the target element[12]. These targets are sealed in Al capsules which fit in holders specially designed for handling and water cooling during bombardment. The targetry makes provision for beam degradation as well as for the simultaneous bombardment of more than one target in tandem, if required. Gas targets have also been developed for the production of ^{18}F and ^{81}Rb/^{81m}Kr, from Ne and Kr gas respectively[13,14].

Target handling and transport between the processing hot cells and bombardment vault are done by means of remotely-controlled devices and a rail and transporter system. Bombardments take place in a bombardment station[15-18] fitted with a neutron shield. An even distribution of the beam over the target faces during bombardments is ensured by means of a double-magnet circular beam-sweeping device.

Chemical Procedures and Quality Control

Procedures for the recovery and purification of various radionuclides from bombarded targets, the preparation of labelled compounds as well as quality control have been developed[19-26]. Special enclosed hot cell systems (see Fig. 1) have been devised for the processing of targets and the handling of radionuclides. Ion exchange chromatography is extensively utilized for chemical separations and the transfer of liquid samples between different stages is mostly done with peristaltic pumps. A high premium is placed on quality assurance and, in order to maintain "good

manufacturing and dispensing practices" for the radiopharmaceuticals, special facilities were established. For radiometric measurements the back-up of the NAC's Radioactivity Standards Laboratory[27-28] is available.

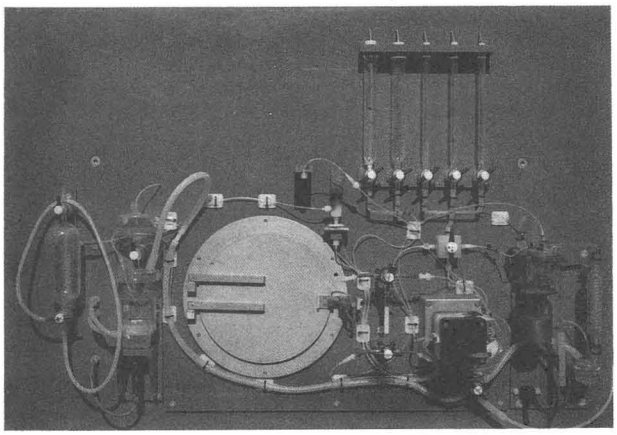

Figure 1: System for recovery of ^{67}Ga from Zn targets.

3 Beam time utilization

The cyclotron is operated on a fixed weekly schedule to accommodate the various user groups (see Fig. 2). Although time slots of 8 hours are indicated for energy changes, some of the changes (such as from 66 MeV to 200 MeV protons, or vice versa) have been streamlined to considerably shorter periods (< 2 hours), allowing more time for beam utilization. In addition, all bits of idle 66 MeV proton beam-time, including the periods when patients are being set up for neutron therapy, are used for the production of long-lived radionuclides in order to optimize beam utilization.

4 Production of radionuclides

Some targets are bombarded with beam currents as high as 80 μA (maximum currently available for 66 MeV protons). Details of the radionuclides which have been produced so far are presented in Table 1. The most important radiopharmaceuticals which are produced every week are: ^{67}Ga-citrate (300 GBq p.a.), ^{81}Rb/^{81m}Kr gas generators (139 GBq p.a.) and ^{123}I-sodium iodide and ^{123}I-labelled compounds (80 GBq p.a.). We are actively engaged in the preparation of ^{123}I-labelled compounds and a variety of products have already been prepared for evaluation and research purposes[29-31]. South Africa has not yet acquired a PET-facility but the production of ^{18}F and ^{18}F-FDG has been started for PET-type studies at institutions with dual-headed SPECT cameras, fitted with 511 keV collimators, as a forerunner to an eventual PET-programme. Gallium-67 is still being produced by the bombardment of Zn targets but, it is planned to use a tandem Ge/Zn target[32] to increase the production rate substantially as soon as the necessary procedures and facilities have been developed.

As far as the longer-lived radionuclides are concerned, over 15 GBq of ^{22}Na have already been produced in a single target. Manganese and CsCl targets have been bombarded successfully in tandem with Mg targets, and are soon to be processed for the recovery of ^{55}Fe and ^{133}Ba respectively.

MONDAY	08:00	Energy change to 200 MeV protons
	16:00	Proton therapy / Energy change to 66 MeV protons
TUESDAY	08:00	Radioisotope production
	16:00	Neutron therapy
WEDNESDAY	08:00	Experiments
	16:00	Radioisotope production
THURSDAY	08:00	Neutron therapy
	16:00	Radioisotope production
FRIDAY	08:00	Neutron therapy
	16:00	Energy change to 200 MeV protons
SATURDAY		Proton therapy calibrations, etc.
SUNDAY		Proton therapy
		Energy / Particle change
		Nuclear physics and other experiments

Figure 2: Weekly schedule of cyclotron operation.

Table 1: Production details.

Radionuclide	Production Reaction(s)	Target Material	Bombardment Energy (MeV)	Production Yield (MBq/μAh)
^{18}F	$Ne(p,X)^{18}F$	Ne	63.0 – 58.3	930
^{22}Na	$Mg(p,X)^{22}Na$	Mg	61.5 – 40.0	0.61
^{52}Fe	$Mn(p,4n)^{52}Fe$	Mn	63.3 – 48.0	12.1
^{55}Fe	$Mn(p,n)^{55}Fe$	Mn	35.2 – 11.0	0.22
^{67}Ga	$Zn(p,xn)^{67}Ga$	Zn	36.7 – 21.9	36
	$Ge(p,X)^{67}Ga$	Ge	61.5 – 38.5	75
$^{81}Rb/^{81m}Kr$	$Kr(p,xn)^{81}Rb$	Kr	52.5 – 45.0	518
	$Rb(p,X)^{81}Rb$	RbCl	62.9 – 57.7	245*
$^{82}Sr/^{82}Rb$	$Rb(p,xn)^{82}Sr$	RbCl	62.9 – 40.0	5.4
^{85}Sr	$Rb(p,xn)^{85}Sr$	RbCl	20.8 – 0	2.2 †
^{111}In	$In(p,xn)^{111}Sn \rightarrow {}^{111}In$	In/In_2O_3 (55/45)	62.6 – 54.2 , 53.0 – 43.4	27.7**
^{123}I	$I(p,5n)^{123}Xe \rightarrow {}^{123}I$	NaI	62.9 – 47.9	265***
^{133}Ba	$Cs(p,n)^{133}Ba$	CsCl	20.8 – 0	0.01
^{139}Ce	$Pr(p,X)^{139}Ce$	Pr_6O_{11}	61.5 – 20.0	83 †
^{201}Tl	$Tl(p,xn)^{201}Pb \rightarrow {}^{201}Tl$	Tl	28.6 – 21.0	11.4****

* yield at EOB for 2 h bombardment
** yield at 30 min after EOB for 1.5 h bombardment (total yield - not recovery)
*** yield at 4.5 h after EOB for 2.33 h bombardment
**** yield at 32 h after EOB for 8 h bombardment
† expected

5 Conclusion

After seven years of operation, the routine production of radiopharmaceuticals with 66 MeV protons at the NAC is well established. During this period the SSC has proved itself as one of the world's most reliable machines, with an extremely low frequency of breakdowns (which is absolutely essential for successful medical radionuclide production and particle therapy programmes). It has been demonstrated that it is possible, through proper planning, to utilize such a facility efficiently as a multidisciplinary facility to accommodate a large number of a variety of users. All the local needs for short-lived medical accelerator radionuclides are currently satisfied, and the capability exists to accommodate increased future needs of both local users and neighbouring countries.

6 References

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