# TRENDS IN CYCLOTRONS FOR RADIONUCLIDE PRODUCTION

H. VERA RUIZ
*Industrial Chemistry and Applications Section, International Atomic Energy Agency, A1400 Vienna, Austria*

R. M. LAMBRECHT
*Department of Chemistry, University of Wollongong, NSW 2522 Australia,*
*and Medical & Natural Sciences Research Center, University of Tübingen, Germany*

The IAEA recently concluded a worldwide survey of the cyclotrons used for radionuclide production. Most of the institutions responded to the questionnaire. The responses identified technical, utilisation and administrative information for 206 cyclotrons. Compiled data includes the characteristics, performance and popularity of each of the different commercial cyclotrons. Over 20 cyclotrons are scheduled for installation in 1998. The expansion in the number of cyclotron installations during the last decade was driven by the advent of advances in medical imaging instrumentation (namely, positron emission tomography (PET), and more recently by 511 KeV emission tomography); introduction of user friendly compact medical cyclotrons; and recent governmental decisions that permit reimbursement for cyclotron radiopharmaceutical studies by the government or insurance companies. The priorities for the production of clinical, commercial and research radionuclides were identified. The emphasis is on radionuclides used for medical diagnosis with SPET (e.g. $^{123}$I, $^{201}$Tl) and PET (e.g. $^{11}$C, $^{13}$N, $^{15}$O, $^{18}$F) radiopharmaceuticals, and for individualised patient radiation treatment planning (e.g. $^{64}$Cu, $^{86}$Y, $^{124}$I) with PET. There is an emerging trend to advance the cyclotron as an alternative method to nuclear reactors for the production of neutron-rich radionuclides (e.g. $^{64}$Cu, $^{103}$Pd, $^{186}$Re) needed for therapeutic applications.

## 1 Introduction

The Directory of Cyclotrons used for radionuclide production is an update of the data base on cyclotrons that was compiled in 1982 by the International Atomic Energy Agency. The Directory contains technical, utilisation and administrative information supplied to the Agency as of October 1997. The Directory was prepared through information collected by questionnaires sent to institutions that either have a cyclotron , or that were identified to be in the process of installation of a cyclotron. The Directory [1] is considered to include most of the cyclotrons of the world that are used at least in part for radionuclide production because most of the institutions responded. A few institutions declined to participate for reasons of their own.

### 1.1 Number of Cyclotrons

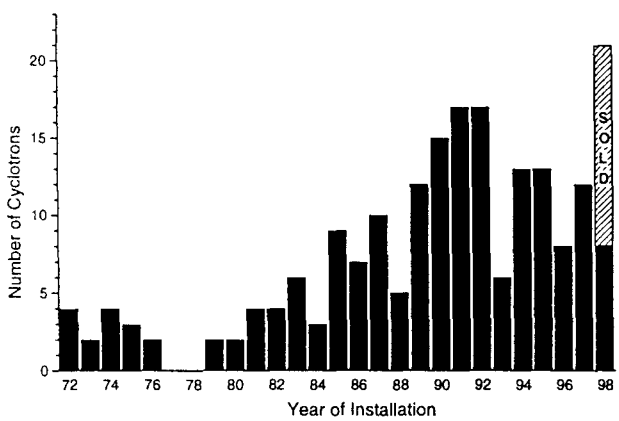


**Figure 1. Number of cyclotrons commissioned since 1972**

Figure 1 depicts the number of cyclotrons used for radionuclide production, and the year of installation. The expansion in number of cyclotrons during the last decade are driven by the advent of advances in medical imaging instrumentation (namely, positron emission tomography (PET), and more recently be 511 KeV emission tomography); introduction of user friendly compact medical cyclotrons from several companies that manufacturer and install cyclotrons; and recent decisions that $^{15}$O-oxygen PET studies in Japan, and $^{18}$FDG PET studies in Germany are eligible for re-imbursement by government or insurance companies. A emerging trend is to integrate a low energy cyclotron into corporations formed by physicians in private practice. Another factor contributing is the introduction of the PETNET concept of distribution of positron emitting radiopharmaceuticals from a central cyclotron to satellite hospitals that have the imaging technology and the patients, but not the cyclotron.

### 1.2 Choice of Cyclotron

Table 1 summarises the characteristics of the cyclotrons that are presently manufactured by eight (8) different companies. It is interesting to note the trends in the number of particle, beam energy of the installed cyclotron, as well as the contemporary trend in characteristics of the cyclotrons.
Table 2 summarises the expected production yields of the most commonly used $^{11}$C, $^{13}$N, $^{15}$O and $^{18}$F precursors required to synthesise PET radiopharmaceuticals

### 1.3 Priorities of Medical Radionuclides

Table 3 provides a definition of the priorities for cyclotron produced radionuclides. There are 52 radionuclides listed of which 5 are generator systems. The driving force for new cyclotron installations is the production of positron emitting radiopharmaceuticals for PET.

Table 1. Statistics concerning cyclotrons (October 1997)

| Model | Description | Number of Cyclotrons: Operational | Number of Cyclotrons: Being installed |
|---|---|---|---|
| **CTI, Inc.** | | | |
| RDS 111 | 11 MeV $H^-$ | 5 | 10 |
| RDS 112 | 11 MeV $H^-$ | 22 | 1 |
| **EBCO TECHNOLOGIES** | | | |
| TR 13 | 13 MeV $H^-$ | 2 | |
| TR 19 | 10-19 MeV $H^-$ | 1 | |
| TR19/9 | 10-19 MeV $H^-$, 5-9 MeV $D^-$ | 0 | |
| TR 30 | 15-32 MeV $H^-$ | 1 | |
| TR 30 | 15-32 MeV $H^-$, 15 MeV $D^-$ | 1 | |
| **D.V. EFREMOV INSTITUTE** | | | |
| MGC-20 | 18 MeV p, 10 MeV d | 3 | 2 |
| **General Electric** | | | |
| PETtrace | 16.5 MeV $H^-$, 8.4 MeV $D^-$ | 8 | 3 |
| **Ion Beam Applications s.a.** | | | |
| CYCLONE 3 | 3.8 MeV d | 0 | 4 |
| CYCLONE 10/5 | 10 MeV $H^-$, 5 MeV $D^-$ | 1 | 2 |
| CYCLONE 18/9 | 18 MeV $H^-$, 9 MeV $D^-$ | 7 | 4 |
| CYCLONE 18+ | 18 MeV | 4 | 6 |
| CYCLONE 30 | 15-30 MeV $H^-$, 15 MeV $D^-$ | 16 | 1 |
| CYCLONE 235 | 240 MeV p | 1 | 3 |
| **JAPAN STEEL WORKS LTD.** | | | |
| BC168 | 16 MeV p, 8 MeV d | 4 | |
| BC1710 | 17 MeV p, 10 MeV d | 8 | |
| BC2010N | 20 MeV $H^-$, 10 MeV $D^-$ | 1 | |
| BC2211 | 22 MeV p, 11 MeV d | 1 | |
| BC3015 | 30 MeV p, 15 MeV d | 1 | |
| **OXFORD INSTRUMENTS GROUP PLC** | | | |
| OSCAR | 12 MeV $H^-$ | 7 | 3 |
| Isotrace(Superconducting) | | | |
| **SCANDITRONIX MEDICAL AB** | | | |
| MC17 | 17.2 MeV p, 8.3 MeV d 12 MeV $^3He$, 16.5 MeV $^4He$ | 16 | |
| MC30 | 30 MeV p, 15 MeV d | 1 | |
| MC32NI | 15-32 MeV $H^-$, 8-16 MeV $D^-$ 11-23 MeV $^3He$, 15-31 MeV $^4He$ | 2 | |
| MC40 | 10-40 MeV $H^-$, 5-20 MeV $D^-$ 13-53 MeV $^3He$, 10-40 MeV $^4He$ | 8 | |
| MC50 | 18-52 MeV $H^-$, 9-25 MeV $D^-$ 24-67 MeV $^3He$, 18-50 MeV $^4He$ | 2 | |
| MC60 | 50 MeV p | 1 | |
| K130 | 6-90 MeV $H^-$, 10-65 MeV $D^-$ 16-173 MeV $^3He$, 20-130 MeV $^4He$ | 1 | |
| **SUMITOMO HEAVY INDUSTRIES LTD** | | | |
| CYPRIS 325 | 16 MeV p, 8 MeV d | 2 | |
| CYPRIS 370 | 16 MeV p, 10 MeV d | 6 | 1 |
| HM 18 | 18 MeV $H^-$, 10 MeV d | 6 | 2 |
| HM 12 | 12 MeV p, 6 MeV d | 0 | 1 |
| 480 AVF | 30 MeV p | 1 | |
| AVF 680 | 40 MeV p | 1 | |
| AVF 715 | 50 MeV p | 1 | |
| AVF 750 | 70 MeV p | 2 | |
| AVF 930 | 90 MeV p, 35 MeV d (K = 110) | 2 | |
| AVF 1000 | 80 MeV p (K = 140) | 1 | |
| Ring Cyclotron 400 | 400 MeV p, (K = 400) | 1 | |
| Ring Cyclotron 540 | 240 MeV p, (K = 540) | 1 | |
| C 235 | 240 MeV $H^-$ | 1 | |

**Table 2. Expected production yield (mCi) of synthetic precursors of PET radiopharmaceuticals with selected proton and deuteron energies and irradiation at 20 μA to 35 μA as recommended by the manufacturer of the various cyclotrons**

| Precursor | 16-18 MeV p 8-9 MeV d | 9-10 MeV p 4-5 MeV d | 12-13 MeV p |
|---|---|---|---|
| $^{11}CO_2$ | 2800 | 1000 | 1500 |
| $^{11}CO$ | 1400 | 350 | 1000 |
| $^{11}CH_3I$ | 700 | 350 | 1250 |
| $^{11}CNH$ | 1200 | 250 | 750 |
| $^{13}NH_3$ | 450 | 100 | 200 |
| $^{15}O_2$ | 1200 | > 150 per min. | 1000 |
| $^{15}OC$ | 700 | > 75 per min. | 500 |
| $^{15}OCO$ | 700 | > 150 per min. | 500 |
| $^{15}OH_2$ | 1000 | 200 | 750 |
| $^{18}F^-$ | 800 | > 500 | 700 |
| $^{18}FF$ | 300 | | |

**Table 3. Priorities for cyclotron radionuclides**

| Application | Radionuclide |
|---|---|
| **PET and 511 KeV SPET** | |
| Emphasis on: | $^{11}C$, $^{13}N$, $^{15}O$, $^{18}F$ |
| Emerging | $^{64}Cu$, $^{124}I$ |
| Research Interest | $^{38}K$, $^{45}Ti$, $^{62}Zn$ / $^{62}Cu$, $^{73}Se$, $^{75}Br$, $^{76}Br$, $^{82m}Rb$, $^{94m}Tc$, |
| **SPET** | |
| Clinical | $^{67}Ga$, $^{111}In$, $^{123}I$, $^{201}Tl$ |
| Therapeutic | $^{64}Cu$, $^{67}Cu$, $^{103}Pd$, $^{186}Re$, $^{211}At$ |
| **Standards and Sources** | $^{22}Na$, $^{57}Co$, $^{139}Ce$ |
| **Commerical -Medical** | $^{18}F$, $^{67}Ga$, $^{81}Rb$ / $^{81m}Kr$, $^{103}Pd$, $^{123}Xe$ / $^{123}I$, $^{201}Pb$ / $^{201}Tl$ |
| Emerging | $^{124}I$ |
| Various | $^{22}Na$, $^{57}Co$, $^{88}Y$ |
| **Others** | $^{7}Be$, $^{10}C$, $^{28}Mg$, $^{48}V$, $^{75}Se$, $^{87}Y$ / $^{87m}Y$, $^{93}Mo$, $^{99m}Tc$, $^{147}Gd$, $^{195}Au$, $^{206}Bi$ |

There are reports that

1) A 2 hour irradiation at 65 μA with 12 MeV protons on a a single recirculating $H_2{}^{18}O$ (> 98%) target yields > 4 Ci of $^{18}F$-Fluoride;
2) The simultaneous irradiation of two targets of $H_2{}^{18}O$ (>98 %) with a 18 MeV cyclotron can produce > 5 Ci of $^{18}F$-Fluoride.
3) There are cyclotron gas targets available that are routinely operated at 25 to 50 μA for production of $^{11}C$ and $^{15}O$

Fluorine-18 ($^{18}$FDG), Oxygen-15 (Water, Oxygen, Butanol and Carbon Monoxide), Carbon-11 (Acetate, Methionine), and Nitrogen-13 (Ammonia) are the most widely used positron emitting radiopharmaceuticals. Essentially all PET centers regularly produce $^{18}$FDG for clinical use. In addition a significant number of center also use specific $^{18}F$ and $^{11}C$ labelled ligands for neuroreceptor studies. These include: $^{18}$F-DOPA, $^{18}$F-Altanserin $^{11}$C-Raclopride, $^{11}$C-Flumazenil, $^{11}$C-WAY 100635, $^{11}$C-SCH 23390, etc.
Many research orientated institutions have radiochemists developing a wide range of radiopharmaceuticals and labeled compounds for diagnosis and or monitoring treatments of various diseases.

It is noteworthy to mention that some institutions commit excess beam time for either solid target irradiation's for companies, or act as a distribution center of radiochemicals or radiopharmaceuticals to customers in the region of the cyclotron facility.

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## References

[1] Directory of Cyclotrons Used for Radionuclide Production in Member States, IAEA-TECDOC-1007, International Atomic Energy Agency, Vienna, March (1998).