COMMERCIAL COMPACT CYCLOTRONS IN THE '90s

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Cyclotrons continue to be efficient accelerators for radio-isotope production. In recent years, developments in the accelerator technology have greatly increased the practical beam current in these machines while also improving the overall system reliability. These developments combined with the development of new isotopes for medicine and industry, and a retiring of older machines indicate a strong future for commercial cyclotrons. In this paper we will survey recent developments in the areas of cyclotron technology, as they relate to the new generation of commercial cyclotrons. Design criteria for the different types of commercial cyclotrons will be presented, with reference to those demands that differ from those in a research oriented cyclotron project. We will also discuss the possibility of systems designed for higher energies and capable of extracted beam currents of up to 2.0 mA.

1 Introduction

For many decades accelerators have been used to produce proton-rich isotopes, as a complement to the neutron-rich isotopes produced in reactors. Initially this production was done in a parasitic mode, on accelerators originally constructed for nuclear physics research. However over the past couple of decades there has been a large number of commercial facilities designed solely for the production of isotopes. In particular the production of isotopes with long enough half-lives that regional distribution is practical, and yet sufficiently short that "just-in-time" production is required, has developed into a specific market. In this market cyclotrons in the energy range of 20 to 40 MeV have become the accelerator of choice. Two firms, Ion Beam Applications (IBA) and Ebco Technologies are currently producing cyclotrons to serve this market.

The production of PET isotopes also represents a significant new market. The requirements of these very short-lived isotopes however leads to different approaches. In particular they must be produced at or very near the PET centre, and the required beam currents for adequate make-rates are much lower, typically in the few tens of micro-amps. Both IBA and Ebco have adapted their larger cyclotron designs for PET production use. In the PET market these two firms are joined by Oxford Instruments with their superconducting cyclotron OSCAR [1], and by CTI with their conventional second generation cyclotron the RDS-112.

In recent years a couple of other commercially designed cyclotrons have been produced for specialized applications. At Michigan State University a 50 MeV, superconducting deuteron cyclotron was constructed for neutron therapy at Harper Grace Hospital in Detroit [2]. This cyclotron has an internal neutron production target, and revolves around the patient on an isocentric gantry. In this manner expensive beam swinger hardware is not required. This cyclotron is presently marketed by IBA under license from MedCyc corp.

IBA is also currently developing a 235 MeV proton cyclotron[3] to be used in proton therapy at Massachusetts General Hospital in Boston. While not exactly a compact cyclotron it shares many characteristics of its smaller kin. It remains to be seen how this cyclotron will compare with the synchrotron[4] currently operating at Loma Linda Hospital in California.

Cyclotron technology has matured significantly since EO Lawrence built the first one in 1929. Over time we have learned to make systems that are reliable and relatively simple to operate. Also being circular machines, cyclotrons are very compact, and therefore require minimal shield volumes compared to other accelerators. For these reasons cyclotrons are a particularly appropriate technology for the commercial environment. For most of the applications mentioned above, the high energy efficiency of cyclotrons and continuous wave (CW) beam delivery are deemed advantageous.

2 The Commercial Isotope Market

In North American and Asia the cyclotron produced isotope business has grown about 20% per year for the past decade, predominantly reflecting the increased use of ^{201}Tl in the US and ^{123}I products in Japan. While the Japanese market is expected to continue to grow (10%/yr) for the next few years, many people have predicted that the ^{201}Tl usage in North America will decline although no evidence of this has yet emerged. While other products continue to be developed, none have truly blossomed. Therefore the market stability is hard to predict, and this generates uncertainty when making decisions about future facilities. The most important commercially produced isotopes used in medicine are shown in table 1. Aside from medical isotopes, there is significant trade in ^{57}Co (produced using ^{58}Ni(p,2n)^{57}Co at 23 MeV), which is used for material inspection, pipeline leak detection and other industrial purposes. However because of its long half life (271 days), it can be inventoried avoiding many of the rigors of medical isotope production. It should also be noted that all these isotopes

Table 1: The most common cyclotron produced radioisotopes used in medicine.

Radio-Isotope	Reaction	Half-Life
Thallium	$^{203}Tl(p,3n)^{201}Pb$ $^{201}Pb \rightarrow {}^{201}Tl$	73.5 hr
Gallium	$^{68}Zn(p,2n)^{67}Ga$	78.3 hr
Iodine	$^{124}Xe(p,2n)^{123}Cs$ $^{123}Cs \rightarrow {}^{123}Xe \rightarrow {}^{123}I$	13.2 hr
Indium	$^{112}Cd(p,2n)^{111}In$	67.2 hr
Bromine	$^{78}Kr(p,2n)^{77}Rb$ $^{77}Rb \rightarrow {}^{77}Kr \rightarrow {}^{77}Br$	57 hr

can be optimally produced at beam energies less than 30 MeV. As a result 30 MeV machines have become the cyclotron of choice for this market.

The commercial production of short-lived isotopes, imposes certain important conditions and constraints on the business. In particular;

- Irradiation, processing and shipping are on a "just-in-time" basis.
- Round the clock operation
- Weekly scheduling with much flexibility to handle customer requirements and recover from system failures.
- Costs are dominantly fixed, ie. little scaling with the level of production (for a given facility).
- Radiation dose accumulated by maintenance and repair personnel represents a serious cost component.

To respond to these requirements, the cyclotron system must be reliable, flexible, and designed to minimize personnel dose. As the market for isotopes matured, producers learned that the increased cost of production enhancing features in these areas could be quickly recovered. As a result there has been a demand for cyclotrons designed to specifically meet this market.

3 The PET Isotope Market

The most commonly used radio-isotopes in Positron Emission Tomography (PET) are shown in table 2. As can be seen, all these isotopes have very short half lives, the longest being less than two hours. As a result these isotopes must be produced in the same city as the PET camera system is located. In most cases this is done on a cyclotron owned by the hospital performing the PET scans. In all cases sufficient activity for a normal day's needs can be produced in less than 1 hour at beam currents below 20 μA. As well these production rates can be achieved using a proton beam with an energy of only 11 to 13 MeV.

Table 2: Principle PET Radiochemicals

Radio-Chemical	Reaction	Half-life
FDG, F_2 Gas, FDOPA	$^{18}O(p,n)^{18}F$	110 min
CO, CO_2, HCN, CH_3I	$^{14}N(p,\alpha)^{11}C$	20 min
Ammonia	$^{16}O(p,\alpha)^{13}N$	16 min
O_2, H_2O, CO, CO_2	$^{15}N(p,n)^{15}O$	122 sec

These requirements are very modest for a cyclotron. As a result the driving goal in this market has been to produce cheap yet very reliable and easy to operate accelerator systems. As well since most hospitals wish to purchase complete systems, these cyclotrons are marketed with a variety of targets and fully automated chemistry systems.

4 Commercial Cyclotron Generations

The first generation of cyclotrons built solely for commercial production of isotopes appeared in 1965. These machines were often the simplest and cheapest possible derivatives of the research machines. Representative of these machines would be the CS series produced by The Cyclotron Corporation (TCC) and the early MC series produced by Scanditronix. These cyclotrons were usually proton-only machines, with internal sources and internal production targets.

In the 1970's TCC proposed to construct a cyclotron to accelerate H^- particles. With simplified extraction from the cyclotron, this allowed improved targetry, and offered a fully variable energy. This machine[5] was called the CP42, as it maximum energy would be 42 MeV. Five of these machines were ordered even before a working prototype had been constructed. Unfortunately the effort to bring these machines online contributed to the downfall of TCC. However all but one of these machines are still in operation and several form a key component of isotope production programs. Other cyclotron designs that fall into the 2^{nd} generation designation are the RDS-

112 built by CTI and the MC32NI from Scanditronix.

In 1984 Yves Jongen [6], then at Cyclotron Laboratory at University of Louvain in Louvain-la-Neuve, proposed that advances in the technology would allow significant improvements in H^- cyclotrons, and that a new attempt to market them should be made. This proposal subsequently spawned the formation of Ion Beam Applications (IBA), by Dr Jongen. With initial government funding, a prototype 30 MeV cyclotron (the CYCLONE 30) was constructed. This machine rapidly met design goals [7], and stimulated strong interest from many commercial isotope producers.

One such producer was Nordion International located in Vancouver. After discussions with people at TRIUMF, it was decided that a Vancouver firm Ebco, would produce a similar cyclotron for Nordion using technology developed at TRIUMF. This cyclotron [8] was called the TR30. As third generation commercial cyclotrons, the TR30 and the CYCLONE 30 share many characteristics. However different philosophies resulted in machines with different strengths.

Subsequently each firm has produced cyclotrons of lower energy for different markets, most notably for PET. For Ebco Technologies this was the TR13, also capable of being produced as a TR19/8, and for IBA there are the CYCLONE 18/9 and CYCLONE 16/8, (note these latter two have internal ion sources). Table 3 lists most of the commercially manufactured cyclotrons available today.

5 The choice of H^-

As in all circular accelerators, one of the most difficult problems is extracting the beam once it has reached the desired energy. For positive ion cyclotrons only in a few exceptional cases have extraction efficiencies as high as 98% been meet, and efficiencies in the 75% region are not uncommon. Isotope production machines need to be reliable yet operate at high current with moderate spills. It is very hard to meet these requirements with a positive ion machine with extracted beams.

Internal targets are limited to metallic compounds, and each of the frequent target changes affects the main tank vacuum. As well they provide very little flexibility as to the shape and distribution of the beam on target, while beam diagnostics are very difficult. Finally and perhaps most importantly their use means that the neutrons created in the target produce induced radioactivity in the cyclotron components. Typically fields of many Rads are present after a few years of operation, making hands on maintenance very difficult. By contrast if H^- particles are accelerated, they can be extracted simply by stripping, using a thin foil to intercept the beam.

However everything has its counter-balancing problems. The second H^- electron is fairly weakly bound

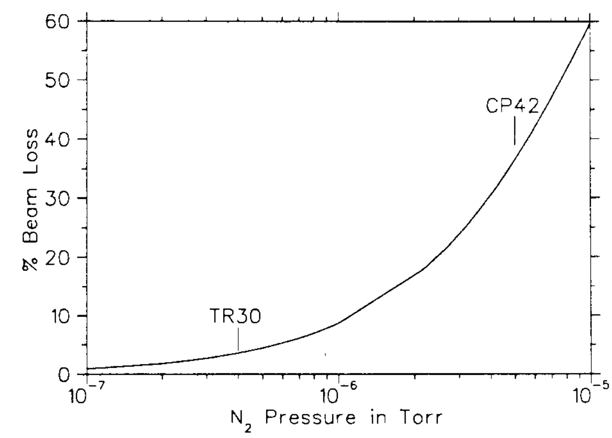


Figure 2: Beam losses due to gas stripping as a function of pressure for a 30 MeV cyclotron.

(0.755 eV) and so may be lost due to interaction with the background gas (vacuum stripping), or by electromagnetic disassociation. This lost beam causes heating and induces significant radioactivity in the cyclotron components. To reduce vacuum stripping, H^- cyclotrons need to operate at vacuum pressures at least one order of magnitude better than proton machines, for the same loss ratios. Electro-magnetic stripping is easily avoided at low energies, but becomes a significant problem at higher energies (eg. The TRIUMF Cyclotron). For commercial cyclotrons, the aim is to keep losses due to electro-magnetic stripping below a few percent in the worst case. For example losses due to EM stripping have been estimated to be less than 0.01% in the TR30.

6 Improvements of the Third Generation

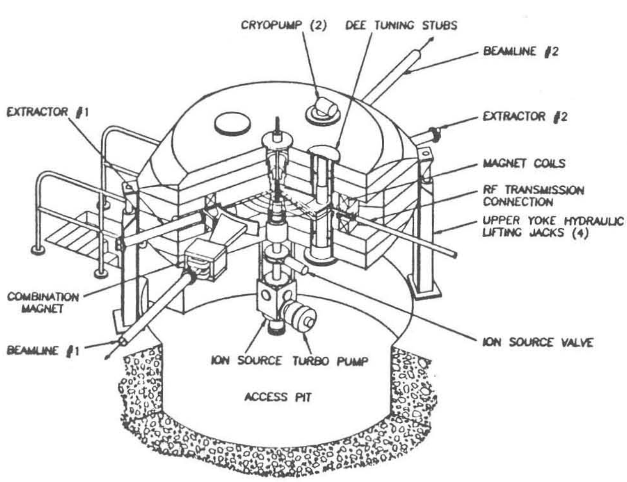
The third generation commercial cyclotrons offer significant improvements over previous generations. Examples of these machines are shown in the schematic drawings of figure 1. Perhaps the most obvious change is the use of external ion sources. Made possible by recent advances in high current DC H^- sources, this modification removes the high hydrogen gas load of the ion source to outside of the main cyclotron vacuum. Combined with cleaner pumping systems (commercial cyropumps are preferred), the third generation cyclotrons operate in the low 10^{-7} Torr range compared to the mid 10^{-6} Torr range of the CP42. The effect on stripping losses is shown in figure 2. Having the ion source outside, also makes ion source maintenance easier. On these machines the source filaments are typically changed every three weeks, but since this does not involve the main vacuum system it can be performed in a matter of a few hours.

Traditionally cyclotrons under 100 MeV have used

Table 3: Available compact commercial cyclotrons used for isotope production

Supplier	Model	Particle Accelerated	Energy MeV	First Operation	Number Sold	Source Type	External μA	Internal μA
IBA	Cyclone 10/5	H^-,D^-	10/5	1988	2	Internal	100	
IBA	Cyclone 18$^+$	H^+	18	1994	4	Internal		2000
IBA	Cyclone 18/9	H^-,D^-	18/9	1992	8	Internal	100	
IBA	Cyclone 30	H^-	30	1986	16	External	500	
Ebco	TR13	H^-	13	1994	2	External	150	
Ebco	TR30	H^-	30	1990	1	External	600	
Ebco	TR30/15	H^-,D^-	30/15	1994	1	External	400	
GE	PETtrace	H^-,D^-	17/8.5	1992	10	Internal	100	
JSW	BC168	H^+,D^+	16/8	1982	4	Internal	70	150
JSW	BC1710	H^+,D^+	17/10	1981	8	Internal	70	150
JSW	BC2010N	H^-,D^-	20/10	1995	1	Internal	70	100
JSW	BC2211	H^+,D^+	22/11	1989	1	Internal	70	150
JSW	BC3015	H^+,D^+	30/15	1985	1	Internal	70	150
NIIEFA	PIC-10	H^-	11	1996	0	Internal	50	
NIIEFA	MGC-20	H^+,D^+	18/10	1974	8	Internal	100	200
SCX	MC30	H^+	30	1987	1	Internal		500
SCX	MC32NI	H^-,D^-	32/16	1990	2	Internal	60	
SCX	MC35,40	H^+,D^+	40/20	1979	12	Internal	75	300
SCX	MC50	H^+,D^+	50/25	1989	2	Internal	50	200
SCX	MC60PF	H^+	60	1984	1	Internal	35	100
Oxford	OSCAR	H^-	12	1990	9	External	100	
CTI	RDS-112	H^-	11	1987	21	Internal	100	

IBA	Ion Beam Applications Chemin du Cyclotron B-1348 Louvain-la-Neuve Belgium
Ebco	Ebco Technologies 7851 Alderbridge Way, Richmond B.C. V6X 2A4 Canada
GE	General Electric Medical Systems, Husbyborg S-75229 Uppsala, Sweden
JSW	Japan Steel Works 4 Chatsumachi, Muroran, Hokkaido Japan
NIIEFA	Efremov Scientific Research Inst. St Petersburg, 189631 Russia
SCX	Scanditronix, Husbyborg S-75229 Uppsala, Sweden
CTI	CTI PET Systems, 810 Innovation Drive, Knoxville, TN 37932 USA



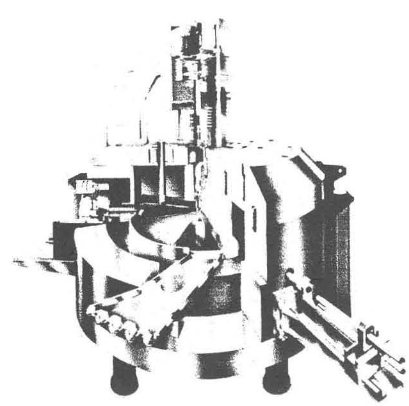


Figure 1: Schematic views of the TR30 cyclotron (on left) and the CYCLONE 30

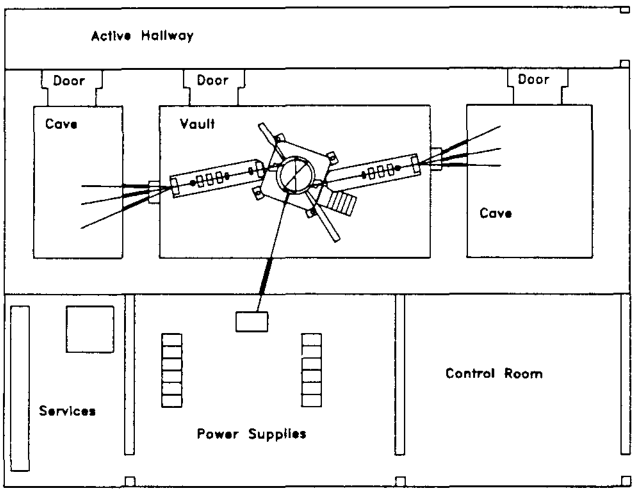


Figure 3: A typical layout for a third generation cyclotron being used for isotope production

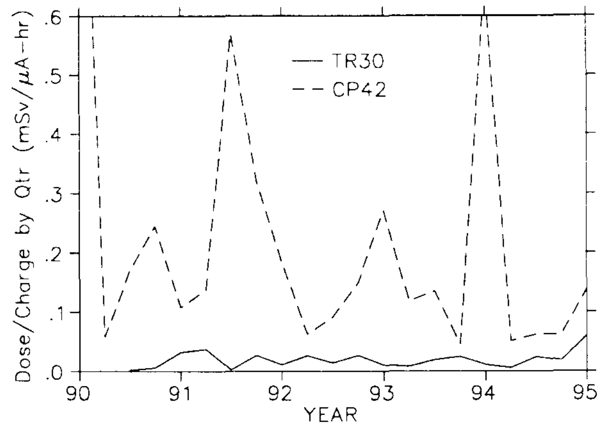


Figure 4: Accumulated personnel radiation dose, by quarter for the TR30 and CP42 cyclotron. Major repairs lead to the large spikes in the CP42 curve.

H frame magnet designs. However both of the third generation manufacturers have opted for the pill box shaped magnets initially used in the superconducting cyclotrons [9]. As shown in the layouts in figure 1, the yoke steel completely surrounds that vacuum chamber except for small holes to allow access to the median plane and for beam extraction. In both cases the RF systems are completely contained in the relatively deep valleys, and no trim coils used. Pole faces are used to form the top and bottom of the vacuum vessel, so no vacuum liner is required. All these items allow for a small magnet gap in the hill region (30-40 mm), but nearly all this space is available for beam. This particular hill/valley combination generates strong vertical focussing and significantly reduces the magnet power consumption. Careful attention to the beam dynamics, combined with the increased control offered by the external ion source has resulted in improved beam quality. With smaller halos and better uniformity, the beams from these cyclotrons are more stable and are less prone to hot spots on target.

In third generation cyclotrons the beam is always extracted and transported in a beamline away from the machine. A typical facility layout is shown in figure 3. As can be seen the isotope production targets are located in target caves that are completely shielded from the main cyclotron vault. In the facility shown, the beamline has been optimized so that all elements are located in the vault. During operation neutron fields in the target caves are several orders of magnitude higher than in the cyclotron vault. This division reduces the radiation damage to cyclotron and beamline components, and results in fairly low residual fields in the vault, thus making service much easier. Target systems on the other hand must be designed for fully remote operation, easy maintenance and the use of radiation hard components throughout.

Many of the above mentioned improvements are aimed at reducing the amount of unnecessary induced radioactivity. In cases where some beam interception is unavoidable, the new machines use low activation materials, typically those with short half lives such as carbon. The results of these efforts have been very successful. As an example we offer a comparison of accumulated personnel dose between the CP42 and TR30 machines operating at TRIUMF in figure 4. As seen in the figure there is nearly an order of magnitude improvement over the previous generation, particularly when compared on a dose per charge delivered basis. This improvement represents both a significant cost saving and an improved work environment for the staff.

The third generation machines also sport more sophisticated control systems using industrial programmable logic controllers (PLCs) and commercial graphics based user interfaces. There has also been a trend to remove equipment such as power supplies from the vault. These changes tend to improve operator efficiency, and reduce downtime.

All these improvements lead to increased average operating beam current, and lower costs to produce isotopes. While typical CP42 operation is limited to extracted beams of 150 to 200 μA, the CYCLONE 30 is guaranteed to deliver 350 μA and the TR30 400 μA. In fact however, versions of these machines are operating regularly at currents in excess of 500 μA. As an example of the improved production capability of these machines, in figure 5 we compare the charge delivered on target for the TR30 with that for the CP42, and in table 4 we show production rates for a typical commercial isotope (^{201}Tl), as a function of year.

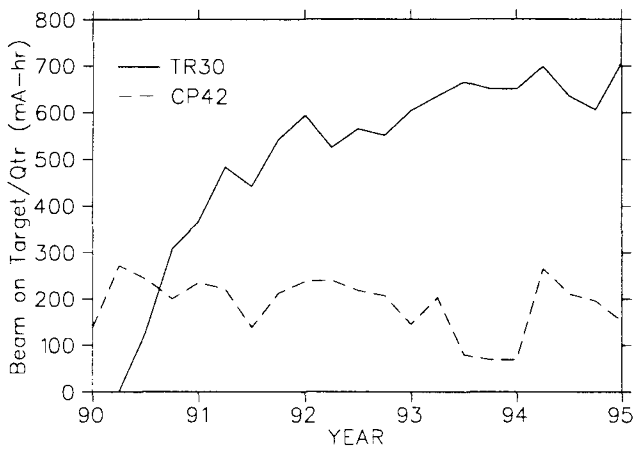


Figure 5: Total charge delivered on target each quarter by the TR30 and CP42 cyclotrons located at TRIUMF, and owned by Nordion Int.

Table 4: Make Rates of ^{201}Tl for representative Commercial Cyclotrons

Year	Cyc.	Current (μA)	Energy (MeV)	Make-Rate (mCi/beam-hr) [EOB+56hrs]
1989	CS30 CP42	350 180	26.5 29	190 160
1992	CYC30 TR30	360 360	29 29	320 320
1994	TR30	440	29	400
1995	TR30	800	29	710
1996	TR30	1000	29	890

Table 5: Installed and operating commercial cyclotrons used for isotope production

	1989	1992	1995
Europe	8 H^+ 2 H^-	8 H^+ 4 H^-	8 H^+ 6 H^-
North America	13 H^+ 1 H^-	13 H^+ 4 H^-	13 H^+ 5 H^-
Asia-Pacific	5H^+	5 H^+ 4 H^-	4 H^+ 10 H^-
Total H^+ Total H^-	26 3	26 12	25 21
Total No. Cyc.	29	38	46

7 Sales

Over the years sales of commercial cyclotrons has fluctuated, but there has been steady growth. As shown in table 5, all cyclotrons purchased since 1989 to be used for the production of commercial isotopes have been third generation cyclotrons. (Note: Four CYCLONE 18$^+$ machines have been purchased recently for a very specific isotope production and are not include in our table, these are positive ion machines.) This shows their complete dominance of the market place.

In recent years it has been indicated that the regulatory agencies in several countries intend to lower the dose that may be accumulated by atomic energy workers. Should this happen, there will be added incentive for many isotope producers to replace their aging first generation cyclotrons with the cleaner third generation machines.

8 Future

In the past month a successful collaboration between Nordion International and TRIUMF to upgrade Nordion's TR30 has resulted in extracted beam currents in excess of 1 mA. Figure 8 shows a recent beam test with an extracted beam current of 970 μA over an 8 hour period. We expect to demonstrate 1.2 mA by the end of the year. These initial runs have shown the cyclotron to be very stable at these currents. As well this collaboration demonstrated[10] beam currents of 2 mA in a 1 MeV

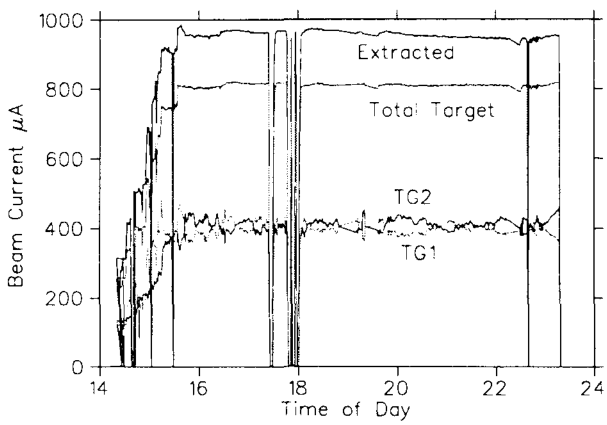


Figure 6: Initial high current beam test with the TR30 cyclotron

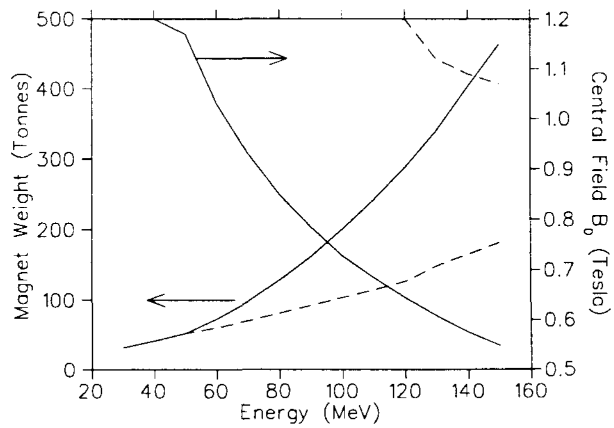


Figure 7: Required Magnet Sizes as a function of Energy for a H^- Cyclotron. The electro-magnetic stripping losses have been constrained to be less than 2% on the solid curves.

model of the TR30 central region. It is therefore reasonable to assume that commercial H^-cyclotrons will soon be operating in this regime. However significant target development work will be necessary as targets capable of handling 1 mA are only now being developed.

An isotope with increasing potential for clinical PET studies is $^{82}Sr/^{82}Rb$ generator systems. As a generator system, it again lends itself to distribution from a central facility, making it very different from most other PET isotopes, that require an onsite production facility. Presently this isotope is produced in North America on higher energy accelerators employing spallation from molybdenum, or by bombardment of rubidium metal with 60-80 MeV protons [11]. The ability to produce this generator has been a strong driving force in the design of cyclotron systems under consideration for the U.S. National Biomedical Tracer Facility [12]. Preliminary studies indicate that the design principles used in the current generation of cyclotrons could be extended to the required 80 MeV. The dominant factor limiting the practical energy of a H^- cyclotron, is electromagnetic stripping of the H^- during acceleration. To reduce activation of the accelerator systems, caused by the resulting beam spill, these losses should be kept to the few percent level. This requires substantially lower central magnetic field values (B_0) with increasing energy, which in turn leads to a very rapid rise in magnet size. In figure 7, the basic system features are held constant except B_0 which is reduced to maintain low stripping losses. This constraint is not maintained for the dashed curves, which are only adjusted to maintain vertical focussing in the centre. (Note: For all cases above 90 MeV the dashed curve would result in 100% beam loss.) It would be possible to make modifications such as increasing the dee voltage, or widening the hills, and thus reduce the cyclotron size. However these changes will also increase the complexity of the overall system. It should also be noted that the reduction in average field will reduce the vertical focussing. It will lower the RF frequency, making the resonators significantly larger. While these considerations do not provide a hard limit on the maximum possible energy, 80 MeV seems to be a practical compromise between the still increasing production cross-section and the accelerator size.

At the present time work is proceeding on production of ^{68}Ge that is a generator for ^{67}Ga. The generator would be produced using $^{69}Ga(p,2n)^{68}Ge$ at proton energies around 26 MeV. At present this isotope is used to calibrate PET cameras. However in the future it is expected to be used as a PET tracer. As such it should become commercially significant in the near term.

There is also hope that cyclotrons can be used to produce some of the isotopes currently produced in aging reactors. One already successful example of this is the production of palladium 103 seeds for brachytherapy with 18 MeV protons. There are also proposals [13] for a cyclotron driven sub-critical neutron source for the production of molybdenum 99, the generator for technetium 99, the most frequently used radio-isotope in nuclear medicine. Such a proposal would require a cyclotron with an energy of 150 MeV and beam currents as high as 1.5 mA. As shown in figure 7, this results in a very large cyclotron. There are also significant technical challenges to be handled at these beam powers. However given the present cost of constructing reactors, this proposal deserves serious consideration.

9 Conclusion

In the thirty years of commercial cyclotrons, the industry has evolved significantly. After some financially difficult times, the industry appears to be considerably more stable. However sales tend to fluctuate on a year to year basis depending on different perception of market possibilities. Nevertheless cyclotron designers continue to increase the capability of these machines so we expect to see many new developments in the next few years. Sales of PET cyclotrons will also probably continue to grow but not as rapidly as predicted a few years ago. In the PET market the dominate effort will be to reduce the costs of the cyclotrons while improving reliability.

10 Acknowledgements

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