FUTURE CYCLOTRON SYSTEMS : AN INDUSTRIAL PERSPECTIVE

N.R. STEVENSON

TRIUMF, 4004 Wesbrook Mall, Vancouver, B.C., Canada V6T 2A3

W.J. DICKIE

Nordion International Inc., 447 March Road, Kanata, Ontario, Canada K2K 1X8

The use of commercial cyclotron systems for the production of radioisotopes continues to grow on a world-wide scale. Improvements in technology have significantly increased the production capabilities of modern cyclotron-based isotope production facilities. In particular, the change to negative ion acceleration and new high power systems have resulted in dramatic improvements in reliability, increases in capacity, and decreases in personnel radiation dose. As more and more older machines are retired decisions regarding their replacement are made based on several factors including the market's potential and the cyclotron system's abilities. Taking the case of the recently upgraded TR30 cyclotron at TRIUMF/Nordion, we investigate the requirements industrial/medical users are likely to impose on future commercial cyclotron systems and the impact this will have on cyclotron technology by the end of the century.

1 Introduction

The use of cyclotrons for commercial isotope production has dramatically increased over the past two decades. The implementation of modern technology (negative ion machines, high power ion sources and RF systems, high power external targetry, etc.) has helped to keep these facilities competitive with alternative production methods (e.g. reactors)[1]. On the other hand, market stability and predictability for cyclotron-based radioisotopes are difficult issues to handle and this generates uncertainty when making decisions regarding the future of commercial facilities.

2 Market Considerations

In the long term, the use of cyclotron-based radiopharmaceuticals is expected to increase. This is due to the difficulties inherent to the production of the alternative reactor isotopes. Generally, reactor and cyclotron production of radioisotopes can be characterized as follows :

Reactors
- Make-rate (yield) is high
- Fission products i.e. neutron-rich
- High capital infrastructure
- Relatively large waste product problem

Cyclotrons
- Lower make-rate (but increasing)
- Neutron-poor products
- Lower capital cost
- No significant long-term waste issues

The inherent difficulties associated with operating reactors, in particular the problem of waste production, is slowly depleting the world supply of industrial and research reactors capable of isotope production. Isotope production has traditionally been run parasitically on research reactors but a general reduction in the mandate and funding for these reactors has depleted their numbers. To some extent, cyclotrons could be used to fill in this void. However, since cyclotrons generally only produce proton-rich isotopes there will always be a need for complimentary reactor isotopes unless suitable (cyclotron) alternatives are available and universally accepted.

In North America and Asia the cyclotron isotope business has grown at about 20% per year for the past decade predominantly reflecting the increased use of ^{201}Tl in cardiac studies in the U.S. and ^{123}I products in Japan. While the Japanese market is expected to continue to grow (~10%/year) for the next few years it is anticipated that the ^{201}Tl usage in North America will decline. Other products (e.g. ^{111}In) have failed to meet expectations.

Despite this, major manufacturers of radiopharmaceuticals have added some cyclotron capacity during the past few years and are now running close to their limit. However, the continuing short-term market uncertainty has reached a point where it is prudent for these radioisotope producers to put-off any further cyclotron purchases. Instead, they often look to back-up bulk radioisotope producers to fill any additional requirements.

There are inherent difficulties with running a cyclotron-based isotope production facility. These can be seen from the typical characteristics of this business which are :

- Irradiation, processing and shipping is on a "just-in-time" basis. It is, therefore, subject to unexpected hardware problems in cyclotron and processing equipment and to shipping delays etc.

- Inventory buildup is generally not possible as most product isotopes are short lived (few hours or days).
- Round-the-clock activity to satisfy the above two criteria.
- Weekly scheduling with many last minute changes to accommodate new orders or to reschedule production runs cancelled by hardware failures etc.
- High dose maintenance. This is particularly true in the case of sites running aging positive ion cyclotrons which require extensive cooldown times to repair internal cyclotron damage.
- Costs are generally well defined and fixed although occasional unexpected major repairs can significantly increase expenses (and impact on radiation dose management).

Given these issues, some radiopharmaceutical manufacturers have decided not to operate their own cyclotron facilities but to sub-contract this business to specialized bulk radiochemical production companies.

3 Cyclotron Considerations

A general overview of the commercial isotope-producing cyclotrons (~30 MeV) is shown in table 1 which indicates some recent trends. Clearly, the retiring of aging positive ion machines is being complimented by newer negative ion cyclotrons coming on-line. While pressure continues to close down the dose-intensive older positive ion cyclotrons the modern technology associated with new negative ion machines provides flexibility in output capacity and diversity (multiple external beams and targets).

The advantages of using negative ion cyclotrons include the following :

- Can easily extract high currents with variable energy.
- No activation from internal targets.
- Multiple simultaneous beams at the same or different energies.
- The removal of targetry to separate irradiation rooms results in lower radiation fields.
- Facilities can readily meet the new ICRP radiation dose limit.

The dominant isotope produced on most commercial cyclotron facilities is thallium-201. In this regard, an examination of the capabilities of various cyclotron facilities during the past few years indicates the trend towards higher more efficient output (see table 2).

The useful economic life of a commercial cyclotron is probably around 15 years and several positive ion cyclotrons have recently been retired with several more planned in the near future. Their replacements, if any, will invariably be negative ion and have a larger beam capacity and flexibility.

Table 1: Commercial isotope producing cyclotrons.

	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

Age is not the only determining factor for the retirement of older positive ion systems. The new ICRP radiation dose limits (20 mSv/yr average dose per ARW) imply severe difficulties to operators of these older machines. Internal targetry and older technology generally results in a considerably more radioactive cyclotron environment than the modern negative ion systems. In addition, frequent breakdowns and more intensive maintenance requirements (requiring longer cooldown periods) result in lower machine up-time and production. For these reasons the future trend is clearly towards replacing aging cyclotrons with negative ion systems.

4 TR30 Considerations

The decision to upgrade the TR30 cyclotron was made based on several factors including cost-effectiveness. For substantially less than the cost of a buying a new cyclotron system (and building expansion) the existing TR30 was upgraded to produce double its previous output.

Another consideration was the desire for operational flexibility. By having cyclotrons capable of delivering more beam than routinely required the following advantages are realised :

1. Less strain on systems; fewer breakdowns and repairs.
2. Ability to rapidly respond to increases in orders.
3. Larger bulk isotope production reduces processing costs.

Table 2: The evolution of commercial cyclotron capacity.

Year	Cyc.	Current (μA)	Energy (MeV)	Tl-201 Make-Rate (mCi/beam-hr) [EOB+56hrs]
1989	CS30	350	26.5	190
	CP42	180	29	160
1992	CYC30	360	29	320
	TR30	360	29	320
1994	TR30	440	29	400
1995	TR30	800	29	710
1996	TR30	1000	29	890

4. Longer cooldown for individual targetry systems with correspondingly lower personnel radiation doses.

As mentioned previously, market uncertainty and increasingly frequent machine breakdowns resulted in a niche market for a reliable back-up bulk supplier of radiochemicals. Having the ability to quickly and reliably respond to immediate needs was a major factor in the decision to upgrade the TR30 at the Nordion facilities in Vancouver, Canada.

The technical ability to upgrade the operating TR30 was supplied by experts from TRIUMF, many of whom were involved in the original design and commissioning of the TR30 in 1990. A feasibility study of the upgrade was made with the following goals in mind :

1. 1 mA beam on-target (~1.2 mA extracted) at 30 MeV.
2. Dual beam operation with 5% stability on each line.
3. No increase in the complexity of operation.
4. No increase in the maintenance schedule.

Some of the considerations that went into the decision to go ahead with the upgrade program were :

- A small central region (1 MeV) cyclotron had been constructed for the original TR30 design investigation. The source of this system had already been able to accelerate up to 7 mA (d.c.) of H^-. With an acceptance of around 14% this would translate to about 1 mA circulating in the cyclotron. Larger power supplies and minor modifications to the source were proposed to increase this by 2-4 mA (d.c.).[2]
- Unlike similar commercial cyclotrons the standard TR30 did not require a buncher in the injection line. By including one it was projected that the apparent acceptance could be increased by 4%. Other injection line modifications were proposed to optimize the existing running system.[2]
- The RF power could be scaled up by building a new larger amplifier and control system.
- The improvements to the targetry required to take the proposed increased beam currents were already proven with 500 μA of beam.[3]
- Other issues (shielding, electrical and cooling services, etc.) were minor and easily handled.

Given the ability to test changes to the source on the centre region cyclotron, the local expertise of the TRIUMF Cyclotron Division, and the probable likelyhood of success the TR30 project was started in the summer of 1994. At this point, the modifications are essentially complete. In mid-August 1995 the machine circulated and extracted over 1 mA of beam (at 30 MeV) with 850 μA delivered onto the targets.[4] By the end of this year the goal of 1.2 mA extracted and over 1 mA on-target should be realized.[5]

5 Future Considerations

Looking further to the future there are additional improvements that could be considered. For example, consider the major sources of inefficiency in the cyclotron isotope business :

- Electroplating, dissolution and recovery of enriched targets results in ongoing (expensive) material losses. This procedure is also very time consuming and labour intensive.
- Batch processing of targets.
- Decay due to production vs. shipping schedules.

To counteract some of these issues the following idealized improvements should be considered :

1. Use encapsulated targets where target material stays in the target station.[6]
2. Continuous vs. batch process.
3. On-line isotope extraction system.

Since these targetry issues are very difficult to realize it is likely that less than idealized use of cyclotron time will continue to be a reality. To counteract this ever higher beam currents may be demanded from fewer running commercial cyclotrons.

At some point the higher beam powers will require that the conventional use of electroplated targets be superceeded by encapsulated targets. This will have an impact on the basic design of most commercial machines which are generally geared for 30 MeV (the maximum energy required for most commercial isotope production reactions). In order to handle beam energy loss through target windows the cyclotrons of the future may be designed to accelerate negative ions of several milliamps up to about 35 MeV.

It may be necessary to have one or two specialized higher energy commercial cyclotrons for specific products e.g. clinical PET ^{82}Sr/Rb generator systems which are produced by bombarding rubidium at 60-80 MeV.[7] In general, though, the commercial reactions can all be done with protons below 30 MeV.

6 Conclusion

It seems inevitable that cyclotron systems of the future will continue the established trend towards higher levels of power, increased flexibility (beam lines), diversity of beam energies to produce a range of isotopes, high reliability/low maintenance, etc. Negative ion technology will make it possible to extract and deliver several milliamps[2] of beam onto high power external targetry. Clearly, the era of positive ion machines has passed and negative ion technology will pave the way for the next few decades.

Acknowledgments

The authors would like to thank Mr. Phil Larabie of Nordion International Inc., and Drs. Bruce Milton and Tom Kuo of TRIUMF for input into this paper.

References

1. 'Cyclotrons for Isotope Production', B.F. Milton and N.R. Stevenson, *Proc. 1995 Particle Accelerator Conference*, Dallas, USA.
2. 'On the Development of 2 mA RF H^- Beams for Compact Cyclotrons', T. Kuo, proceedings of this conference.
3. F.M. Nortier *et al.*, Nucl. Instrum. Meth. **A355**, 236 (1995).
4. 'The TR30 Cyclotron and Targetry Upgrade', N.R. Stevenson, *Proc. VIth Workshop on Targetry and Target Chemistry*, Vancouver, Canada (1995).
5. 'Commercial Compact Cyclotrons in the 90's', B.F. Milton, proceedings of this conference.
6. 'On-line Production of Radioiodines with Low Energy Accelerators', N.R. Stevenson *et al.*, *Proc. VIth Workshop on Targetry and Target Chemistry*, Vancouver, Canada (1995).
7. M.R. Cackette *et al.*, Appl. Radiat. Isot. **44**, No. 6, p 917 (1993).