ACHIEVING BALANCE AS A SURVIVAL STRATEGY FOR A SMALL CYCLOTRON FACILITY

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Positron emission tomography (PET) forms the rationale for several dozen new cyclotron installations across the world. The success of these small accelerators has resulted in an excess production capacity. This suggests fanning out as a regional distribution center or, as in our case, reaching out to provide Argonne Nat'l Lab with F-18 for the study of astrophysical reaction rates with radioactive ion beams. The challenge to scale up our target yields has greatly benefitted our medical mission. The diversification vitalizes our PhD training, and the collegial relationship provides a needed measure of balance.

1. Introduction

The cyclotron is celebrating its 65th anniversary, filling a major role among accelerators. This longevity is due to its ability to accomodate a broad spectrum of demands, from basic physics research to a host of medical applications. Positron emission tomography, with its appetite for biocompounds labeled with the short-lived radionuclides C-11, N-13, O-15 and F-18, does not challenge a cyclotron's performance; the setting does. An 11 MeV proton cyclotron with 50 microamps of beam can easily satisfy the PET tracer needs for an entire city. However, running that machine in a clincal site, as a radiopharmacy, with staff having minimal accelerator expertise but subject to overzealous regulatory scrutiny, and finally, with no tolerance for technical downtime, is very challenging. Today's class of PET cyclotrons have met the demands for reliable tracer production, and have managed to provide the raw material for metabolic imaging in over fifty new installations in the past decade.

A number of reviews [1] have correctly pointed out a graded approach that sensibly allocates small cyclotrons to single purpose groups, and successively larger, multiparticle machines to those research centers with more ambitious programs. Although this is common sense, most academic institutions about to commit many millions of dollars in a new technology do not have a modest, or realistic, self perception. To marshal these financial resources in a hospital today requires large scale promotion, cheerleading, with binding promises to clinical specialties for their support. It is not surprising that sooner or later, departmental tectonics will leave one clinical group as the major player, dictating the focussed thrust of the PET work to be done at that site.

Now, in the mid-90's, the US health care system is under considerable pressure to throttle its ever-spiraling costs. New diagnostic techniques must be justified more rigourously. PET is hostage to its high capital cost, continuing struggle for reimbursement and the prospect of new levels of governmental regulation. Against this backdrop, the single specialty PET clinic faces all of the costs, but enjoys none of the buffering advantages of the more broadly based operation. The experience at

the University of Wisconsin serves as a counter example, perhaps being of some use in showing that a small cyclotron serving a small PET client group can try to achieve an operating stability through a balance of aspirations. Some lessons are obvious: the major function of a university is to train young people, hence providing solid research opportunities for Medical Physics PhD candidate's dissertations is of prime importance. If this is the first of a set of concentric circles, it circumsciribes the targetry, innovative chemistry and detector development that make up the specific research interests of the cyclotron group itself. Reaching out beyond this inner circle is the second group of collegial research projects, captivating in their science, but for which our cyclotron group efforts act as essential support. And in the third more distant circle, the daily conduct of clincial PET imaging requires a reliable source of a few PET agents (FDG, ammonia, F-DOPA), without fail, and without fanfare.

2. The balancing act.

The UW cyclotron, the first CTI RDS 112, purchased in 1985 entirely from intramural funds, operates within the Medical Physics Department. It is administered under a state-audited charge-back account that expects it to be self supporting, providing cyclotron products and services to users on the UW campus, the state and beyond with operating costs levied on a fair share basis. Initial uncertainties about operating costs have settled out over the past decade, with a rather steady operating budget of approximately $70K, covering three graduate student stipends and supplies. All accelerator repairs are performed in house, with counsel that continues thanks to a warm relationship that persists with the manufacturer. The major ambiguity concerns the ultimate replacement schedule of the cyclotron, and how to amortize its capital replacement cost over a lifetime that is made uncertain as the RDS becomes *more* robust over the years. The initial conditions, then, at installation in 1985, were that the cyclotron was a UW resource, operated by physicists, for training, research and routine production of PET tracers. Without a startup burden of debts or unsupportable promises, the UW cyclotron group could enjoy a freedom that is not known in most cyclotrons serving clinical PET centers that are integrated from top-down.

2.1 Examples of the basic cyclotron research projects.

It is immediately apparent that the 11 MeV proton-only cyclotron is well-suited to make a far-wider palette of radionuclides that the CNOF quartet that dominates PET. A double-focussing, vertical switching magnet was installed, so as to be able to direct the beam downward to bombard corrosive or molten targets. A systematic advance through the periodic table was performed, irradiating elemental targets of natural abundance, relying on a high resolution germanium spectrometer of calibrated efficiency to determine thick target yields [2,3]. The results to date include over 124 products, ranging from C-10 through the rare earths, where the Coulomb barrier finally throttles the entrance channel. While most of the reactions lead to agents with little medical potential, or suffer from low yields or natural abundances, a short list of (p,n) and (p,alpha) reaction products is shown in Table 1 below are

seriously pursued at Wisconsin, providing the feedstock for radionuclide studies in basic medical research [4-8].

Table 1: Other UW cyclotron products

Products	Target	Use
^{14}O	nat N_2	flow
^{48}V,^{56}Co	Ti, Fe	phantoms
^{55}Co,^{52}Mn	Ni, Cr	cell status
$^{60,61,67}Cu$	Ni, Zn	Cu-PTSM
$^{79m,81m}Kr$	LiBr	gas age
^{86}Y,^{89}Zr	Sr, Y	MoAbs
$^{94m,95m,96}Tc$	Mo	Tc-ligands

2.2 The Argonne National Lab (ATLAS) / UW radioactive ion beam collaboration.

Over the past two years, a cooperative project has resulted in the successful acceleration of an ^{18}F-ion beam, first on the SNICs source test bench at the National Electrostatics Corporation, Middleton WI; then in a study of the $^{18}F(p,\alpha)^{15}O$ reaction at astrophysical energies on the ATLAS facility at Argonne National Lab [9]. This collegial outreach was pivotal in spurring the development of high yield targets[10], making 2 Ci of aqueous $^{18}F^-$ with 40 uamps of protons on 500 ul water inventory at 45 bar overpressure. Five decades of ^{18}O-removal is performed by sequential drydown from ^{18}O-depleted water. The aqueous $^{18}F^-$ is then deposited on the SNICs source insert, followed by transport by small aircraft to ANL. Initial studies employed electrodeposition, but these suffered from ion-source sparking. Later studies have used a gentler evaporation technique, which provides several picoamps of $^{18}F^-$ beam out of the ion source for acceleration through the FN Tandem to the proton target, where a gas filled magnetic spectrometer takes advantage of the inverse kinematics to cleanly resolve the reaction products.

Astrophysics and PET tracer production are not obvious bedfellows, but the practical consequences of the outreach collaboration with the ANL group has revolutionized our $^{18}F^-$ production. With the scale-up in yields, we are now able to make record batches of FDG[11] and F-DOPA. This excess capacity can be translated into a wider distribution radius, or the ability to satisfy our local needs by irradiating low (10%) enrichment target material.

2.3 PET tracer production service.

The UW PET program has served the UW Clinical Science Center and the Wm S Middleton VA Hospital since the arrival of the Ortec ECAT II in 1979. That venerable scanner has been succeeded by a CTI 933/04 (1986) and a GE Advance (1994), the former now installed at the cyclotron site and the latter at the clinical site 3 miles away. Transport is performed by a dedicated vehicle, with no delivery failures even for 10-minute ^{13}N-ammonia. Currently, the scan requests break down as: FDG (80%, oncology, neurology), F-DOPA (10%, movement disorders), ^{13}N-ammonia, ^{62}Cu and ^{94m}Tc-ligands (10%, cardiology). At two to three hundred studies per year, the production capacity of the CTI RDS is barely exercised, so that outside requests (eg. for ^{18}F or ^{96}Tc) are welcomed. The major thrust now occupying our attention is the upgrade of our facilities to comply with current good manufacturing practices (cGMP), soon to be

required of all US PET cyclotron sites by the FDA.

3. Plans for the future.

Our first decade of cyclotron operation has taught us the benefits of a realistic self perception, with

- a clear training mission
- some unique facilities and talents for radiotracer research
- an exciting invitation to be a small part of the "big science" of radioactive ion beams for astrophysical studies
- while minding the store, providing the PET tracers needed for clinical diagnosis.

Our future plans extend these avenues, integrating our newly relocated CTI PET scanner into a seamless resource for the imaging of labeled agents in research animal preparations. Having the scanner finally contiguous with the cyclotron facilities should open up new avenues of basic PET research applied to pharmacology.

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