The Production of Short-Lived PET Isotopes at Low Bombarding Energy with a High Current Electrostatic Accelerator

R.E. Shefer and R.E. Klinkowstein
Science Research Laboratory, Inc.
Somerville, MA

M.J. Welch and J.W. Brodack
Department of Radiology
Washington University
St. Louis, MO

A radiopharmaceutical delivery system based on a Tandem Cascade Accelerator (TCA) capable of producing clinically significant yields of the PET isotopes ^{15}O, ^{13}N, ^{11}C and ^{18}F is under development at Science Research Laboratory (SRL). The TCA is conceived as a low cost, reliable and easy to operate alternative to a cyclotron for PET which exploits the advantages of target irradiation with low energy (3-4 MeV) protons and deuterons. At these energies, low-cost electrostatic acceleration technology may be utilized. The TCA comprises a linear tandem electrostatic accelerator capable of producing saturated yields of 1-2 Curries of the short lived PET isotopes in solid or gas targets. Recent technological advances in high voltage solid state circuit components and in high current negative ion sources make possible the design of an accelerator which is very compact and lightweight and which can deliver ample particle current to the target chamber for PET applications.

The preferred proton and deuteron reactions for low energy target activation along with the calculated yields for ^{11}C, ^{18}F, ^{13}N and ^{15}O as a function of bombarding energy are shown in Fig. 1. SRL, in collaboration with the Mallinckrodt Institute of Radiology at Washington University, is investigating the use of gaseous, liquid, and solid targets with the TCA. Very thin ($<$ 0.5 μm) diamond film target windows capable of withstanding the high thermal loading produced by a high current, low energy ion beam are being investigated for use with the TCA. The use of solid target materials eliminates the need for target windows and may be particularly advantageous at low bombarding energies. For illustrative purposes, it is assumed in the calculations displayed in Fig. 1 that ^{11}C is produced in a boron nitride target, ^{18}F is produced in an enriched boric oxide target, ^{13}N is produced in a graphite target and ^{15}O is produced in lithium nitride. It is evident from Fig. 1 that clinically significant yields (1-2 Curies) of the four PET isotopes can be obtained with proton or deuteron currents of 500 μA or less at an energy of 3.7 MeV. These beam parameters may be realized through electrostatic acceleration.

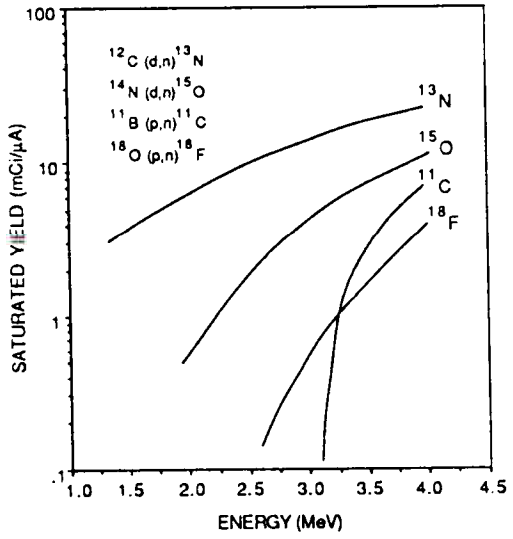

Fig. 1: Preferred reactions for low energy radioisotope production and saturated yields versus bombarding energy.

The inherent simplicity of the TCA stems from the fact that the accelerator geometry is linear, the applied accelerating potential is dc, and no magnetic fields are required. Linear geometry enables very high beam extraction efficiency to be achieved. High extraction efficiency impacts maintenance, reliability, and shielding requirements since the loss of particles at high energy both damages and activates surfaces within an accelerator. The high gradient cascade rectifier power supply is power efficient, and the tandem design allows both the ion source and target to be at ground potential and easily accessible during operation. A high degree of compactness is achieved by a patented SRL design which matches the power supply gradient to the accelerating column gradient. This allows the power supply to be mounted directly onto the accelerating column and eliminates the requirement for external power supply chassis. The TCA requires no magnetic fields which greatly reduces the system weight, power dissipation and heat load on auxiliary systems. The 3.7 MeV accelerator weighs less than 2000 lbs and has an overall length of approximately 10 ft.

The choice of a 3.7 MeV particle energy for the TCA is dictated by trade-offs between the required beam current to produce sufficient activity for clinical applications, beam energy and accelerator size and cost. These trade-offs are illustrated in Fig. 2 which shows the maximum current for the present TCA design and the required proton current for a 2 Ci saturated yield of ^{18}F via the $^{18}O(p,n)^{18}F$ reaction on $B_2{}^{18}O_3$ as a function of proton energy. The ^{18}F reaction is chosen here because it has the lowest yield at the energies of interest. The maximum available TCA current is limited by negative ion source performance at energies between 1 MeV and 2.5 MeV and by electrical current limitations of the cascade rectifier power supply at higher energies. For an electrostatic accelerator in which the accelerating gradient is fixed, both the size and cost of the system are minimized by choosing the lowest possible beam energy compatible with PET isotope production. A beam energy of 3.7 MeV allows for the production of ample activity of all four short-lived isotopes at currents compatible with accelerator limitations.

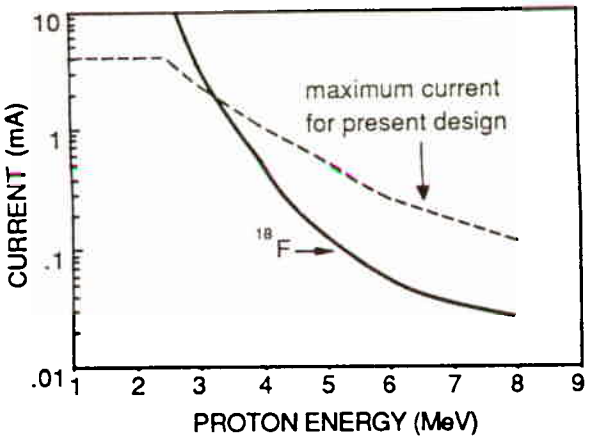

Fig. 2: Maximum TCA current and required current for 2 Ci saturated yield of ^{18}F via the $^{18}O(p,n)^{18}F$ reaction on boric oxide versus proton energy.

In a clinical system, the TCA will be integrated with a fully automated radiopharmaceutical synthesis unit. The full system comprises three major sub-units: 1) the accelerator, 2) the target chamber and neutron and gamma shield and 3) the robotically controlled chemical synthesis hot cell. A tentative layout drawing of the system components is shown in Fig. 3. The fully shielded facility, including the final processing laboratory and control room requires less than 400 sq. ft. of floor space. In Table 1, the operating parameters and capital costs associated with a TCA suitable for clinical production of the short-lived PET isotopes are compared with those of two commercially available small cyclotrons. The facility considered here comprises a fully shielded TCA capable of delivering up to 1 mA of proton and deuteron current at an energy of 3.7 MeV to a target chamber and does not include the radiopharmaceutical synthesis system. A prototype TCA with these parameters is currently being fabricated at SRL. The accelerator, with shielding, occupies a floor area of approximately 6 ft. by 20 ft. and is 6 ft. in height. The system is lightweight enough to be compatible with installation on any floor of a hospital building with minimal structural modification. The power consumption is sufficiently low that the accelerator can operate on stan-

dard 220 V circuits. Comparable yields of the PET isotopes may be obtained with all three systems. It is projected that the TCA system will require a capital outlay approximately 3 times lower than a small cyclotron and can be installed in a hospital with minimal structural modifications and minimal load on auxiliary systems.

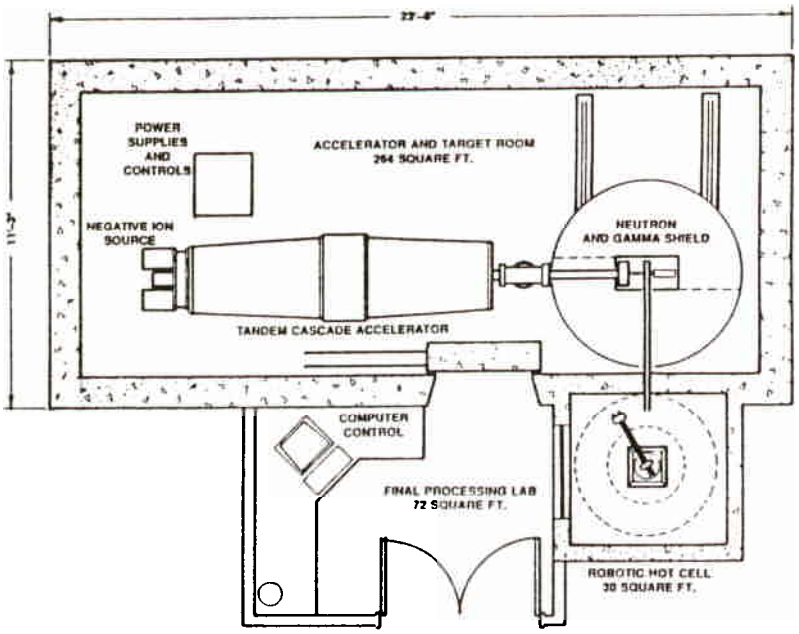

Figure 3: Layout of TCA radiopharmaceutical system.

Table 1: Comparison of TCA with Two Commercially Available PET Cyclotrons

	TCA	Scanditronix MC16F	CTI 112
Accelerator Type	Electrostatic	Cyclotron	Cyclotron
Particle Delivered	Protons and deuterons	Protons and deuterons	Protons only
Energy	3-4 MeV	16 MeV p, 8 MeV d	11 MeV
Beam Current	1 mA	50 μA	50 μA
Floor Space	265 ft^2	450 ft^2	450 ft^2
Weight (including shield)	9 tons	40 tons	42 tons
Input Power	11.4 kW	90 kW	100 kW
Heat Load			
- Air	6.3 kW	6 kW	7.5 kW
- Water	5.1 kW	85 kW	92 kW
Peak Floor Loading	500 lb/ft^2	N/A	2500 lb/ft^2
Capital Cost (Approx)	$400,000.†	$1,400,000.	$1,200,000.

† Projected cost