allowed to multiply for 5 days at 37°C, and the resulting individual colonies were stained with methylene blue. The number of colonies per 2.3-mm interval was counted. Unirradiated cultures with 10^4 cells in each flask were used as controls and were counted in the same manner. Survival was calculated as the number of colonies in a 2.3-mm band divided by the average number of colonies in the corresponding band in the control cultures. The resulting data give cell survival as a function of distance along the beam path. These are presented in Fig. 1 for four doses of nitrogen ions. It can be determined from the data that about 110 rads at the Bragg peak resulted in 55 percent cell survival on the uppermost curve of Fig. 1. Uncertainty in the dose estimation is about 15 percent.

Reference radiation (gamma ray) experiments were performed under the same conditions with dose rates of 0.16 and 350 rad/min. The doses required for 50 percent survival were 350 and 240 rads, respectively, so that the relative biological effectiveness of Bragg-peak nitrogen ions for this end point is between 2.2 and 3.0 at the dose rates used. The survival values are in quantitative agreement with predictions based on survival data for low-energy heavy ions (*1, 5, 12*).

These results confirm the favorable depth-dose profile and high efficiency of cell killing at the Bragg peak. An extensive experimental program to investigate the remaining relevant properties of high-energy heavy ions is necessary; however, the present evidence suggests that cancer therapy and other biomedical applications of high-energy heavy ions are distinct possibilities.

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Acceleration of Heavy Ions at the Bevatron

Abstract. *Substantial beams of deuterons, α-particles, and nitrogen ions have been accelerated to high energies (nitrogen to 36 billion electron volts) in the bevatron. Beams of various energies were successfully extracted for experimental use. Modifications of the ion source, the injector, and the main acceleration system made the production of high-energy heavy ions possible. Our computer control system played an important part.*

The bevatron, a proton synchrotron of 6.2-Gev energy with a long history of having been used for research in elementary particle physics, has been modified to provide the additional capability of accelerating heavy ions to very high energies. We have verified its potential in several fields of physics, in biology, and in medical research. So far, deuterons, α-particles, and nitrogen ions have been accelerated and extracted from the machine; experiments with the nitrogen ions in radiobiology and in physics are under way (*1, 2*). Table 1 gives the energies and intensities of the extracted heavy ion beams. For comparison, the usual extracted proton beam is 3×10^{12} particles per pulse.

The duoplasmatron source normally used to produce protons could be used without difficulty in forming the $^2H^+$ and $^4He^{2+}$ ions. But since these ions have only one-half the charge to mass ratio of protons, they are not accelerated in the usual (1 $\beta\lambda$) mode in the injecting linear accelerator, which is designed for 20-Mev protons. Instead, they are accelerated in the 2 $\beta\lambda$ mode, which is only one-tenth as efficient, to 5 Mev/nucleon—or to one-half the velocity of protons. In the 2 $\beta\lambda$ mode, the ions take two radio-frequency periods to pass from one drift tube to the next; their lower velocity (compared with protons) requires that the starting frequency of the bevatron accelerating system be reduced by one-half. This capability had already been built into the original conservative design.

Particles can be accelerated in the bevatron to energies that are determined by the radius and magnetic field. For deuterons, this maximum is 5.2 Gev and for α-particles, 10.4 Gev. Lower energies can also be obtained, presently down to about 280 Mev/nucleon, a limit imposed by the design of the extraction system.

Getting a beam of nitrogen ions was much more difficult (see Fig. 1). Nitrogen ions are produced in the ion source in various charge states, in the ratio $N^{a+}:N^{(a+1)+} \simeq 0.1$ for charge states higher than + 3. With a cold-cathode

Table 1. Intensities (particles per pulse) for various energies E (billion electron volts per nucleon) of extracted heavy ion beams. The letters ND mean not done.

Particle	$E = 2.1$	$E = 1$	$E = 0.28$
Deuterons	10^{11}	ND	2×10^{10}
α-Particles	5×10^9	5×10^9	10^9
Nitrogen ions	7×10^5	ND	1.4×10^3

Penning discharge source of the type developed for the Hilac (heavy-ion linear accelerator), the highest charge state we can produce in useful quantities is N^{5+}; the current of this ion species is about 40 μa. The charge to mass ratio of 5:14 required that both the electrical gradient in the linac (injector) cavity and the quadrupole magnetic field in the drift tubes be increased by about 40 percent over their normal values. This was achieved and gave a 2-μa beam of 70-Mev N^{5+} ions.

However, it is not possible for N^{5+} ions to survive acceleration in the bevatron; at the ambient pressure of 10^{-6} torr a change in charge state resulting in a loss of particles is almost certain. To overcome this problem we converted the particles to N^{7+}, with an efficiency of about 50 percent, by passing them through an aluminum stripping foil of 40 μg cm^{-2}. About 10^9 nitrogen ions per pulse were then available for injection into the bevatron.

When this number is compared with the usual 10^{13} protons per pulse, it can be appreciated that this nitrogen beam current is too low to provide usable signals for operating the present closed-loop systems controlling the acceleration system of the bevatron. We solved this problem by tuning up the bevatron on α-particles, whose charge to mass ratio is the same (within 0.04 percent) as that of $^{14}N^{7+}$, and storing on tape the frequency program and the settings for the 15 magnets used in the extraction. Nitrogen ions were then injected and the bevatron controlled entirely by computer, without beam signal. The last signal prior to acceleration is the Faraday-cup signal of the injected beam; the next signal is from the counter at the target. Losses of ions during trapping and acceleration, and from the capture of electrons by fully stripped ions, left us with 7×10^5 nitrogen nuclei per pulse. We can increase this beam substantially in the near future.

Beams are extracted from the bevatron by a technique that utilizes a resonance of the radial (betatron) motion of the particles, which is driven by a controlled magnetic-field perturbation. This method depends on the fact that a magnetic field causes the same deflection for all particles of the same rigidity $B\rho$ (the guidefield multiplied by the radius of curvature of the beam). Hence, for an extraction scheme employing only magnetic fields the setting of the currents is entirely prescribed by the rigidity of the particles. Therefore, once the extraction and beam-guiding system has been set up for protons or α-particles, it will be equally correct for nitrogen ions of the same rigidity. Beams of energies above 1 Gev/nucleon can at present be extracted with 50 to 70 percent efficiency.

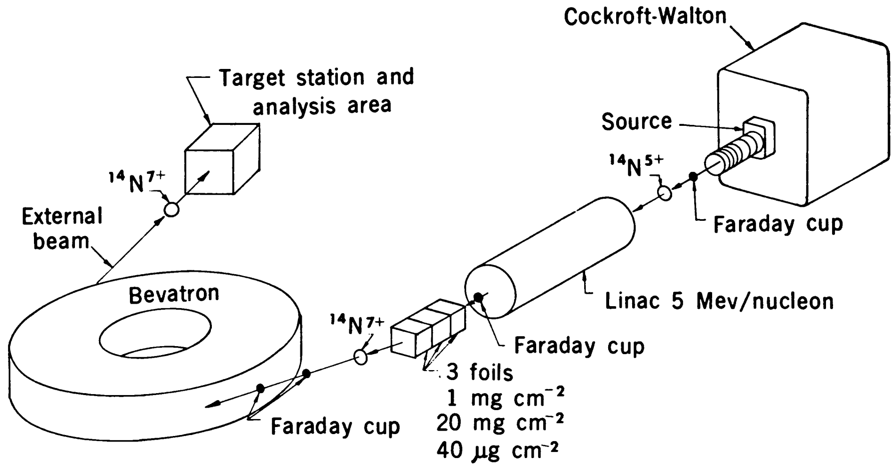

Fig. 1. Diagram of the bevatron acceleration systems for heavy ion work.

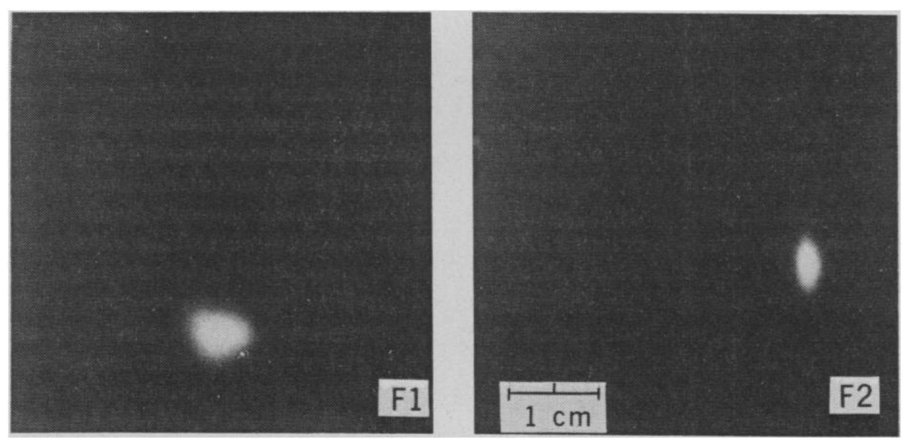

Fig. 2. Quality of the heavy ion beams accelerated at the bevatron is indicated by the sizes of the beam spots at the two focal points; *F1*, first focal plane; *F2*, second focal plane. The scale shown is 1 cm.

Heckman *et al.* have unambiguously identified the nitrogen ions by using a solid-state counter telescope (*1*). The quantity measured by this particle identifier gives the profile of the energy loss along the particle's path through the detector system. We found the beam to have some contamination (less than 5 percent) of singly and doubly charged ions resulting from breakup of nitrogen ions by restrictive apertures.

Beam quality is characterized, in part, by the size of the beam spot (see Fig. 2). At the first focal plane (*F1*), 10 m downstream from the beam exit, the beam spot was 5 mm in diameter. Transporting the beam to the experimental "cave" resulted in a spot size (at *F2*,) 50 m downstream) of 2×5 mm^2. In more precise terms, the beam emittance at 2.1 Gev/nucleon is 20 mm-mradians in the horizontal plane and 100 mm-mradians in the vertical plane.

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