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Bevalac Operations 1991

Accelerator and Fusion Research Division
Lawrence Berkeley Laboratory
University of California
Berkeley, California 94720

March 1992

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Foreword

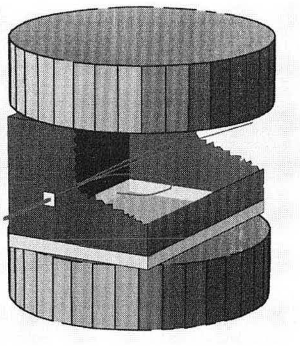
The history of accelerated heavy-ion beams at Lawrence Berkeley Laboratory goes back to the very beginning of cyclotron development under E.O. Lawrence. As early as 1940, C^{+6} was accelerated to a total energy of 50 MeV in the 37-inch Cyclotron. The first heavy ion induced nuclear reactions were produced in 1950, again with C^{+6}, at 120 MeV in the 60-inch Cyclotron.

In August 1971, acceleration and extraction of nitrogen ions from the Bevatron's injector succeeded, and August 1974 the Bevalac was operational, delivering intense beams of medium-mass ions from the SuperHILAC at energies up to 2 GeV/amu. Regular operation of the Bevalac began almost immediately for biomedical research and nuclear science, as the physicists restructured their research programs to delve into multi-nucleon interaction and nuclear equation-of-state studies.

The Bevalac was designated as a national heavy-ion facility in 1975, and since that time, multiple research programs have been carried out in nuclear science and biomedical research.

By 1981, continuing upgrades had made the Bevalac capable of delivering ions throughout the periodic table. The range of ion energies and intensities produced here are presently unavailable at any other accelerator complex in the world. Researchers are now planning to use the Bevalac for a new program of space radiation effects, which should add a new chapter to the long history of heavy-ion research at LBL.

Benedict Feinberg
Bevalac Operations Manager
March 1992



7.

BEVALAC OPERATIONS

ASTRONAUTS ON LONG MISSIONS BEYOND EARTH'S MAGNETIC field will be exposed to cosmic rays to an extent whose effects are unknown. As we plan for the phaseout of the Bevalac's nuclear-science program sometime in the mid-1990s, other researchers are poised to use it in support of future space exploration, building a data base on the biological and physical effects of heavy ions.

Meanwhile, the Bevalac, guided by its advisory committees (Tables 7-1 and 7-2), continues its traditional mission of serving nuclear science, radiation biology, and clinical radiation treatment. A major effort to prepare for the early-1991 DOE Tiger Team inspection has left it in a strong position both physically and procedurally. Management formalisms, employee attitudes, and facility and equipment improvements combine to ensure protection of safety, health, and environmental quality.

B. Feinberg *(operations manager; head of planning and development)*
G.F. Krebs *(head of research coordination)*
R.M. Miller *(head of operations)*
R. Stevenson *(head of safety and administrative services)*
J.B. Abenojar*
S. Abbott**
R.V. Aita
D.P. Almeida*
T.E. Althar
D. Anderson**
R.L. Anderson§
L. Archambault**
J.J. Ayers**
B.J. Bailey**
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K.M. Baptiste**
R. Barr
D. Beck**
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K. Connelly**
D.N. Cowles
H. Crawford *(guest)*†††
A.W. Cutt*
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M.R. Dickinson**
R.L. Doty*
J.R. Dougherty**
R. Dwinell**
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M. Hui**
D. Hunt**
R.E. Jahnigen
O. Jones
J.G. Kalnins
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A. Lindner**
A. Loop**
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D. Lozano
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M.A. McCloud**
R. McDonald
M. McEvoy**
M. McMahan
S. Meaney
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E. Moldenhauer*
E.K. Moller*
M. Monroy
D. Morris**
M. Morrison**
R. Mueller**
M. Nyman**
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S.L. Patterson**
M. Payne**
E. Perry**
M.R. Photos**
D.D. Pohl
J.L. Pusina
J.F. Quan**
D.E. Reimers*
R. Reimers**
T. Renner
R.M. Richter
W.L. Ridgeway**
S. Rogoff**
B. Rude**
S.E. Ryce**
T.C. Sampson*
B.C. Samuelson**
D.W. Schmeyer§
L. Shalz**
C.R. Siero
K.H. Sihler**
R.P. Singh**
L. Skvarla
R. Sorensen** §
J.W. Staples
L.L. Stout**
G. Stover**
S.A. Stricklin**
D.L. Syversrud**
H.K. Syversrud
R.L. Tafelski**
M.M. Tekawa
R.K. Thatcher
D. Thewlis**
J.R. Thomas**
C.W. Thornton**
P. Torres*
J.C. Walling*
H. Wieman††
K. Williams§
O.S. Wiggins
N. Wong
K. Woolfe**
M.D. Woolfe
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P. Bullocks
S. Fujimura
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K.E. Williams§

* Plant Engineering and Construction and Maintenance Departments
** Engineering Division
† Research Medicine and Radiation Biology Division
†† Nuclear Science Division
††† University of California Space Sciences Laboratory
§ Retired

A proton-therapy project being considered by the University of California at Davis would also draw heavily upon the body of expertise associated with the Bevalac. The accelerator, built at their cancer center in Sacramento, would be designed in a cooperative effort involving oversight from LBL scientists and engineers and strong industrial participation.

These panels of experts recommend beamtime allocations. The LBL scientific director of each program may allocate about 10% of the beamtime on a discretionary basis.

Table 7-1. Program Advisory Committees (PACs) for 1990 and 1991.

Bevalac Nuclear Science PAC

J. Carroll, University of California at Los Angeles, users' representative*
S. Datz, Oak Ridge National Laboratory
B. Feinberg, LBL, operations manager
C. Gelbke, Michigan State University
F. Goldhaber, State University of New York at Stony Brook
M. Gyulassy, LBL†
W. Henning, GSI, Darmstadt, Germany
G. Krebs, LBL research coordinator
F. Lothrop, LBL scheduling coordinator
P. McMahan, LBL executive secretary
F. Plasil, Oak Ridge National Laboratory
R. Scharenberg, Notre Dame University, users' representative*
L. Schroeder, LBL, scientific director
V. Viola, Indiana University, chair

Bevalac Biomedical PAC

S.J. Adelstein, Harvard Medical School, chair
Eleanor A. Blakely, LBL, deputy executive secretary
J.D. Chapman, Cross Cancer Institute
William T. Chu, LBL, executive secretary
Edward R. Epp, Massachusetts General Hospital
B. Feinberg, Bevalac operations manager (*ex officio*)
Robert J. Michael Fry, Oak Ridge National Laboratory
David J. Grdina, Argonne National Laboratory
G.F. Krebs, Bevalac research coordinator (*ex officio*)
Robert E. Krisch, University of Pennsylvania
Amy Kronenberg, LBL
F. Lothrop, LBL, scheduling coordinator
Bernhard Ludewigt, LBL, biomedical experiment liaison
Lester J. Peters, University of Texas System Cancer Center

Table 7-2. Nuclear Science Users' Association Executive Committees for 1990 and 1991.

W. Benenson, Michigan State University†
P. Brady, University of California at Davis
J. Carroll, University of California at Los Angeles, 1991 chair†
S.Y. Fung, University of California at Riverside
R. Madey, Kent State University†
M. McMahan, LBL, executive secretary
D. Olson, LBL*
R. Scharenberg, Notre Dame University, chair-elect
L. Schroeder, LBL, scientific director
K. Toth, Oak Ridge National Laboratory
H. Wieman, LBL

* Beginning in 1991.
† Through 1990.

Accelerator Technology and Operations Summary

A steady program of technology upgrades, combined with long experience at efficient scheduling and with continual fine tuning of operating procedures, has helped the Bevalac staff overcome a long-term trend of decreasing budgets coupled with inflationary erosion. Budget restrictions brought the Bevalac down to 3689 hours of experimental beamtime in 1990, followed by 2975 hours in 1991, after three consecutive years of record-breaking, 4000-hour-plus operation.

1990 and 1991 Performance Statistics

Many factors affect beam delivery, including scheduled and unscheduled shutdowns for maintenance, usage for machine studies and tuning, and seasonal fluctuations in the cost and availability of electricity (traditionally, the facility shuts down during part of the summer). Despite these variations, there have been steady improvements.

The physical sciences—mostly nuclear physics—continued to use about two-thirds of the experimental beamtime at the Bevalac. The life sciences, comprising radiotherapy research and basic radiobiology and radiation biophysics studies, accounted for the rest. Table 7-3 summarizes the year's operating statistics and compares them to figures for past years and projections for the future.

Table 7-3. Operating summary by fiscal year.

	1990 actual	1991 actual	1992 projected	1993 projected
Bevalac Operation (*hours*)				
Research	3689	2975	2800	2800
Machine Studies	243	225	187	187
Tuning	987	706	653	653
Total Operation	4919	3906	3640	3640
Unscheduled maintenance	671	459	535	535
Scheduled shutdowns	3170	4395	4609	4609
Total Downtime	3841	4854	5184	5184
Beam Use for Research (*hours*)*				
Nuclear Science	2535	2034	1867	1867
Life Sciences	1153	941	933	933
SuperHILAC	728	400	0	0
Total	4416	3375	2800	2800
Number of nuclear-science experiments receiving beam	25	6	12	12
Number of participating scientists	189	64	64	64
Institutions represented				
Universities	33	15	18	18
National laboratories	5	3	5	5
Other	7	2	3	3
Total	45	20	26	26
Use of Beamtime (%)				
In-house staff	50	50	50	50
Universities	35	35	35	35
DOE national laboratories	5	5	5	5
Other institutions	10	10	10	10

* These figures include the SuperHILAC parasitic program and therefore may exceed the research beamtime reported for the Bevalac alone.

Facility Development Projects

The Bevalac (Figure 7-1) has an ongoing program of technology upgrades designed to increase efficiency, improve user service, and ensure safety. A multiyear project to modernize the Bevalac's control systems and extend modern computer systems throughout the facility saw additional progress in 1990 and 1991. The computer control system has been extended to the local injector's rf system and drift-tube-magnet power supplies and to the beam transport and diagnostic devices in all beamlines. Conversion from the obsolete ModComp computer control system to the new system, which is based on networked Sun workstations, also progressed.

Our 1991 accelerator-improvement projects were directed toward modernizing the power-distribution system in the beamline areas and bringing it up to today's standards. Another significant improvement,

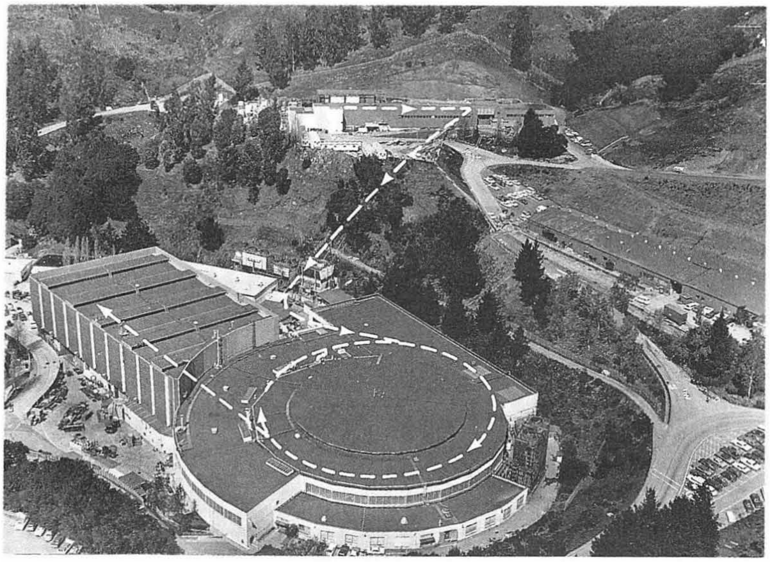

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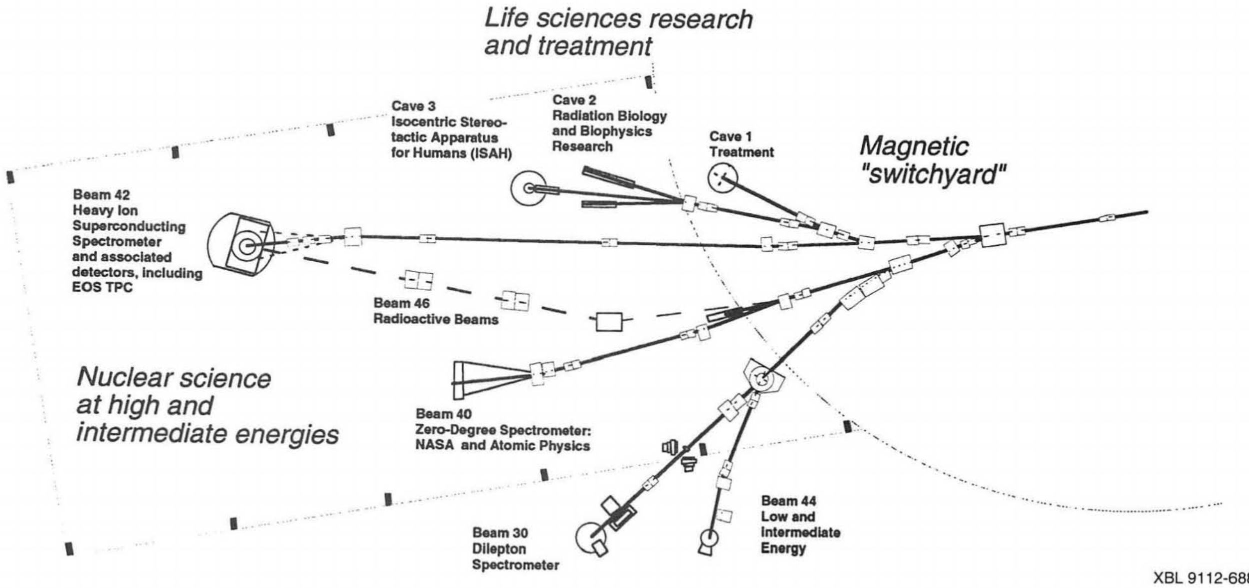
Figure 7-1. The Bevatron, a synchrotron, accelerates beams from either its local injector or the SuperHILAC heavy-ion linear accelerator. The dotted lines in the picture show the beam path from the SuperHILAC through the Bevatron. The SuperHILAC, which has three complementary ion sources, is used when higher energies and heavier ions are needed, as in most of the nuclear-physics programs. The beams are delivered to a variety of users in the External Particle Beam hall. The faint dashed lines in the drawing correspond to the circular and rectangular buildings shown in the photograph. The various experimental areas are separated by a "maze" of shielding blocks.



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planned for 1992, will raise the maximum "flat-top" time of the main guide-field magnet's power supply, and therefore the maximum beam spill time, from 1 second to as much as 4 or 5 seconds. This project requires R&D for new measures to stabilize the magnetic field and to substantially reduce power-supply ripple. This will allow the Bevalac to greatly increase the overall duty cycle, thus providing service that better matches today's emphasis on high-statistics investigations rather than survey experiments.

Improvements to the control of the main guide-field magnet also yielded advantages to the users. After a prolonged search for proper corrections to the field shape at the very low field (about 250 gauss) used at injection, we have achieved very good proton intensities, being able to deliver about 10^{10} particles per second.

In recent months, equipment refinements aimed at improving the optical quality of extracted beams have been getting under way. Major goals are to reduce beam halo (thus cutting the rate of unwanted background events) and to provide feedback instrumentation to aid precision tunings for specific targets.

Support for Space Exploration

The Bevalac presents unique opportunities to NASA because its energetic beams of heavy ions can realistically simulate most of the cosmic-ray spectrum in a laboratory environment. NASA has taken advantage of this capability for many years by conducting materials studies, calibrating detectors, and performing basic space-science research. In support of manned planetary missions beyond the magnetosphere, the program would be expanded greatly into three main areas:

- *Radiation biology, studying the effects of heavy-ion irradiation on cell cultures and animals.*
- *Materials science, characterizing the effectiveness of shielding materials and the radiation resistance of equipment.*
- *Space physics, a basic-science corollary of the manned-mission research, seeking to understand the interactions of cosmic rays with, for example, interstellar gas clouds.*

This pure and applied research builds not only upon the technical capabilities of the Bevalac, but also upon its existing research program.

NASA and the Bevalac

Under this proposal as it currently stands, NASA would significantly increase its current low level of Bevalac usage beginning in fiscal year 1993, sponsoring additional operation on nights and weekends during the 22 weeks per year in which the Bevalac is used solely for the therapy program. The total NASA program would ramp up from its current level of about 300 hours of research beamtime per year to 1000-plus hours. Meanwhile, the current nuclear-science and biomedical programs would continue.

After FY 1994, NASA-supported research would comprise the entire base program at the Bevalac. Other agencies might purchase additional beamtime. It is likely that some present users of the facility, from LBL and elsewhere, would be among the scientists proposing research within the NASA program. The section on "Biomedical Research," presented later in this chapter, gives further details on the some of these research challenges associated with space exploration.

Proton Medical Accelerator

The use of accelerated ion beams to reach tumors precisely in three dimensions is deeply rooted in the history of LBL. Over four and a half decades, radiotherapy with heavy, charged particles has become widely accepted for the treatment of an ever-increasing variety of tumors. Meanwhile, LBL accelerator scientists and their life-sciences colleagues have been thinking from time to time about special-purpose accelerators dedicated to medical use. Now these two lines of inquiry are coming together in a proton-therapy initiative planned for the University of California at Davis Cancer Center, located in Sacramento. This facility, to be built with privately raised funds, will be the second dedicated, hospital-based, clinical charged-particle treatment facility in the world, following the lead of the Loma Linda University Medical Center.

The Davis Initiative

The Davis facility—formally, the University of California at Davis Proton Therapy Center—will be a 250-MeV proton accelerator optimized for medical treatment. Specifications and design decisions for the Davis facility are being developed with the aid of grants from the National Cancer Institute.

In 1991, under the first-year grant, an analysis of the current state of technologies applicable to proton therapy was completed. The synchrotron emerged as the leading candidate, with a conventional (that is, non-superconducting) cyclotron as a close runner-up. (Proton therapy is currently performed or planned worldwide at more than a dozen accelerators, all of which are cyclotrons and synchrotrons.) Specifications for accelerator performance have been developed, and comparisons have been made among the various techniques for creating large radiation fields suitable for therapy, along with isocentric gantry delivery of the beam.

The second year of NCI funding is being used to address a specific design for the Davis site. The Proton Therapy Facility, to be located in a new structure adjoining the recently completed Cancer Center, is currently envisioned as a 250-MeV proton accelerator, probably a synchrotron, delivering beam to three treatment rooms, two of which are equipped with rotary gantries capable of bringing the treatment beam into a supine patient from any angle. Several specific areas are being addressed in this segment of the project:

- Detailed specifications for all parameters of both technical and conventional facilities.
- Conceptual designs covering all elements of the project.
- Cost estimates to provide fund-raising targets for UC-Davis.
- Technical issues identified from the operation of the Loma Linda facility, as well as other medical charged-particle programs around the world. These are recently identified problems that prevent the full implementation of many of the recent innovations in beam delivery. By solving these problems, true "second-generation" performance can be obtained at the Davis facility.

Close collaboration with industry is planned throughout this portion of the project. Conceptual designs and cost estimates will be performed by the private sector once the detailed specifications have been developed. The technical issues will also be addressed primarily by industry, with assistance from LBL. One of the principal goals of this process is to transfer technology to industry, as advanced systems for charged-particle therapy could eventually emerge as a significant market.

Nuclear Science

The Bevalac's ability to provide beams of the heaviest of ions in the GeV/nucleon range gives it a unique role in the U.S. nuclear-science program. The anticipated phaseout of the program in the mid-1990s has led researchers to concentrate upon the experiments that can provide the most-decisive results in the remaining years. They are focusing upon the study of extreme conditions in nuclear matter, the thermodynamic and transport properties of nuclear matter, and the nuclear equation of state (EOS). The prominent achievements of 1990 and 1991 include important new data from the Dilepton Spectrometer and the ongoing preparation of a Time Projection Chamber.

EOS Studies and the Time Projection Chamber

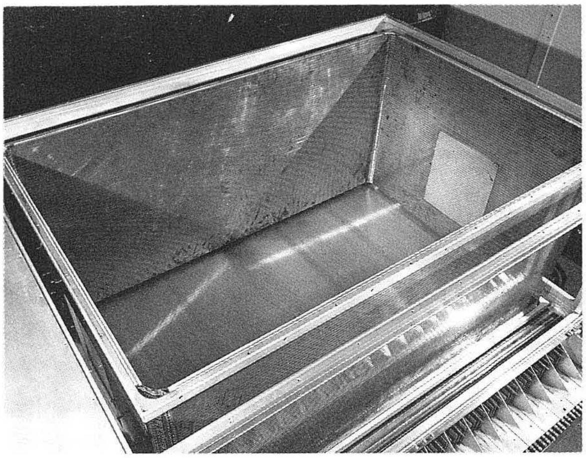
The running theme of the Bevalac's nuclear science program has been the production and examination of extreme conditions in nuclear matter. Early Bevalac experiments, using the Streamer Chamber and Plastic Ball detectors, established that central collisions* between nuclei could create high temperatures (50-100 MeV) and high densities (two to four times normal). The first evidence for "collective flow" in nuclear matter was obtained in these experiments. Such studies reveal the thermodynamic and transport properties of nuclear matter, and thus the equation of state (EOS), as described in the sidebar.

The experimental observables of the EOS are now clear; they include, for example, the dependence of "collective flow" on fragment mass, as well as the correlation of flow with reaction plane, etc. Experimenters have found that the heavier reaction fragments appear to fly away from the reaction at an azimuthal angle closer to the reaction plane than do lighter fragments. Furthermore, the in-plane flow momenta of heavier fragments are significantly larger. However, the effective compressibility of nuclear matter remains uncertain to within a factor of 2, so clearly a consensus on the form of the EOS has not been reached. What is required is a 4π detector capable of analyzing all the particles produced in a central collision between the heaviest nuclei. At the same time, this detector must be able to collect a large statistical sample of such events and study them on an event-by-event basis. At the Bevalac, this next-generation detector will be the EOS TPC (time projection chamber).

The EOS TPC (Figure 7-2), installed and undergoing tests and electronics completion, is an electronic 4π detector that fits inside the Heavy Ion Superconducting Spectrometer (HISS) magnet. The EOS TPC is designed for full-solid-angle coverage, hence the term "4π." It will be able to identify and analyze the momenta of most of the 200 or so mid-rapidity charged particles (mostly protons, deuterium and tritium nuclei, ^{3}He and ^{4}He nuclei, and pi mesons) that are produced when heavy nuclei such as gold collide at Bevalac energies. In the HISS dipole, its functions will be complemented by a variety of existing detectors.

Nuclear multifragmentation will be studied through exclusive experiments (that is, experiments that do not account "inclusively" for all particles and phenomena) using the technique of reverse kinematics. This work will involve heavy beams such as krypton, lanthanum, and gold upon lighter targets such as beryllium and carbon. Flow effects will be studied as a function of mass and energy, and other experiments below 200 MeV/n will

* Central, head-on collisions, as opposed to "grazing" or peripheral collisions.



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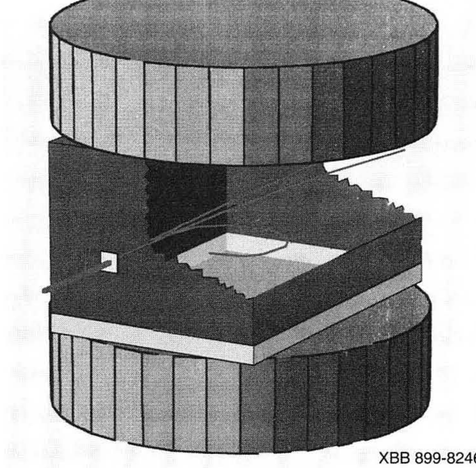

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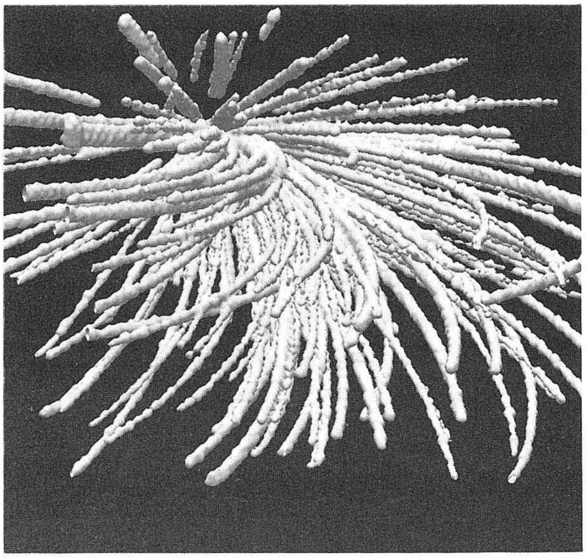

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Figure 7-2. The Equation of State Time Projection Chamber (EOS TPC) will play a key role in optimizing scientific progress during the remaining years of the Bevalac nuclear-science program. The detector system was tested in scaled prototype form in 1988 and installed in 1991; it is scheduled to come fully on-line early in 1992. The TPC, a full-solid-angle detector in the Heavy Ion Superconducting Spectrometer (HISS) magnet, will be able to identify and analyze the momenta of most of the 200 or so mid-rapidity charged particles (mostly protons, deuterium and tritium nuclei, ^{3}He and ^{4}He nuclei, and pi mesons) that are produced when heavy nuclei such as those of gold collide at Bevalac energies. Here an illustration of the EOS TPC concept is shown alongside part of the apparatus *(top left)* and a computer-modeled result of a simulated 800-MeV Au + Au central collision.

search for their decrease and presumed eventual disappearance as incident-projectile energy decreases. Experimental operations will begin in 1992, with 1000 hours of beamtime approved for these initial experiments, and will continue until the termination of the nuclear-science program at the Bevalac.

Pumping and Compressing the Nuclear Fluid

Some of the effects of nuclear collisions are rather exotic, as are the means of observation. However, many of the effects are analogous, in considerable detail, to phenomena one sees in everyday, macroscopic matter. (An example of such behavior is collective flow, which was first observed in the Plastic Ball and Streamer Chamber detectors at the Bevalac.) Nuclear matter can be thought of as a solid, liquid, gas, or plasma, depending on temperature and pressure, as shown in Figure 7-3. The equation of state (EOS) mathematically describes the balance among these phases and the borderlines of the phase transitions. Knowledge of the EOS is of great fundamental importance to nuclear scientists. It is also useful to astrophysicists, because certain hypotheses about mechanisms within supernovae and neutron stars are based on assumptions related to the EOS. The hypotheses are especially sensitive to the value of nuclear incompressibility.

Probing the EOS under conditions far removed from the equilibrium state of nuclear matter requires considerable disturbance of the entire volume of interacting matter. This calls for head-on impacts from beams of heavy ions. The greater the mass of the target nucleus and the projectile, the greater the disturbance and the greater the number of participating nucleons. Therefore, an ongoing highlight of Bevalac research is exploration of the EOS at high temperatures (typically 50-100 MeV of thermal energy) and high densities (two to four times normal).

The Bevalac energy range is especially appropriate because regions of the EOS far from equilibrium can be reached, yet the phenomena are still strongly influenced by the nuclear mean field. In other words, the nucleus still behaves as a unit in the collision.

Dilepton Spectrometry

Another important detector is designed to provide an especially clear view of certain reactions. The Dilepton Spectrometer (DLS), shown in Figure 7-4, is a unique detector that was installed at the Bevalac in 1986. It offers special insights into reaction dynamics by watching for a rare event: emission of an electron and positron correlated in their paths and their time and place of origin.

Dilepton emission is thought to provide an especially undistorted view of nucleus-nucleus, proton-nucleus, and proton-proton collisions because leptons interact with other forms of matter through the weak nuclear force and the electromagnetic force. Thus there is only a small probability of scattering or reabsorption on their way out of the reaction area, and reliable data can be obtained on deep and early phenomena of the collision. In particular, dilepton spectrometry might provide insights into one of the key theoretical unknowns of nuclear collisions: the behavior of pions and other

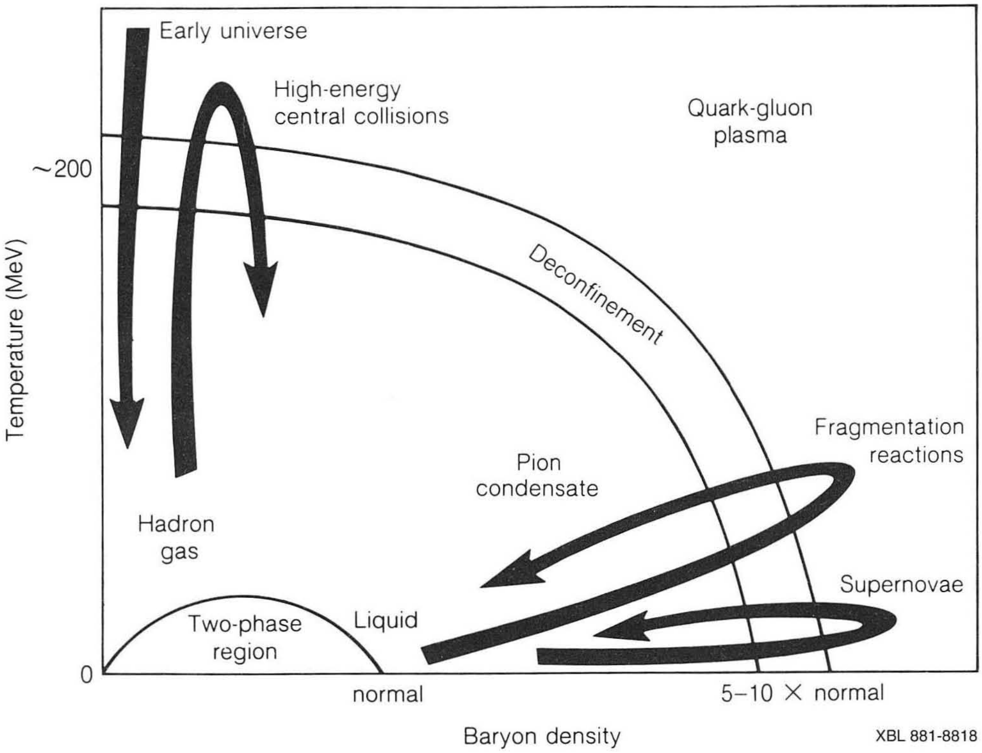

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Figure 7-3. A schematic phase diagram for nuclear matter shows some of the states and transformations predicted by various theories. The normal state of nuclear matter can be characterized as liquid. It may undergo phase transitions to a hadron gas at relatively low densities or, at higher densities, to some condensed phase such as a pion condensate or a superdense nucleus containing thousands of nucleons. Under extreme conditions, the hadrons themselves are expected to break down into "deconfined" quarks and gluons; such conditions are thought to have existed in the first few fractions of a second after the Big Bang, and are thought to exist today in supernovae. Such extreme conditions can be re-created at a laboratory scale through central collisions between nuclei at extreme relativistic energies.

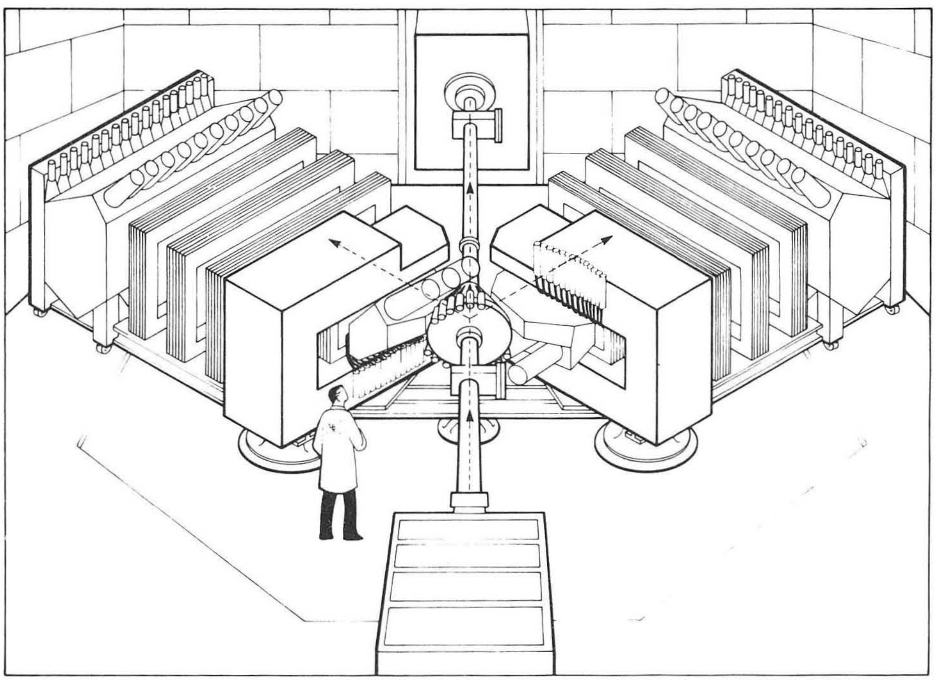

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Figure 7-4. An artist's rendering shows the major elements of the Dilepton Spectrometer (DLS), which in its completed and installed form is difficult to photograph. Electron-positron pairs are detected in the two arms, each of which has a three-cell Cerenkov gas counter, a 16-element scintillation hodoscope, drift chambers and a magnetic dipole, a 20-cell Cerenkov gas counter, and a large 16-element scintillation hodoscope. In 1989, an additional multiplicity detector was added: a 96-element hodoscope configured as a cone surrounding the target chamber. This hodoscope detects charged particles and gives information about the centrality of the event.

mesons. (It is also thought that dilepton production might signify the formation of a quark-gluon plasma in the higher-energy heavy-ion colliders of the future.)

In 1987 the DLS collaboration established that dilepton emission does indeed occur at Bevalac energies. Subsequent work further defined the role of dilepton spectrometry in studying the EOS and other behavioral aspects of hot, compressed nuclear matter. In 2.1- and 4.9-GeV $p+{}^{9}Be$ collisions, and to some extent in 1.95-GeV/n ${}^{40}Ca+{}^{40}Ca$ collisions, the mass spectra have a sharp peak around 300 MeV, which is twice the rest mass of a pion. A great many models have been proposed to explain the early DLS data; in one of them, the peak might be interpreted as the matter-antimatter annihilation spectrum of pion pairs (π^+/π^-).

To verify preliminary interpretations of these DLS data, it was essential to measure the dilepton spectrum for the elementary nucleon-nucleon case. A liquid hydrogen/deuterium target was added to the DLS. In these collisions, which involve elementary nucleons rather than nuclei with a collective "mean field," the sharp peak was expected to disappear, providing dramatic confirmation that dilepton spectra directly reflect the properties and behavior of pions in hot, compressed nuclear collisions. This ability to visualize the early stages of a collision would be a key addition to current techniques, which often cause an interpretational stalemate because they primarily provide data on flow and other phenomena from late in the reaction process.

In fall 1990 a one-month run studying dilepton production in p-p and p-d collisions at 1 and 4.9 GeV was conducted. Several thousand direct pairs were obtained at 4.9 GeV. Even though the production cross section decreased by a factor of more than 50 at 1.05 GeV, a few hundred direct pairs were detected at that energy. The fall 1990 work increased the total DLS sample of direct pairs more than fivefold; the substantial data set is being analyzed to see if the previous structure observed earlier in p-Be is also present in p-p and p-d. The future DLS program will use long blocks of beamtime to finish a high-statistics p-p and p-d study. Then the group will bring back its solid-target scattering chamber for a series of high-statistics experiments on dilepton production in nucleus-nucleus collisions. This will reveal whether the structure observed in the data truly reflects a property of the nuclear medium.

Subthreshold Production

Collective features of heavy-ion collisions can be highlighted through the study of particle production below the free nucleon-nucleon threshold. To test various theoretical models predicting the yields and distributions of antiprotons, substantially improved data are required.

Subthreshold pions in Au + Au collisions have been observed, for the first time, at energies of 180-240 MeV/n. Analysis is in progress to determine if the yield of subthreshold pions has a larger-than-expected dependence on projectile/target mass, indicative of a highly cooperative production mechanism. Other subthreshold-production experiments, such as Si + Si, have also been conducted recently. A new experiment will provide such data and will extend the subthreshold antiproton measurements to lower energies. At the same time, an interesting scaling hypothesis will be tested in which all particle production below threshold, be it production of pions, kaons, or antiprotons, falls on a single curve.

Pion Studies

Pions, the most abundant particles created at Bevalac energies, have long been the subject of experimental scrutiny, especially for studying the effects of central collisions. Pion yields provide unique insights into compressional effects, the π^+/π^- ratio in various regions of phase space can be used to study the role of the Coulomb force in nuclear collisions, and pion interferometry based on the Hanbury-Brown and Twiss effect is used to measure the magnitude of the emission in space and time.

Earlier comparisons between the shapes of pion spectra and the predictions of various models suggested that pions are sensitive to the EOS. The systematic study of two-pion interferometry with the JANUS spectrometer was completed as results came in from La + La studies (with multiplicity selection to aid in determining the degree to which the ions collided head-on rather than grazing each other). Systematic measurements of the size, shape, lifetime, and coherence of the pion source have played a valuable role in our understanding of the dynamics of heavy-ion collisions at Bevalac energies.

Neutrons and Light Charged Particles

Recent theoretical speculation suggests that collective flow should set in at energies as low as 50-100 MeV/n. Earlier data from a Streamer Chamber experiment carried out by researchers from Michigan State University apparently show a disappearance of flow at energies below 70 MeV/n. In 1991, a group from Kent State University began an extensive set of measurements of the triple differential cross section for neutrons produced in the collisions of the heaviest systems, attempting to ascertain the energy at which flow disappears.

Inclusive charged-particle experiments, carried out using the two single-arm spectrometers at the end of Beam 30, are in the final stages of analysis using new data sets. These data, taken with high precision, should be sensitive to effects of the nuclear medium and should also serve as a testing ground for theoretical models of central nucleus-nucleus collisions for heavy systems.

Intermediate-Mass Fragments

An active collaboration exploits reverse kinematics to measure the interaction between substantial currents of heavy projectiles (with atomic number in the range of 100) and lighter targets. These collisions, in the 30-150 MeV/n energy range, produce nuclear matter at intermediate temperatures, but at below-normal densities in the area of the liquid-gas phase transition. The sources and characteristics of complex fragment emission are being studied as functions of mass and energy. The measurements are compared with dynamic calculations of the interactions, followed by examination of the statistical decay of the hot matter to ascertain whether multifragmentation (an instantaneous rather than sequential process) is occurring.

Grazing Collisions and Secondary Radioactive Beams

Although most Bevalac research focuses upon the extreme temperatures and pressures caused by central collisions, other extreme phenomena can be studied in "grazing" collisions. For example, nuclear fragments with extreme numbers of protons or neutrons—out to the "driplines" at the edges of the chart of the nuclides—can be created. Considerable progress continues to be made in using the projectile fragmentation processes to produce and study beams of radioactive nuclei. Initial studies with ^{11}Li showed clear evidence for a two-component structure, which has been interpreted as a sign of a diffuse neutron skin (halo). This has been followed by studying the

A-dependence of the electromagnetic-dissociation (EMD) process for ^{11}Li , an isotope for which a large EMD component was observed.

Another group is completing the measurements of the magnetic moments of polarized unstable mirror nuclei, producing polarizations as large as 5% in unstable nuclei through reaction kinematics.

Nuclear Astrophysics, Atomic Physics, and NASA Instrument Calibration

Many of the Bevalac's capabilities are relevant to astrophysics. HISS is used to study nuclear reaction mechanisms and to measure heavy-ion inclusive fragmentation cross sections. This holds particular interest for those who study cosmic-ray propagation in the interstellar medium. The group performing this research is measuring fragmentation cross sections for projectiles up to Fe on liquid hydrogen and helium (principal components of the interstellar medium).

A variety of work is done at the Bevalac in disciplines other than nuclear science. Bevalac beams are used for instrument calibration by researchers from the National Aeronautics and Space Administration (NASA) and by other cosmic-ray scientists from around the world. They use the beams to calibrate detectors that will be used on balloon, rocket, and satellite flights, and to recalibrate them after retrieval.

Atomic physicists use the Bevalac's ability to provide "hydrogen-like" and "helium-like" uranium ions (that is, ions stripped down to one or two electrons). Because uranium has 92 protons, these highly stripped ions represent an extreme condition of the atom. On their small scale, they have the strongest electric fields found in nature, enabling scientists to address phenomena in quantum electrodynamics, including the Lamb shift.

Production of electron-positron pairs in collisions of fully stripped uranium nuclei on gold targets, with the electron captured by the outgoing nucleus, has consequences for RHIC, the Relativistic Heavy Ion Collider being built at Brookhaven National Laboratory, and is being explored in an upcoming experiment at the Bevalac. And a gas-cell target was developed at the Bevalac in order to measure charge-changing cross sections for ions that are of interest to the designers of new accelerators at CERN and Brookhaven; it also examines the role of electrons in relativistic ionizing collisions. This same gas cell was then used to study resonant transfer and excitation for U^{90+} projectiles in hydrogen. These experiments provide a test of relativistic dielectronic-recombination theory.

Biomedical Research

In addition to nuclear science, a diverse biomedical program has thrived at the Bevalac. This section describes selected 1990 and 1991 highlights in the three primary areas of Bevalac biomedical work:

- *Clinical programs in heavy-charged-particle radiation therapy and radiosurgery.*
- *Radiation biology and biophysics research.*
- *Development of equipment and techniques.*

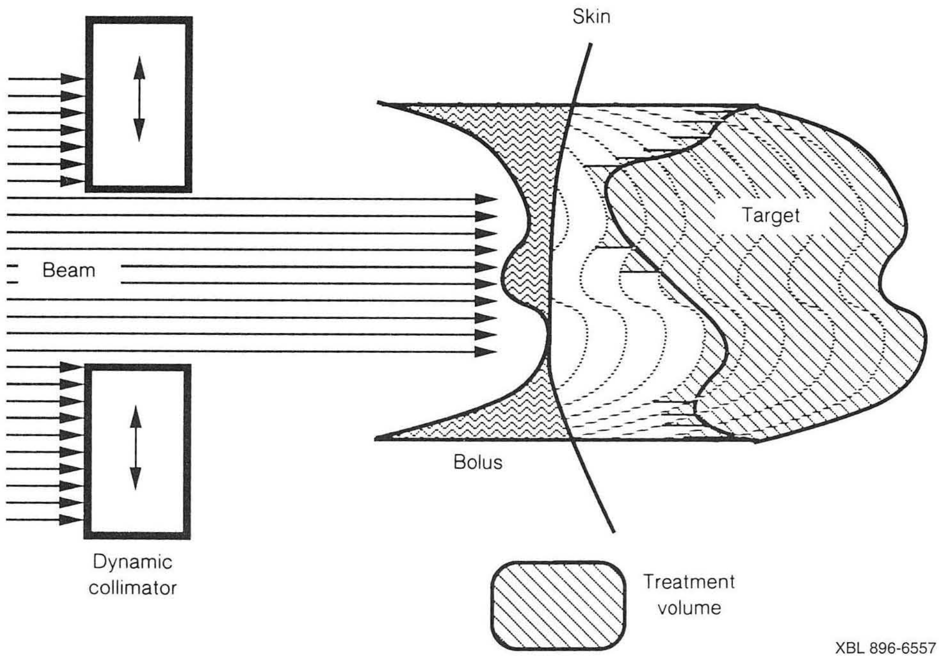
An area of life sciences research at the Bevalac accounting for about 20% of biomedical beamtime involves basic studies of the effects of radiation on both normal and abnormal cells and tissues. In vivo *and* in vitro *experiments examine such subjects as damage and repair of DNA, cell and tissue kinetics, and radiation tumorogenesis. The radiation biology and biophysics programs found their research temporarily curtailed in late 1990 and early 1991 because of the effort to prepare for and support* *the DOE Tiger Team inspection. (The clinical trials, with patients depending on the availability of treatment beamtime, proceeded as usual.) Substantial progress was nonetheless made in a variety of areas.*

A program of technology development, aimed at safer and more effective delivery of the prescribed radiation doses, has gone hand in hand with these research and treatment efforts. The major achievement of 1991 was the clinical commissioning of the Raster Scanner beam-delivery system, a significant step towards dynamic three-dimensional conformal delivery.

Heavy-Ion Radiotherapy and Radiosurgery

Clinical research medicine at the Bevalac focuses primarily on Bragg-peak radiation treatment (Figure 7-5). Two general types of treatments are carried out: radiosurgery of intracranial arteriovenous malformations (AVMs) and radiotherapy of tumors.

Over the years, more than 400 patients with symptomatic, inoperable intracranial AVMs have been treated at LBL with stereotactic Bragg peak radiosurgery in a collaborative program with area medical centers. This program, initiated at the now-decommissioned 184-Inch Synchrocyclotron, now uses helium beams at the Bevalac. A long-term dose-searching clinical-trial protocol has followed more than 250 patients for more than 2 years.



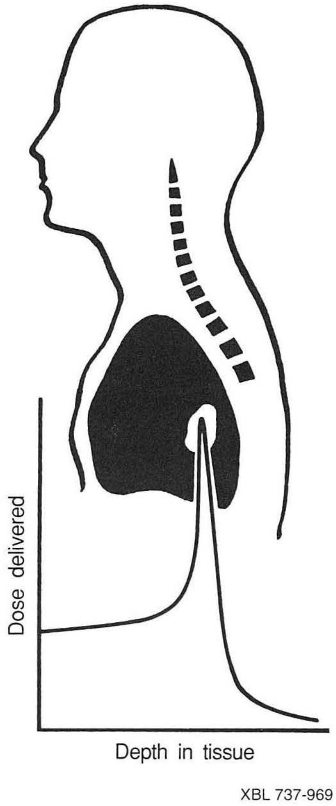


Figure 7-5. The Bragg peak gives charged particles an advantage over electromagnetic radiation (such as x-rays) for radiosurgery. Electromagnetic radiation grows weaker exponentially as it is absorbed, so delivering an effective dose to a deep tumor means considerable damage to healthy tissues in front of and behind the tumor. Particles, by contrast, lose most of their energy in a relatively narrow part of their range; the location of this "Bragg peak" can be accurately predicted and precisely controlled. In the radiosurgical instrument arrangement diagrammed here, an energy-absorbing wax or Lucite bolus matches the depth of the Bragg peak to the thickness of the tumor, while collimators control the cross section of the beam. Not shown is an upstream "binary filter," or absorber, which draws the beam back in sequential layers. Changing these variables can fit the treatment area to the tumor across three dimensions.

Initially, radiation doses ranged from 45 to 35 gray-equivalent (GyE)* now, doses of 25, 20, 15 and, under special circumstances, 10 GyE can be used, depending on a number of factors.

The characteristics of charged-particle beams provide a relatively homogeneous dose distribution with the 90% isodose contour to the periphery of the lesion. When the entire arterial phase of the AVM core is included in the treatment field, the rates for complete obliteration 3 years after treatment are impressive: 90-95% for volumes of 4-14 cm^3 and 60-70% for volumes greater than 14 cm^3. The total obliteration rate for all volumes up to 70 cm^3 is approximately 80-85%. For complete radiation-induced obliteration, dose is primarily related to volume, secondarily to location. The implementation of raster scanning in Cave III opens up the possibility of treating complex intracranial lesions that have previously been impossible to treat effectively, even with beams of charged particles.

A related helium-ion bioeffects research program continues to investigate the reaction to heavy-charged-particle radiation injury. Advances in dosimetry and beam-delivery technologies provide a better understanding of dose localization and dose distribution in the Bragg ionization peak at selected sites. Emphasis is placed on the cellular basis of central-nervous-system damage and repair. Research addresses the biophysical events of DNA damage and repair; oligodendrocyte, neuronal, and endothelial-cell kinetics and homeostasis; perturbations of regional blood flow dynamics and regulatory control; and cell population kinetics under heavy-ion irradiation.

In radiotherapy, more than 1200 patients have been treated in LBL clinical trials. The ongoing trial with helium continues to show excellent results for selected tumor sites, as compared to historical control data. Rates of complications are acceptably low—comparable with those of standard radiotherapy. The initial local control results with neon ion irradiation in the Phase I-II studies have been promising, with rates ranging from 50-90% for salivary gland, locally advanced prostate, advanced paranasal sinus and nasopharynx tumors, as well as for locally residual sarcoma of bone or soft tissue. We continue to search for additional evidence regarding the clinical effectiveness of high-linear-energy-transfer (high-LET)** charged particles and for improved techniques of patient selection, treatment planning, and fractionation scheduling. New randomized protocols have been opened for most of the tumor sites listed above.

We plan continued accrual in randomized Phase II and III studies, which have been established for locally advanced prostate tumors, for sarcoma, and for paranasal sinus, nasopharynx, and "radioresistant" histologies such as melanoma or renal carcinoma. For glioblastoma, a trial has been opened that compares the combination of neon ions with chemotherapy against an existing, well-characterized data base on the combination of low-LET (x-ray) irradiation plus chemotherapy. Other plans for the upcoming year include continuation of uveal-melanoma trials, a chordoma-chondrosarcoma collabo-

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* The gray is a unit of energy deposition by ionizing radiation: 1 joule per kilogram of mass. It is equivalent to 100 rads. The gray-equivalent accounts for differences in relative biological effectiveness caused by the "quality factor" of different kinds of radiation (ions, neutrons, x-rays, and so forth); the linear energy transfer (LET) of the radiation being used; and the vulnerability of the tissue being irradiated.

** LET is the energy transfer per unit length—the rate at which charged particles transfer energy as they interact with electrons when traveling through a medium. Different ions have different LETs, and many other factors come into play.

rative trial, and accrual of patients in the new randomized helium vs. neon protocol for other paraspinal and base-of-skull tumors.

The results of the study in 235 patients with uveal melanoma were excellent. A local tumor control rate of 97% has been observed in follow-up periods of 3 to 168 months (median: 62 months). Tumor control was excellent at all studied dose levels, which ranged from 50 to 80 GyE. Overall, 83% of patients have retained the affected eye. Of 181 patients who had pre-treatment visual acuity of 20/200 or better, 79 (40 %) retained this level of visual acuity. The actuarial survival rate is 80% at 5 years.

Radiation Biology and Biophysics Research

Radiation biology and biophysics research activities at the Bevalac address a broad spectrum of scientific questions. This work is relevant to the missions of several U.S. national agencies as well as to the private sector. A broad spectrum of scientific questions has been addressed by experiments employing a wide variety of beams, ranging from light ions such as helium to heavy ions such as lanthanum and even uranium.

NASA-funded biophysical research at the Bevalac has focused mainly on three space-related problems. First, an investigation is underway to assess the effects of heavy-particle fragmentation on cell killing and transformation (*sidebar*). In particular, the use of polyethylene or water-equivalent shielding material in space is under consideration, so quantitative information is necessary to determine what this material would do to the high-energy, heavy charged particles found in cosmic radiation, such as iron at 600 MeV/n. Iron fragmentation spectra under these conditions are being measured with a time-of-flight spectrometer. In addition, experiments completed to date with mouse 10T1/2 cells *in vitro* show that, in the plateau at 190 keV/μm of linear energy transfer, little change in cell killing or transformation frequency is found with up to 5 cm of polyethylene shielding.

More-fundamental work is in progress on transformation frequency in human keratinocytes subjected to iron at 600 MeV/n. The goal is quantitative assessment of the species-specific differences between rodent systems, which are readily available *in vitro*, and systems of human derivation, which are harder to develop. Assays for quantitative measurement of transformation of human mammary epithelial cells, using argon and iron, have been developed during the past year using anchorage-independent growth as a criterion. Currently in progress is a molecular analysis of the DNA of cells cloned from parent cells which were transformed by heavy ions. The goal is characterization of the kinds of genetic damage associated with the transformation process.

Experiments conducted with corn seeds conducted during space flight have spawned interest in the effects of heavy ions in producing growth inhibition, somatic mutation, and tumor induction in plants. Although the studies are limited, very interesting results have been obtained in ground-based plant studies at the Bevalac. Systematic studies with various heavy ions demonstrated that the frequency of somatic mutation in these seeds increased linearly with dose and that high-LET heavy ions were many times more effective than photons at inducing mutation.

More-recent studies with rice seeds showed significant results: both seedling survival and fertility of plants decreased with increasing doses of argon ions. Interesting mutations such as semi-dwarfism, early maturity, and large grain size were also found. These mutants demonstrate the unique potential use of heavy ions in crop improvement. In addition to the seed studies, preliminary experiments with cultured plant tissues were performed and various developmental effects of heavy ions were observed. Due to the excitement generated by these novel kinds of plant results, both basic and applied heavy-ion research with seeds and plants will surely continue.

As mentioned in an earlier section, both NASA and the Department of Defense are increasingly concerned about the loss of protection from galactic radiation provided by the magnetic field of the earth as astronauts travel deeper into space for longer periods—as in a mission to Mars, for example. Relatively little is known about the potential consequences of exposure to the types of radiation encountered in space in terms of human behavior or other effects on the brain. To reliably estimate the resulting potential for mission failure, we must understand the effects of such exposures on neurobiological systems and on behavior. Previous research showed that iron particles produce a taste aversion (a measure of behavioral toxicity) at significantly lower doses than the other types of radiation that were studied. The earlier data did not allow determination of whether the extreme behavioral toxicity of iron particles is due to their greater LET or to some other characteristics. Experiments are in progress to evaluate the LET dependence of this effect.

Another experiment, which examined mutation induction, has shown a qualitative similarity in the relationship between relative biological effectiveness (RBE) and LET at two different genetic loci (*tk* and *hprt*). The maximum RBE is achieved with ^{28}Si ions with a LET of 61 keV/μm. The *tk* locus, however, proved to be more sensitive to mutation induction for each LET. This is true whether the mutant yield is expressed as a function of dose or of particle fluence. When the mutant yield is expressed in terms of particle fluence, a qualitative difference in LET response is apparent for the two loci. This is due to the contribution of *tk-sg* (slow growth) mutants, which are induced with a vastly different LET response than either *hprt* mutants or *tk-ng* (normal growth) mutants. The spectrum of DNA structural alterations produced by high-LET radiation differs from that produced by doses of x-rays of the same toxicity. Intragenic rearrangements and allele loss are more common among mutants induced by high-LET radiations. Losses of genetic sequences associated with a linked but unselected marker locus are much more common among mutants induced by high-LET radiations.

New data have been obtained on a DOE-funded program of basic cellular and molecular effects that indicate that cellular damage caused by densely ionizing particles can be potentiated with active protein synthesis during post-irradiation heat treatment, and the radiation quality may be important to the regulation of synthesis of some specific proteins. X-rays appear to inhibit the rate of new protein synthesis, while neon ion irradiation appears to stimulate the rate of new protein synthesis post irradiation. Heat applied post-irradiation appears to amplify this response. After a treatment involving neon irradiation followed by heat, the synthesis of 70 kD, 90 kD and 110 kD proteins were enhanced while that of 100 kD protein was depressed. The differential synthesis of some proteins implies that the expression of specific gene products may be important in potentiating heavy-ion-induced radiation damage.

Further progress has been made in describing the kinetics and structures of ion-induced genetic and developmental lesions in the nematode *C. elegans*. These NASA-funded studies include lethal mutation in a 350-gene autosomal region, inactivation of both gonad and somatic blast cells, X-chromosome duplication/translocation, polycentric chromosome formation, and embryo inactivation. A set of radiation-sensitive mutants has been tested in search of specificity in the DNA-repair pathways for ion-induced lesions. Oxygen concentration and DMSO (dimethyl sulfoxide, a free-radical scavenger) were used to discriminate between direct and indirect ionization effects. The work has recently emphasized manipulation of ion-track structure by varying both charge and velocity. These experiments have shown that reducing the velocity and atomic number of the particles leads to important differences in biological effectiveness and lesion structure. This work is aimed at yielding interaction-cross-section data for multiple *in vivo* genetic and developmental endpoints, elucidating the repair pathways used for ion-induced damage, and planning for a 1992 spaceflight experiment.

DOE and NASA have supported studies during the past year directed at understanding the RBE of high-LET radiations for inducing cancer. Using the Harderian gland of the mouse as the test system, tumor prevalence data were obtained for iron (600 and 350 MeV/n), niobium (500 MeV/n), and lanthanum (693 MeV/n). These studies, together with previous results on protons (250 and 2000 MeV/n), helium (230 MeV/n), and neon (670 MeV/n), have provided enough data for regression analysis, resulting in estimates of the initial slope of the dose-versus-tumor-prevalence relationship. Contrary to data on normal tissue responses and from cell transformation studies, no convincing evidence has been found that the RBE drops at very high LET values. These data have important implications for estimating the cancer risk from heavily ionizing radiation.

In addition, dose-fractionation studies, which enable us to assess whether protracting a given particle dose reduces the hazard of tumor induction, have been completed. Early results indicate that a single dose of 40 cGy has the same effectiveness as a dose of 42 cGy given in 7 fractions of 6 cGy every two weeks. This shows that fractionation does not spare the radiogenic cancer response—in other words, that small doses of heavy ions spread out over time can be as risky as a single dose of the same size. Methods are also being developed to determine cells at risk and the transformation rate for *in vivo* irradiations.

Surviving Three Years in Space

According to the calculations for one scenario involving three years outside the magnetosphere, any given cell within an astronaut will probably be hit many times by protons and helium ions. Heavier ions (with atomic number greater than 10), though less common, would still hit one in three cell nuclei, and would have a disproportionate effect. (The calculations refer to the omnidirectional background of galactic cosmic rays. They assume that the astronauts would have a place to take shelter from the intense but short-lived and directional radiation of solar flares.)

The total dose may be as much as one sievert, or 100 rem—much more than a U.S. radiation worker would be allowed to receive in the same period. Deducing the biological effects is a complex matter. Heavy ions can damage a cell either indirectly or directly. They can produce free radicals in water and thus cause a cascade of chemical reactions. The ions can also interact directly with the DNA in the cell nucleus. A cell can be killed outright or damaged in various ways, including DNA alteration.

Radiation-induced cell transformation, one of the more worrisome biological results, begins with molecular events in the DNA, such as deletions of genes, translocations, and other genetic rearrangements. In addition to being massive and thus carrying great energy, heavy ions deposit most of that energy at the "Bragg peak," a single point at the end of their path. There, extensive cellular damage occurs, including greater potential for breaking both strands in the double helix of DNA. This compromises the cell's primary method of repairing damaged DNA, which uses an intact strand as a template.

Additional knowledge on both the physical and the biological effects of radiation will be needed for spacecraft design as well. The simplest approach would be to include massive shielding, but this could backfire, at least for the amount of overall shielding that a mechanically and financially practical spacecraft could accommodate. Naively designed shielding might make matters worse by turning the incoming particle into a shower of fragments. It would be virtually impossible to build a shielding wall that stops all these secondary particles; thus the shielding must be designed to admit the least-harmful spectrum of radiation. Clearly, a mission to Mars will require new knowledge in many fields, including the effects of heavy-ion irradiation.

Based upon an *LBL Research Review* article by Jeff Kahn of the Public Information Department.

Biomedical Operations and Quality Assurance

Procedures for safe conduct of operations in patient treatments at the Bevalac were instituted in the early stages of the clinical trials more than twelve years ago. These procedures span a wide range of activities, including treatment protocols, treatment recordkeeping, and daily calibration of dosimetry instruments. Some important procedures, such as the patient-treatment protocols, have been reviewed and approved by external committees. Our self-assessment of these procedures during the DOE Tiger Team inspection confirmed that the procedures already in place have been satisfactory for safeguarding the patients and personnel. Our quality-assurance program, as well as the training of personnel to adhere to these safety procedures, has been also judged quite adequate.

We have also maintained sufficiently detailed documentation of the daily operations, daily calibrations, testing, and maintenance at the facility. As a result of the Tiger Team inspection, we have formalized the quality-assurance schedules and have strengthened the bookkeeping procedures for the personnel training records. We believe that these changes will improve the biomedical facility's performance, decrease its downtime, and therefore improve the patient throughput.

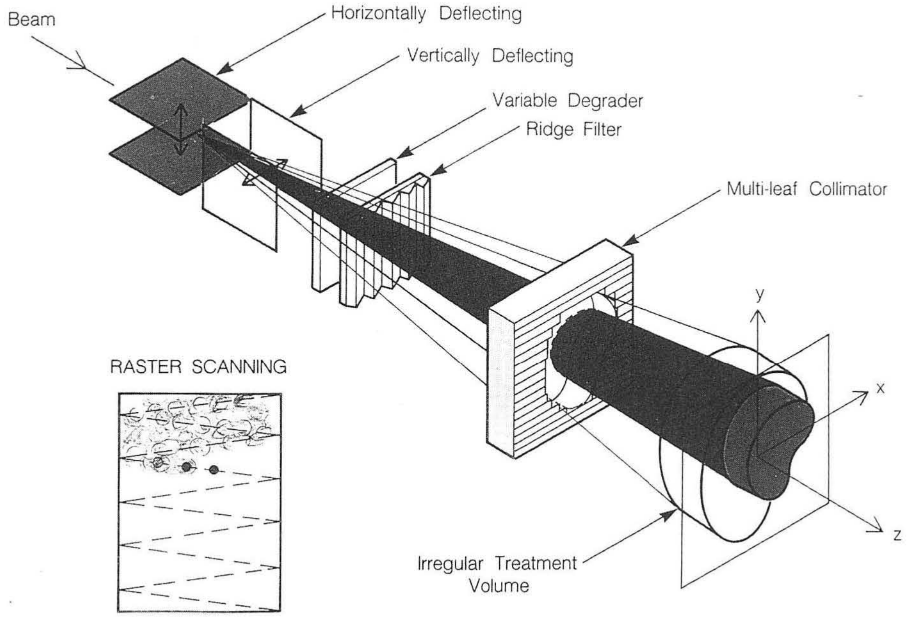
Equipment Development

The most important attribute of heavy charged-particle beams for radiotherapy is their dose-localizing property. We continue to develop the hardware necessary to achieve the optimum dose delivery—that is, delivering a uniform dose within the entire tumor volume with minimum damage to adjacent healthy tissues. The most significant advance of 1991 was commissioning of the Raster Scanner for clinical use. The Raster Scanner, commissioned in mid-1991 after extensive testing, has been shown to produce large fields with uniform dose distribution using helium and neon beams.

The Raster Scanner (Figure 7-6) represents an advance over systems currently in use, including the "wobbler" we developed in the mid-1980s. It scans the beam across the treatment area, much like the electron beam in a television's picture tube is scanned across the screen. Because the ion beams used at the Bevalac are so much more "rigid" than the low-energy electron beam in a picture tube, it was difficult to implement. Considerable effort has gone into its power supply and control system so that sharp-edged fields could be produced and the scan speed could be modulated to control the dose. Biological measurements in the proximal peak of the field, using neon ions, gave results as good as those of the wobbler.

Development of dynamic conformal treatments has continued with the construction of a multileaf collimator. We tested it with helium and neon ions for transmission through the gap between the fingers and found that leakage of the particles was suppressed sufficiently for use with patients. Other important systems currently in progress are a multi-element ionization chamber, an integrated circuit for measuring charge, and further improvements in Bevalac beam intensity control.

These results are a promising indication that the ultimate goal of implementing dynamic conformal particle therapy will be achieved. Human-use approval was very recently obtained to allow the Raster Scanner to be used with human patients in clinical trials. The therapy program at the Bevatron has already initiated a Phase I study using the Raster Scanner on selected tumor sites.



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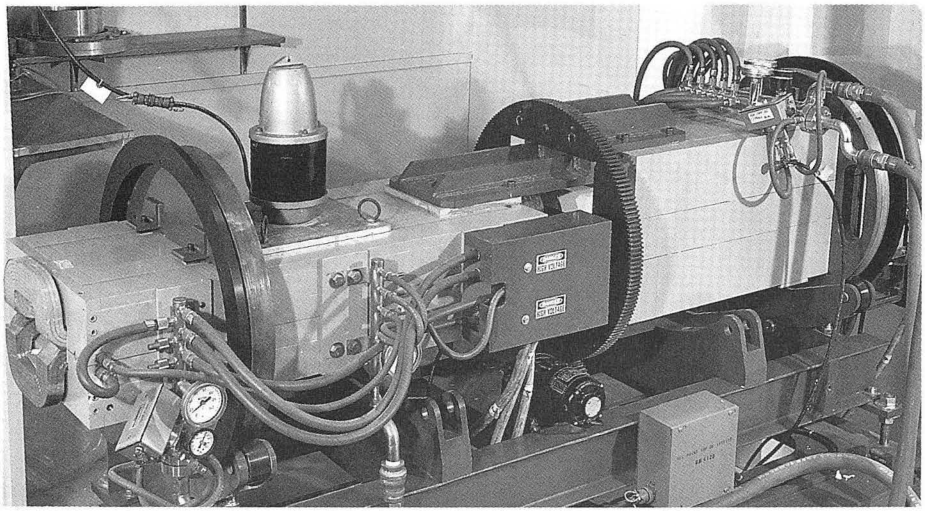

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Figure 7-6. One of the 1991 highlights in Bevalac biomedical technology development was the commissioning for clinical use of the Raster Scanner. It scans the rigid heavy-ion beam back and forth much like the electron beam in a television's picture tube. Biological measurements in the proximal peak of the field, using neon ions, have shown results as good as those of the "wobbler" beam-delivery system.

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