Title
Proton Therapy Research and Treatment Center Proposal

Author
Alonso, J.

Publication Date
1992-05-01

PUB-5348

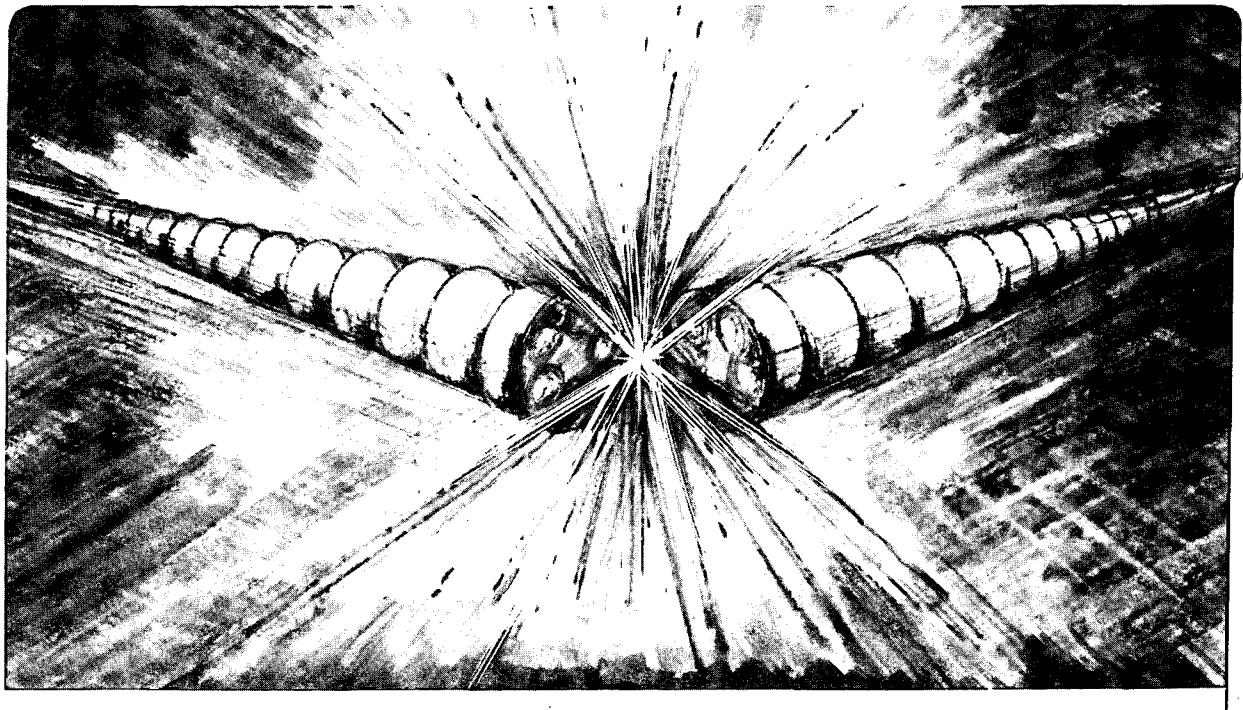
Lawrence Berkeley Laboratory
UNIVERSITY OF CALIFORNIA

Accelerator & Fusion Research Division

Proton Therapy Research and Treatment Center

J.E. Goodnight, Jr., and J.R. Alonso

May 1992



Prepared for the U.S. Department of Energy under Contract Number DE-AC03-76SF00098

DISCLAIMER

Proton Therapy Research and Treatment Center

Grant Proposal

submitted to the

National Cancer Institute

May 1, 1992

Principal Investigator:

James E. Goodnight Jr, M.D., Ph.D.
Director, UC Davis Cancer Center
UC Davis Medical Center
Sacramento, California

Co-Principal Investigator:

Jose R. Alonso, Ph.D.
Assistant Division Director,
Accelerator and Fusion Research Division
Lawrence Berkeley Laboratory

I. PROJECT OVERVIEW

A Design and Construction Project

This Grant proposal outlines the steps that will be undertaken to bring the UC Davis Proton Therapy Research and Treatment Center, known locally as the Proton Therapy Facility (PTF), through its design and construction phases. This application concentrates on the design phase of the PTF project; a follow-on application will be submitted in February 1993 to address the details of the construction and technical component procurement process.

The design process is divided into several sections. The technical component design consists of designs for the accelerator, beam transport lines, gantries, nozzles, dosimetry systems, patient positioning and verification systems, control systems and technical support facilities associated with the PTF. Collectively these items are known as the Proton Treatment System or "System." The building design effort, Proton Therapy Building or "Building," concentrates on the design for the structure housing all the technical components, as well as the regulatory, operational and planning issues associated with integrating the PTF into the overall hospital environment.

A third component of the process, although not one included in the scope of this grant application, is the fund raising program. Considerable effort is going into this area, funded directly by the UC Davis Medical Center, to first conduct a feasibility study of fund raising potential for the PTF, then to actually launch and carry through the campaign. The first phase should be completed by early fall 1992.

The technical design efforts will focus on the selection of the "design-build" industrial firm and on working with this firm to produce detailed designs and costs for the accelerator and other technical components. This is an optimal strategy for this type of technical design, and offers the best way of ensuring that the technology and experience available at a major national laboratory, the Lawrence Berkeley Laboratory (LBL), can be effectively transferred to the industrial sector, and through this to the PTF. With its extensive experience in the field of heavy-charged-particle radiation therapy, LBL is a logical choice for partnership in the System design effort. Furthermore, the excellent relationship between LBL and the UC Davis Medical Center established in the earlier phases of this project provides a solid basis towards the successful completion of the PTF. (Note, protons or heavier ions are all called "heavy charged particles" or HCPs.)

The process of selection of the System design firm is straightforward, although time-consuming, to meet the procurement requirements. A System Design RFP will be written, soliciting proposals for facility designs capable of meeting desired specifications. The specifications will be directed primarily at beam characteristics at the patient treatment site, and will leave open many questions such as accelerator type or gantry design. The proposals are expected to be in the form of conceptual designs in which these technical choices are made by the proposer, evaluating for their chosen design the expected performance and technical risks in meeting the published specifications. Once selected, the design firm is expected to work with LBL personnel in developing their design into its final form, producing detailed drawings and cost estimates for fabrication and procurement. Where necessary, prototypes of critical components must be built as part of the design process, to ensure that performance in practice meets theoretically calculated values.

The initial stage of the above process, from the start of the writing of the System Design RFP until the selection of the winning vendor, is expected to take about eight months. This time estimate is based on a careful evaluation of the steps that must be followed, on allowing interested firms adequate time to prepare their proposals, and on experience gained in the current year in which contracts are being issued to perform preliminary "critical technology" studies. As a result, it is imperative that the process commence as quickly as possible. In fact, work is already underway, and it is anticipated that the RFP will be issued well before the beginning of the grant year. Selection and awarding of the design contract will occur early in the grant year.

The Building design process follows a well-established path in the University of California system and should be quite straightforward. The land is owned by the University of California and is available for this project, no environmental concerns are expected and site conditions are well suited for the type of construction anticipated. Architectural firms will be selected early in the process, and will work with the University A&E staff throughout the design process. Planning documents and an architectural design guide are developed, leading to two reports, the Detailed Project Program (DPP) and the Program Planning Guide (PPG). University review of the project occurs upon submission of these documents, leading to approval by the UC Regents, expected in May 1993. Receiving this approval allows the commencement of detailed design work, including Schematic Design, Design Development and Construction Documents.

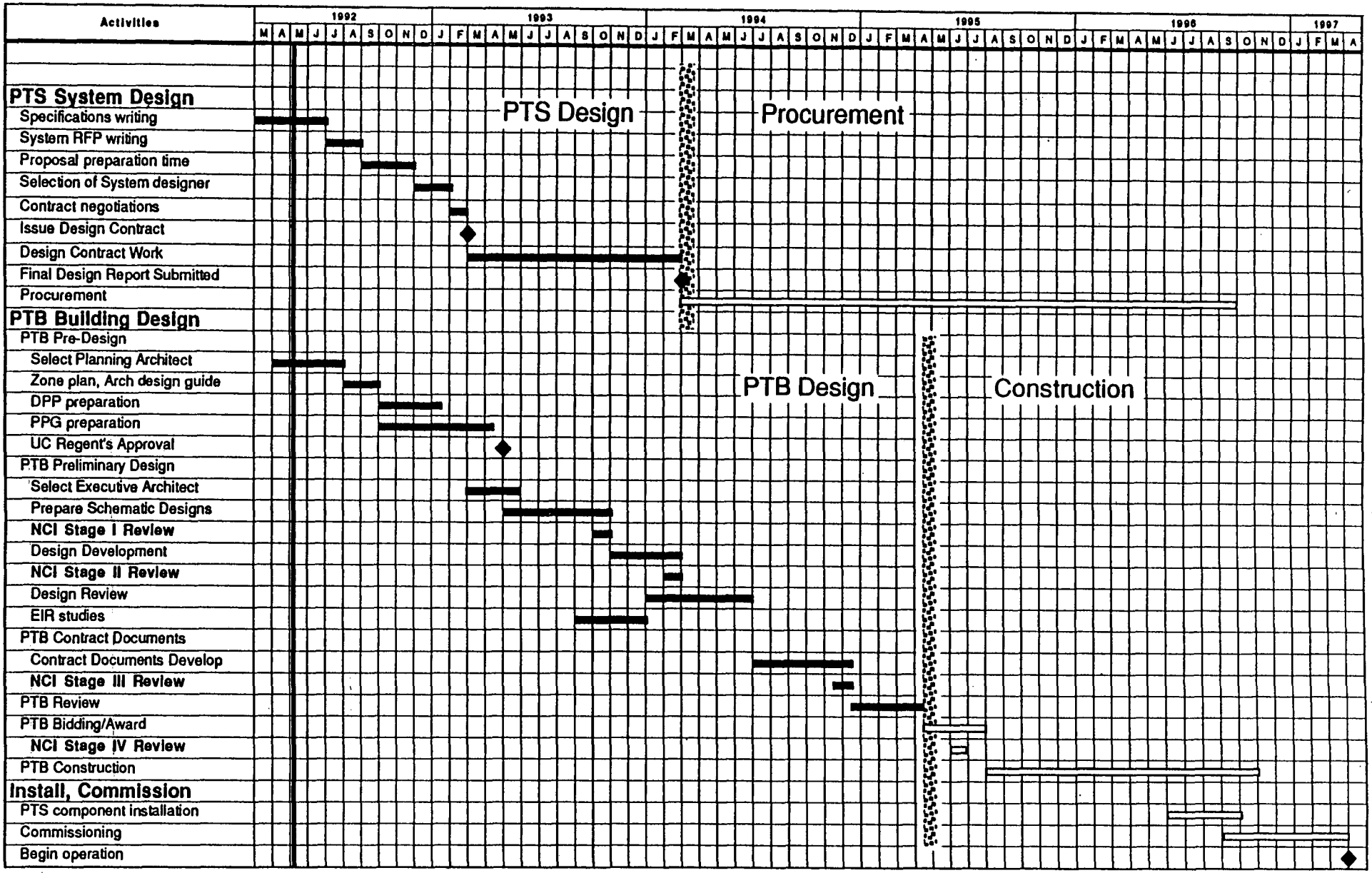
The building design process will require 31 months from the start of the grant year. Throughout this time period, numerous reviews are required to satisfy University requirements for project management. It was with some satisfaction that we learned that the University review process was essentially parallel to the NCI review requirements, and that the timing and nature of these respective reviews were quite similar. There should be no difficulty in accommodating the NCI review process within the overall schedule proposed for the PTF construction project.

The time-line chart attached below provides a general overview of the design project timetable, summarizing the information given in the paragraphs above. Note that the technical design efforts will be completed one year before the end of the building design. The preparatory efforts for the building design have only recently commenced, and as indicated above, the process is a lengthy one that requires following proper procedures. In fact, this staggering of design completion dates may serve in good stead because usually the fabrication process for accelerator systems is somewhat longer than actual building construction times, so that schedules for completion of technical components and building should mesh quite well for integration of all elements.

Interfacing of the technical and building design efforts is accomplished through the management structure for the PTF project. Dr. Goodnight provides overall leadership for the project, leaning on his previous clinical and management experience, to bring the UC Davis Cancer Center through the planning, design and construction stages. Dr. Alonso, as co-principal investigator, provides continuity with the earlier LBL-based design studies, and will supervise the technical design activities. Since Dr. Alonso is also principal investigator of the ongoing NCI funded studies at LBL, he provides the necessary management ties between LBL and UC Davis. The relationship between LBL and UC Davis has been excellent; a Memorandum of Agreement signed by LBL Director Shank and UC Davis Chancellor Hullar to foster collaboration towards design and construction of the PTF, as well as a Working Agreement between UC Davis and LBL identifying the detailed roles and responsibilities of the two institutions during the initial design phases of the project. This Working Agreement will be updated to cover subsequent phases.

Capital Building construction and System procurement commence immediately following the end of their respective design stages. A procurement contract with the System designer will be issued in the spring of 1994, and components should be ready for installation in early 1996. A construction contract award will be issued in the summer of 1995, and the building will be available to begin installation of technical components by mid 1996. Interior finishing of the building can occur during equipment installation and commissioning. Since commissioning exercises of the accelerator and beam delivery systems should begin in the summer of 1996, and research will commence in the spring of 1997.

Proton Therapy Facility Design Process



II. KEY PERSONNEL

Key Personnel:

Goodnight, J.E., M.D., Ph.D.	Director	Cancer Center University of California, Davis Medical Center
	Professor Chief	Department of Surgery Surgical Oncology Division University of California, Davis Medical Center
Alonso, J.R., Ph.D.	Physicist Assistant Div Director	Accelerator & Fusion Research Division, Lawrence Berkeley Laboratory, Berkeley, Calif.
	Physicist (appt pending)	Cancer Center, Univ. of Calif. Davis Medical Center, Davis
Castro, J.R., M.D.	Sr. Radiotherapist	Life Sciences Division, Lawrence Berkeley Laboratory, Berkeley, Calif.
	Professor Vice Chair	Department of Radiation Oncology, University of California, San Francisco
	Professor	Dept. of Surgery, Section of Radiation Oncology, Univ. of California, Davis
Chu, W.T., Ph.D.	Sr. Physicist	Life Sciences Division, Lawrence Berkeley Laboratory Berkeley, California
Kubo, H., Ph.D.	Professor	Department of Radiation Oncology University of California, San Francisco
	Professor	Division of Radiation Oncology Department of Surgery, Univ. of Calif, Davis
Lelevier, K.M., M.B.A.	Manager (Acting)	UC Davis Cancer Center University of California, Davis, Medical Center
Ludewigt, B., Ph.D.	Biophysicist	Life Sciences Division, Lawrence Berkeley Laboratory Berkeley, Calif.

Phillips, T.L., M.D.	Sr. Radiotherapist	Life Sciences Division, Lawrence Berkeley Laboratory, Berkeley, Calif.
	Professor Chairman	Department of Radiation Oncology, University of California, San Francisco
	Professor Chief	Dept. of Surgery, Section of Radiation Oncology, Univ. of California, Davis
Renner, T., Ph.D.	Physicist	Accelerator & Fusion Research Division, Lawrence Berkeley Laboratory, Berkeley, Calif.
Rush, T.A., M.A.	Sr. Architect	Architects & Engineers University of California, Davis, Medical Center
Smith, T.H., Ph.D.	Sr. Adm. Analyst	Medical Science Planning University of California, Davis, Medical Center
Staples, J.W., Ph.D.	Physicist	Accelerator & Fusion Research Division, Lawrence Berkeley Laboratory, Berkeley, Calif.
Verhey, L.J., Ph.D.	Medical Physicist Chief	Division of Physics Department of Radiation Oncology, University of California, San Francisco
	Professor (appt. pending)	Dept. of Surgery University of California, Davis

III. PROGRAMS FOR THE UC DAVIS PROTON THERAPY FACILITY

A. Cancer Research Programs to be Conducted at the PTF

A long term clinical research program in the use of heavy charged particles in the treatment of cancer has been carried on at LBL utilizing the Bevatron accelerator, as well as the 184-inch synchrocyclotron until its closure in 1987. The long term goal of this clinical study has been to compare low (protons, helium ions) and high (neon ions) LET irradiation. While the 184-inch synchrocyclotron was operational, this machine served as the source of helium ions both as low-LET control arm for neon studies, and for research in the application of low-LET charged particles in their own right. These studies when coupled with the experience with protons in other facilities have provided a strong basis for extension of proton radiotherapy to hospital-based facilities. When the 184-inch synchrocyclotron was decommissioned in 1987 to make way for the Advanced Light Source, the low-LET helium ion clinical research was transferred to the Bevatron. At the present time, beam time is scarce on the Bevatron and is mainly devoted to heavy ion clinical research. Therefore, only limited helium ion low-LET studies have been possible in the past few years.

We expect that the Bevatron will continue operation for NASA related space biology, and important high-LET neon ion clinical research and related radiobiology programs.

The low-LET proton research would best be carried out by moving to a new source of particles. We regard the PTF at UC Davis as an ideal source and expect that this important low-LET clinical research will be expanded when the PTF is commissioned. This would include control arms for the high-LET neon work at LBL, and, more importantly, the cooperative clinical research with protons which is discussed below. A major effort is being mounted for proton facilities to cooperate in clinical research studies so that optimization of proton therapy can proceed expeditiously.

1. UC Davis Low-LET Radiation Research Program with Protons at PTF

The Department of Radiation Oncology, UCSF; Division of Radiation Oncology, Department of Surgery, UCD; and the Radiation Oncology Department, Life Sciences Division at LBL have underway a long-term program of low-LET radiation research using proton and helium ions. This has been supported by a Clinical Program Project Research Grant (NCI, J.R. Castro, P.I.) from the National Cancer Institute, with ion beams provided by Department of Energy support at the Bevatron accelerator at LBL. Additional physics and biological research supporting the clinical trial at LBL is funded by NCI, NASA and DOE and involves such studies as improved beam delivery through dynamic conformal therapy (NCI, W. Chu, P.I.), and evaluation of heavy ion biological effects, and development of predictive assays for use in patient selection (DOE, E. Blakely, P.I.).

The goal of the clinical research trial has been to study the application of the advantageous physical dose parameters of protons and helium ions in the treatment of unresectable tumors in critical anatomical locations.

The major sites treated at LBL have been in the head and neck area (skull base, paranasal sinuses, nasopharynx), juxtaspinal area and selected lesions in the retroperitoneum, pelvis and bone or soft tissues. Particular emphasis has been placed on treatment of uveal melanoma, paranasal sinus tumors, nasopharynx tumors invading into the base of skull, and tumors arising in the paraclival and juxtaspinal regions such as chordoma, chondrosarcoma and meningioma. The results have been most encouraging with a significant increase in local control and survival. In the patients with unresectable or residual chordoma or chondrosarcoma, of whom more than 85 have been treated, actuarial local control and survival rates range from 60%-85% at 5 years, representing an approximate doubling of results when compared to historical data for x-ray therapy. In uveal melanoma, local control is 97% with 5 year actuarial survival at 80% because of distant metastases.

The eye has been preserved in 88% of patients and useful vision in approximately 50% of patients. Other localized tumors which have been successfully treated with protons and helium ions include prostate tumors, periaortic lymph nodes, and residual tumors in soft tissue and bone sites.

Promising work has also been seen in the use of proton and helium ions in the treatment of unresectable arteriovenous malformations where a high rate of shrinkage has occurred and more than 85% of patients treated no longer have episodes of bleeding. Charged particles appear uniquely suited for the use of complex and large arteriovenous malformations, which cannot be well treated with stereotactic x-ray therapy or embolization.

We expect that the proton research to be carried out at UC Davis will build on the exciting results obtained to date. The chief tasks are to extend further the number and range of tumors treated and refine the techniques of proton therapy learned in the physics laboratory accelerators at LBL, MGH-HCL (Boston), NIRS, Japan and others.

The initial emphasis will be on Phase I-II studies in tumor sites which limited facilities and beam time have prevented us from studying, such as selected upper aero-digestive tract, paranasal sinus, brain, lung and GI tumors. Dose-searching studies will help to optimize the use of protons and maximize local control while minimizing normal tissue late reactions.

While we have used helium ions at LBL because of the physical characteristics of our accelerators, pretherapeutic studies have shown only a small amount of high-LET in the distal portion of the helium beam. Clinically the results are identical to proton therapy. Therefore the transfer of the low-LET ion research program to UC Davis with continuation using proton therapy is not expected to show any significant clinical differences from the helium studies at LBL. This has been borne out already by the quite similar results obtained with helium ions at LBL and protons at MGH-HCL in eye and skull base tumors.

These new research studies will be carried out under the aegis of the Proton Radiation Oncology Group (PROG): H. Suit, Chairman; L. Davis, Executive Officer. This is a newly formed clinical cooperative group of which the founding members are LBL-UCSF-UCD, MGH-HCL and LLU (Loma Linda Proton Accelerator Facility). This group has just received support from the National Cancer Institute to organize and begin development of cooperative clinical research protocols in proton radiotherapy. The initial studies include the following: completion of an on-going protocol in head and neck chordoma-chondrosarcoma started by LBL and MGH in 1985; commencement of new dose searching protocols in uveal melanoma and meningioma which were instituted at MGH and are now expanded to the entire group; and Phase I study of the use of protons in treatment of tonsil and base of tongue tumors. A clinical protocol development committee has been established (J. Slater), as has a quality assurance/physics review committee headed by Dr. L. Verhey of UCSF.

Establishment of additional research protocols will take place as the Loma Linda Facility comes fully online, and will be strengthened by the addition of the UC Davis Facility. Additional group members will be enrolled from around the world, including the Centre Protontherapie de Orsay, France, the newly forming proton facilities at Paul Scherrer Institute, Switzerland, and the National Accelerator Center in South Africa.

We anticipate that eventually more than 10 facilities worldwide will be available for inclusion in this cooperative research group; at UC Davis, all patients will be entered on either PROG or local research protocols.

2. Control Arm for Heavy Ion Research with Neon Ions at LBL

In addition to the proton and helium ion research, LBL conducts a unique program of heavy-ion research concentrating on the use of neon-ion irradiation. The goal of this research is to determine whether high-LET beams are more useful in the clinic for certain selected tumors than

low-LET beams such as protons. This research will continue at LBL since at present it has the only accelerator in the world capable of producing these beams in sufficient intensity for clinical research.

With the construction of the proton accelerator at UC Davis Medical Center, all of the low-LET ion research at LBL will be transferred to Davis. This will free all of the available beam time at LBL for concentration on the unique heavy-ion research and provide even better use of the valuable heavy-ion beam time available at LBL.

3. Other Cancer-Related Research Initiatives for the PTF

Many disciplines are expected to become involved in the cancer-related research endeavors at the PTF. Some of these are closely related to understanding and improving factors associated with the patient treatment research efforts, while others probe more basic areas of cancer risks and mechanisms.

In direct support of the therapy program, studies associated with improvements in beam-delivery techniques will become an active element of the PTF research program. Currently there is a very strong and successful effort ongoing in this area at LBL, and many significant strides have been made in the field. The Wobbler and Raster Scanner systems, now in clinical use, were developed by Dr. W. Chu and his group with NCI funding, and continued research is progressing towards development of 3-dimensional "dynamic conformal therapy." Development efforts at LBL are focused around the Bevalac and its heavy-ion beams. Plans are being developed to shift much of this effort to the PTF when it is available, for optimization of beam-delivery technology for protons. Systems utilizing protons can be developed and very quickly placed in clinical operation. Much of the group's experience is directly applicable to this new focus.

A new area of research will be an exploration of the potential for proton radiography. Early experiments performed as long ago as 18 years demonstrated some interesting possibilities for direct use of proton and heavy-ion beams for radiography. The motivation to explore proton radiography is to develop techniques for rapidly verifying patient positioning and target volume localization with the patient in the treatment position immediately prior to treatment.

Members of the UC Davis physics department and the Crocker Laboratory have expressed interest in examining the effects of nuclear reactions undergone by the proton beam as it traverses tissue in the patient prior to reaching the target volume. Reaction mechanisms and effective dose delivered to normal tissue due to these reactions are among the topics this group has expressed interest in studying.

NASA has initiated a program of basic research into radiation effects of cosmic rays, with the goal of assessing risks to astronauts on deep-space, long-duration missions. LBL and Colorado State University are participating in a program called NSCORT to perform studies involving carcinogenesis, mutation, neoplastic transformation, chromosome aberrations, DNA damage and repair (double strand breakage and base damage), and other effects of ionizing radiation. With both high LET and low LET components to this research effort, this group has expressed strong interest in using beams from the PTF for the elements of the program best done at UCDMC rather than at the Bevalac.

Biological studies are needed to explore late effects, such as mutagenesis and carcinogenesis, and to elucidate molecular mechanisms that may underlie these late sequelae. A large void also exists in our understanding of the chronic and late consequences of single particle traversals of muscle, the brain and the spinal cord. The full potential of combined proton radiotherapy and chemotherapeutic drugs has also not been examined.

DOE and NCI currently fund several other lines of basic biomedical radiation research at the Lawrence Berkeley Laboratory that with the development of collaborative arrangements could

be continued at PTF. In addition, the specific genetic effects of proton-particle probing of seeds to develop plants with valuable phenotypes could also draw major agricultural interest to a proton research facility. As mapping of the human genome progresses worldwide, proton damage to specific human genes could become a tool to resolve specific gene functions.

Dr. Eleanor Blakely of the Life Sciences Division at the Lawrence Berkeley Laboratory and Dr. Marvin Goldman of the Department of Radiological Sciences, School of Veterinary Medicine, University of California, Davis are among those interested in developing a basic proton research program at the PTF. Other interested biologists in the Medical School and Veterinary Medical School, as well as in the basic sciences, will be contacted for interest in using the proton facility.

SUMMARY OF CANCER RESEARCH IN PROPOSED FACILITY

Program Activity Principal Investigator	Grant or Contract Number/Other Funding Agency	Title	Percent of Effort	Grant Period	Current Annual Award ($) (Direct Costs)
Dr. J.R. Castro	CA19138	Treatment of Cancer with Heavy Charged Particles (low–LET arm to be transferred to UCDMC)	80	7/92–6/97 (pending)	$1,770,496 recommend
Dr. W. T. Chu	CA49562	Beam Scanning & Treatment Planning for Conformal Therapy	50	12/92–11/9 (pending)	$369,231 requested
Dr. A. Chatterjee (LBL) Dr. S. Curtis (LBL) Dr. E. Blakely (LBL) Dr. E. Gillette (LBL)	NASA	Cosmic Ray Effects on Cancer (low–LET research to be performed at UC Davis) Helium Ion Induced Human Cateractogenesis (proton portion)		1/92–12/96	$707,000
TOTAL					$2,846,727

New Research Activities Made Possible by Completion of the PTF

Program Activity Principal Investigator	Grant or Contract Number/Other Funding Agency	Title	Percent of Effort	Grant Period	Current Annual Award ($) (Direct Costs)
Dr. E. Blakely (LBL) Dr. M. Goldman (UCD)	DOE	Radiobiology, Predictive Assays of Cancer	1997	New	To be proposed
Dr. W. T. Chu (LBL) Dr. H. Kubo (UCD)	NCI	Proton Radiography & Cancer Treatment	1997	New	To be proposed
Dr. P. Brady (UCD) Dr. J. Romero (UCD)	DOE	Nuclear Reactions Effects on Dose Delivery	1997	New	To be proposed

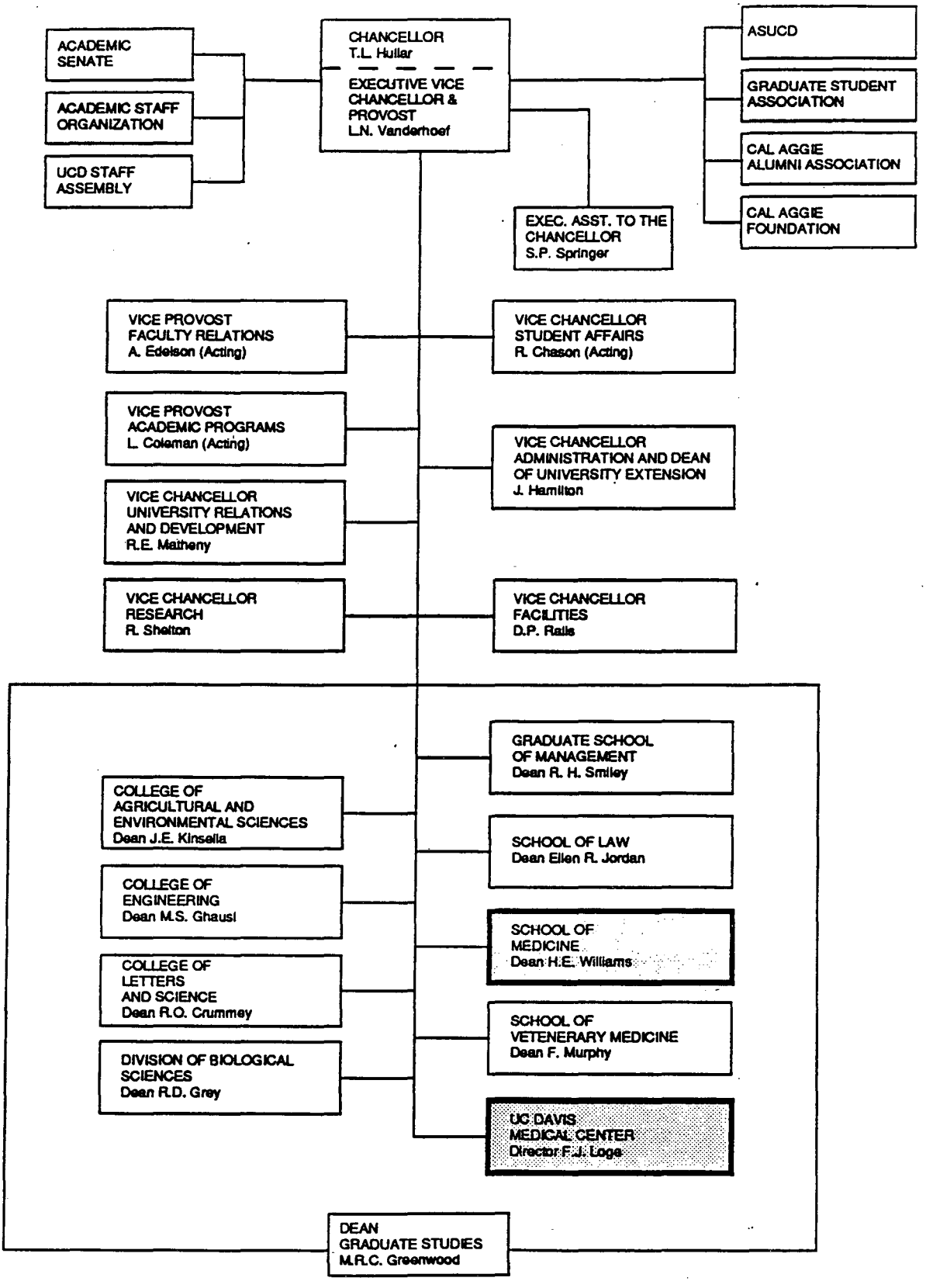
B. Administration, Organization of the PTF

The PTF will serve as a major cancer research center for UC Davis serving the Medical School, the hospital (Medical Center), as well as other departments within the UC Davis campus with interests in proton beams for cancer research. Additionally, the PTF will be available for peer-reviewed research projects from other institutions, on an equitable beam- and facilities-use recharge basis. The UC Davis and Cancer Center organizations will reflect the ability to support such research activities, through user support resources to effect proper scheduling, preparation, and other activities necessary to properly interface external research efforts to a flexible user facility.

In the organization charts that follow, we first describe the overall organization of the University of California at UC Davis, showing the relative positions of the teaching hospital at the Medical Center, which is an entity separate from the School of Medicine. The second chart shows the organization of the Medical Center, identifying the Cancer Center within this hierarchy. The third chart gives an indication of the organization of the Cancer Center itself once the PTF has been placed in full operation.

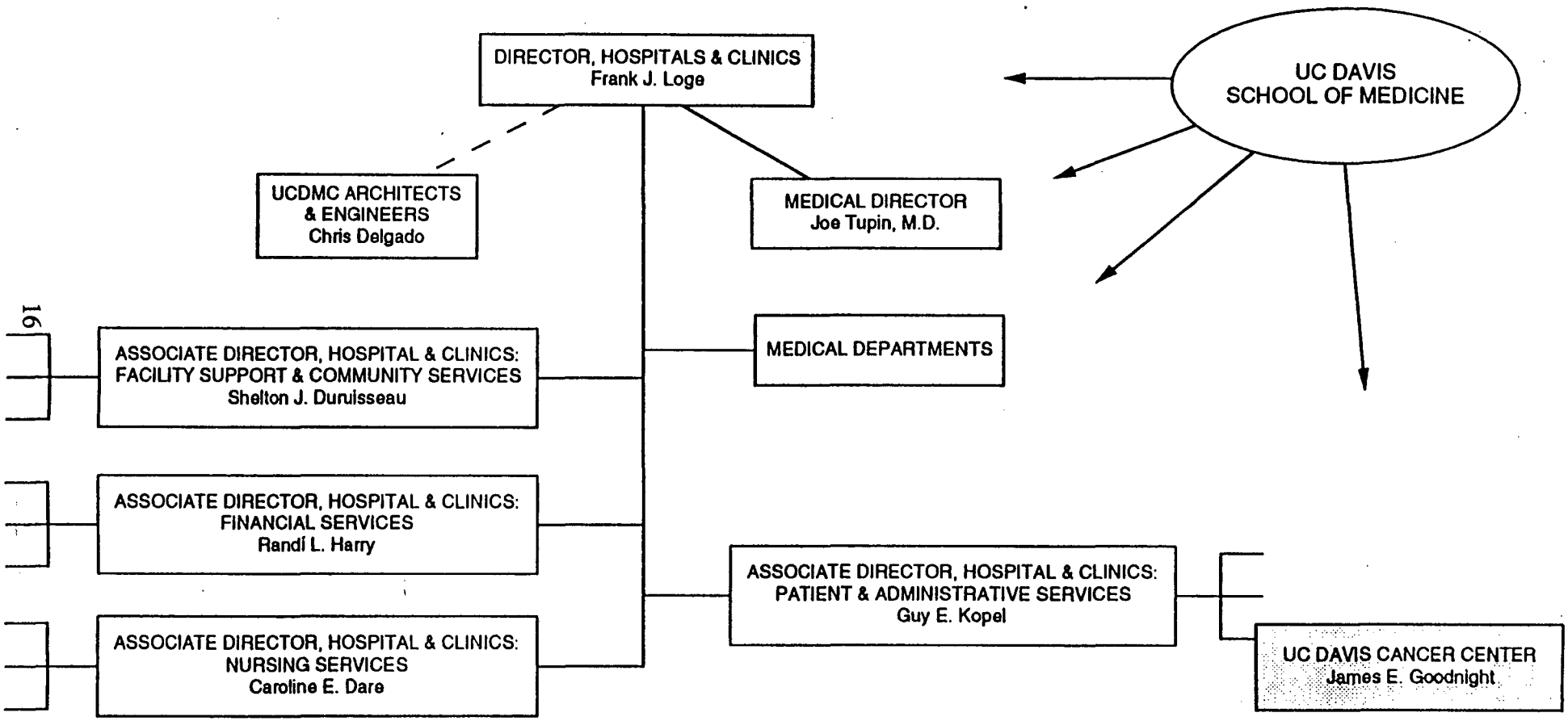
Under the Director of the Cancer Center, the PTF will be directed by the head of the Radiation Oncology Department, an MD radiotherapist. Clinical and research operations of the PTF will be integrated into the normal operation of the Radiation Oncology Department. The Research Coordination group will perform proper liaison and support of the research activities conducted at the PTF, on both a scientific and administrative level. Separate PTF Operations and Facility Development groups, within the PTF organization itself, will be responsible for operations, maintenance and improvements of the System components.

UNIVERSITY OF CALIFORNIA, DAVIS
ADMINISTRATIVE ORGANIZATIONAL CHART

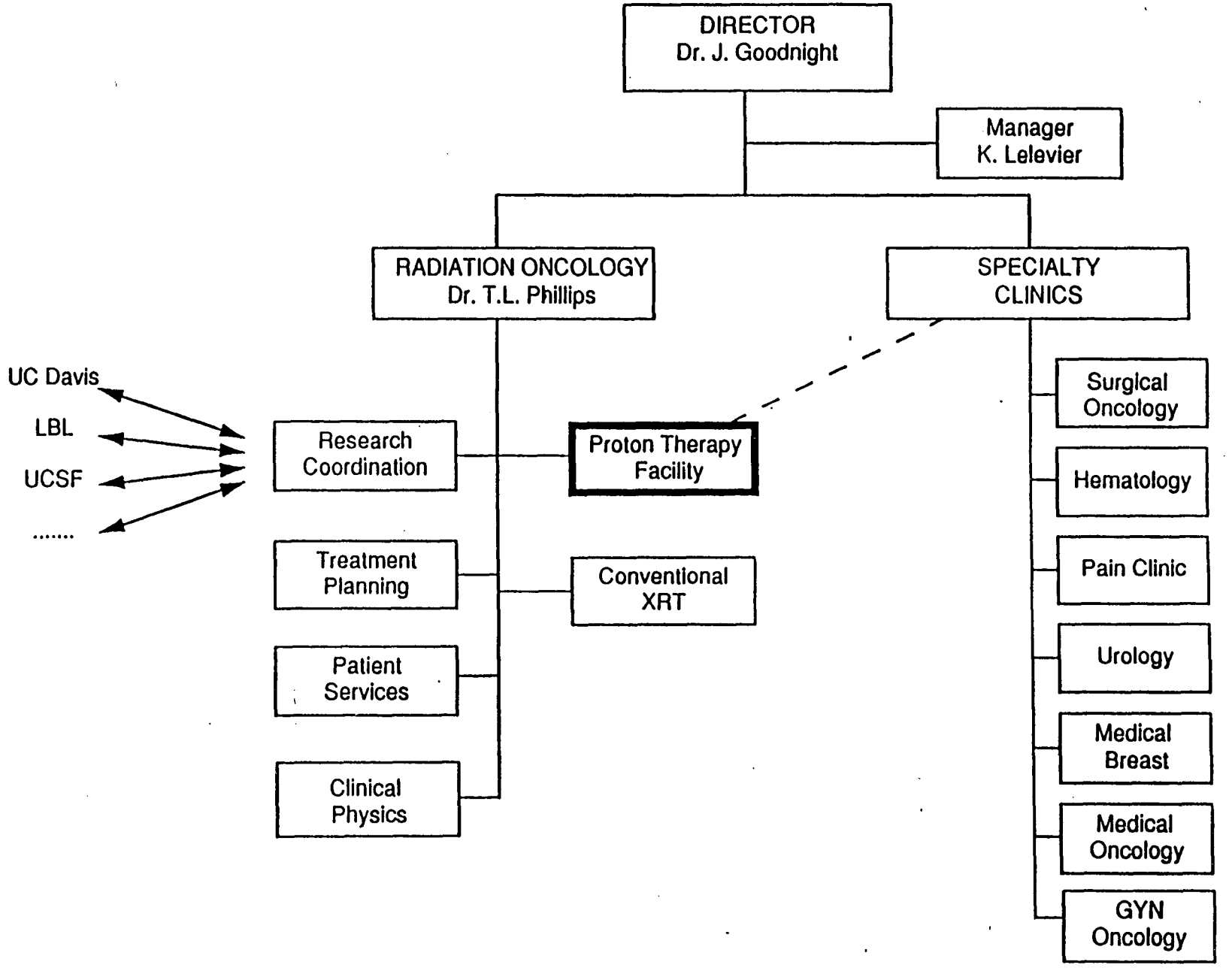


UC Davis Medical Center

Administrative Organization Chart



UC Davis Cancer Center



C. Institutional Support

UC Davis institutional managers enthusiastically support the development of the PTF to be located at the UC Davis Medical Center in Sacramento. Attached as the next pages, is a letter to Dr. James Goodnight from Dr. Theodore Hullar, UC Davis Chancellor, Dr. Hibbard Williams, Dean of the School of Medicine, and Frank Loge, Director of UCD Medical Center, affirming the University's continued support for the project. There is also strong support among the Medical Staff of the UCDMC, including the Cancer Center Staff. A feasibility study for raising significant funding for the UC Davis Proton Treatment Facility has been commissioned. The funding goal is believed to be within the University's realm. The purpose of the feasibility study is to test the general attitudes of prospective donors; gauge community support for a specific project; uncover problems in the public's perceptions of the purpose of the project; research the magnitude of the goal; discover strong promotional themes; cultivate early support; and evaluate internal readiness to conduct the campaign. The hiring of a consultant firm has taken place and work will start immediately. Note, no NCI funds are being used in these fund-raising activities.

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DAVID PIERPONT GARDNER
President of the University

THEODORE L. HULLAR
Chancellor at Davis

OFFICE OF THE CHANCELLOR
DAVIS, CALIFORNIA 95616-8558

29 April 1992

Dr. James E. Goodnight, Jr.
Director, UC Davis Cancer Center
UCDMC
Sacramento, California 95817

Dear Jim:

By this letter, we affirm our continuing support for the development of a proton beam therapy research and treatment center at the UC Davis Medical Center. We envision the proton center as facilitating the development of a whole new focus of cancer research at our campus, with a synergistic impact on current cancer research. This would be an exciting addition to the Cancer Center, our outpatient imaging complex, our expanding acute care 500+-bed hospital, a major Radiology Department, and our new research complex. We have, therefore, initiated the development of a financial plan to fund the building and technical components.

Our desire to create this facility results from the interest we and our faculty colleagues find in the demonstration at LBL and other institutions of the efficacy of charged particle therapy resulting from the modality's excellent dose-localization possibilities. We feel that proton therapy has progressed to the point where its introduction into the academic medical center environment will facilitate applications research in areas of demonstrated effectiveness and will speed up research in other areas.

We would like LBL's continuing assistance in bringing this project to completion. The direct experience of its staff with accelerator, beam-delivery, and dosimetry technology for radiotherapy with heavy charged particles makes LBL one of the few centers in the world capable of designing the proton system we envision. LBL staff assistance with parameter selection, design, construction oversight, and commissioning of the proposed system will be vital to the success of the project. It is for this reason that we have signed a memorandum of agreement to develop this project with LBL.

We are grateful that you agreed to be the chair of the Proton Therapy Task Force and its subcommittees in order to muster, coordinate, and guide the resources necessary for project implementation. UCDMC Architects and Engineers, as well as the Office of Medical Sciences Planning, have been asked to make this a high priority project. We have committed the land adjacent to the Cancer Center for the project. Our recruitment process for a campus urban design (master) plan consultant is down to two finalists; the selected consultant will include site planning for the proton center in the urban design plan.

Finally, we have commissioned a feasibility study through our development office to lead to a financing plan for the project. It remains a high campus priority and we encourage you to pursue wholeheartedly the development of the proton therapy research and treatment center.

Sincerely,

Theodore L. Hullar
Chancellor

Hibbard E. Williams, Dean
School of Medicine

Frank J. Loge, Director
Hospital and Clinics

IV. PROGRESS REPORT

A. Overall Strategy for the Design Study Process

The multi-year nature of the NCI design-study process has allowed an orderly approach to the subject, permitting a high degree of confidence that the end result will lead to optimized plans for clinical implementation of proton therapy in a hospital setting. In broad terms, efforts in the first year were focused on technology assessment; in the second year we are conducting preliminary design studies; and we propose that the third year be devoted to detailed design and costing exercises. Following this design sequence, construction can commence immediately.

Year One activities were conducted entirely in-house; LBL has the necessary qualifications and expertise to analyze appropriately the current status and recent developments in the field. Our report summarizing work conducted in Year One has been published as a separate report (LBL-32053). We will elaborate further on our basic conclusions from the Year One studies below. In Year Two (the current year), we have emphasized establishing contacts and performing technology transfer to the private sector. It is clearly inappropriate for LBL to perform the ultimate design and construction of the technical components of the facility for UC Davis; this is in the domain of the private sector. The appropriate role for LBL is to transfer accelerator and medical technology to assist the private sector to design successfully and build such facilities. The current year is a transition year, with LBL establishing contacts with industry, and beginning the process of identifying firms with the willingness and capabilities to enter seriously into this field. The process we have selected for this is the commissioning of studies by industry of specific topics we have labelled as "critical technology" areas, identifying problem areas with presently operating facilities or technologies which limit their ability to satisfactorily meet clinical requirements. We have currently identified a list of topics to be studied, and are in the final stages of preparing the first of several "critical technology" RFPs soliciting proposals from industry. The results of these studies will be collected into a report, a reference guide for the ultimate designer of the PTF, or for any entity interested in designing a clinical proton facility. More details of the process will be described below.

B. Progress in Year One

Our studies in Year One concentrated on three areas: an evaluation of the existing state of different types of accelerators applicable to radiotherapy with protons; a study of optimization of beam delivery techniques and methods for most effectively placing the dose into the desired target volume while reducing complications due to normal tissue involvement; and an assessment of tumor sites suitable for proton therapy. These studies searched for potential implications for facility size and layout, with an eye towards establishing the most desirable clinical specifications.

To assess current accelerator technology and identify problems relevant to a new proton therapy accelerator, we studied the design and performance of the Loma Linda accelerator, as well as our own Bevalac, plus cyclotrons used now or previously for therapy (Harvard, LBL), as well as the characteristics of operating proton linear accelerators. Our conclusion was that the overall best choice for the accelerator remains the synchrotron, although a cyclotron-based system has not yet been ruled out. Although new ideas for a linac have been proposed, no technological demonstration currently exists and basing a new facility on such a linac would carry significant performance and cost risks at this time. This is not to say that the cyclotron or synchrotron designs of today are completely without problems. Certain areas have been identified that are limiting the performance of all of these machines for the most advanced applications desired today. Solutions to these problems may tilt the choice towards one or the other of these options. Examples of problems are: the elimination of spill structure from the synchrotron beam that presently prevents Loma Linda from employing a scanning system; how to most effectively achieve a large beam energy variation with a cyclotron, again to facilitate beam scanning. These problems have been further defined, and are the subject of Year Two (current year) "critical technology" studies.

Beam delivery studies were conducted along two fronts: a study of gantry designs, both "separated function" and "compact" types, and an evaluation of benefits of 3-D conformal and multi-port treatments. Design parameters were identified for the different gantry types, as well as some topics for further study that would further optimize designs and integration of beam transport and beam delivery systems. The "separated function" gantries, of which those at Loma Linda serve as examples, are physically larger because the beam spreading systems are located entirely between the last bending magnet of the gantry and the patient. "Compact" gantries integrate the beam spreading system with the bending magnets, allowing for a smaller overall radius for the gantry and thus a smaller shielded enclosure. This integration process does not come without cost in some limitation of available options for beam spreading systems, so the optimization of the gantry-beam spreading system is not altogether straightforward.

The importance of gantry beam delivery for an optimized treatment facility has become very clear. Although treatment delivery with fixed horizontal beams are certainly possible, and has been accomplished satisfactorily for many years, the added flexibility of the gantry, coupled with the ability to treat supine patients, points clearly to this method being preferable in a clinical setting. The importance of a supine patient is twofold: first in added comfort of the patient, leading to easier immobilization and the potential for more accurate positioning, and, second, the more direct applicability of high quality diagnostic information from CT and MRI scans in which the patient is almost always scanned in the supine or prone position. Such diagnostic information is critical for treatment planning, and any scans below the head and neck area must be taken with the patient in the actual treatment position owing to substantial gravity-induced shifting of organs and tissue. LBL and MGH have specially modified CT scanners capable of imaging a seated patient, although these machines are now more than 10 years old, are difficult to service and do not produce images as good as those from more modern scanners. It would be difficult for a hospital-based therapy facility to rely on this type of CT device as a primary data source for treatment planning. Additionally, no rotatable MRI unit as yet exists anywhere. These problems could be overcome to a limited extent, and indeed some horizontal beam programs will continue in existing facilities in Japan, France and Russia so that there may be a demand for rotatable CT and/or MRI devices. However, the preferred technique is isocentric delivery of charged particles. Although this requires large and expensive hardware, it provides great flexibility to the clinical implementation of proton therapy. We believe, therefore, that optimization of gantry designs is a worthwhile endeavor.

Gantry optimization cannot be performed independently from the choice of accelerator to be used. Most relevant is the relationship between the beam spreading system and the stability of beam intensity provided by the accelerator. If excellent beam stability is possible, the large therapy fields can be produced by active magnetic scanning. Such scanning allows the greatest flexibility in treatment delivery, and is viewed as the more desirable technique to be used. However, the intensity stability required for scanning has proven difficult to obtain for synchrotrons, so conservative designs call for being able to produce the clinical field sizes with passive scattering systems. While integrating scanning systems into a "compact" gantry design is relatively straightforward, such gantry designs which will accommodate a scattering system require much larger magnets and become somewhat unwieldy. As a result, the "separated function" (Loma Linda-type) gantry, although quite a bit larger, offers added design flexibility.

While suitable intensity control from a cyclotron should be quite easy to accomplish, the problem is more difficult with a synchrotron. Tight specifications for regulation of the main guide-field power supplies, and high-quality feedback systems are required to obtain proper performance. Such performance has been in fact demonstrated from some existing machines, but not without very careful design and attention to proper engineering. For a synchrotron-based facility, then, specifying a "compact" gantry that requires a scanning system to produce the desired field size carries a definite element of risk. Note that the performance specifications of proton linear accelerators are not conducive to beam delivery via scanning systems. Since such machines typically produce very short pulses (< 10 usec) of beam at a relatively low repetition rate (<50 Hz), producing large uniform treatment fields with a scanning system would be difficult. Pulsed

electron linacs that do use sweeping magnets to make large fields run at around 300 Hz, and sweep a beam that is several centimeters in diameter, much larger than an optimally-sized proton beam.

3-D treatment delivery was also studied in Year One activities. As the greatest effectiveness of the beam is achieved by placing stopping particles in the desired treatment volume, tailoring the distribution of stopping particles into an arbitrarily-shaped volume becomes a desirable attribute of a treatment delivery system. Just how desirable, however, has not been clear, and as achieving this type of delivery is quite complex, we undertook a study to assess quantitatively the benefits of 3-D conformal scanned beam delivery. By comparative treatment plans on patients actually treated, we assessed normal tissue complication probability for 2-D and 3-D delivery, and for few- or multi-port treatments. In initial clinical studies, only about 6-8 anatomical sites have been evaluated to date, 3-D conformal scanned beam delivery shows a small, but significant benefit for HCP treatments. Details of these studies are given in the final report from our Year One activities. There appears to be a promising potential for reducing the number of treatment ports as well as improving therapeutic ratio (ratio of tumor dose to dose in normal tissues) with the 3-D conformal technique. We expect that this will be a vital improvement in beam delivery and want to preserve flexibility in design of our proton facility to permit this type of scanning system.

Many of the advanced concepts in beam delivery, such as scanning systems and 3-D delivery, have not been developed to the state of clinical readiness at this time. Enough developmental work has taken place, though, that it is reasonable to expect that they will be incorporated into treatment facilities within a few years. Ultimate development of beam- delivery technology is sure to produce performance far superior to that available now or in the near future. The implication of such potential developments on new facilities being designed, is that one must ensure that enough flexibility is built into these designs to allow for implementation of new techniques as they become available.

Another important observation from our preliminary studies has been that one of the operational problems with existing treatment techniques is the reliance on a large amount of patient- and port-specific hardware. Each port requires a customized collimator and range compensator. Fabrication of these devices is labor-intensive and adds significantly to the cost of treatment. A highly-desirable goal is to develop a dynamic conformal treatment delivery system that minimizes reliance on such hardware. At LBL, we are ready to begin testing of a multi-leaf collimator for charged particles, which may reduce reliance on poured cerrobend collimators for many treatment fields. A variable-speed scanning system, also nearing readiness for clinical use, coupled with range-stacking techniques may allow for performing some treatments without compensators. These systems will require clinical testing but should be optimized before the PTF is completed.

In summary, our Year One activities have served to strengthen the case for readiness of proton accelerator technology for clinical implementation. As outcomes of these studies have come several well-defined topics that need to be further developed to increase the confidence that a given technology will in fact perform at the desired level. These topics, discussed further below, are being actively pursued in our Year Two currently ongoing studies.

C. Evolution of Relationship between LBL and UC Davis

During Year One activities, it became necessary to change the site for development of the Proton Therapy Facility from the University of California at San Francisco to UC Davis. Leadership at UC Davis and UC Davis Medical Center have enthusiastically supported the idea of a joint venture to build a Proton Therapy Facility as part of a planned expansion of the UC Davis Cancer Center. The site visit for the Year Two grant was conducted at the UC Davis Cancer Center and a message of a strong institutional commitment from UC Davis management was evident.

There continues to be strong and increasing support at UC Davis for the construction of the PTF as evidenced by the institutional support letter in Section IV. The necessary committee and

task force structure has been established to develop the infrastructure for the planned PTF. Activities and membership of these committees will be detailed below and in succeeding sections.

A noteworthy activity for this past year has been the development of a Memorandum of Agreement between UC Davis and LBL for development of the PTF. This document, written and thoroughly reviewed by both LBL and UC Davis management, was signed by the Chancellor of UCD and the Director of LBL at the March 19th meeting of the UC Regents at UCLA. The basic agreement calls for LBL to take responsibility for oversight of the specification, fabrication, installation and commissioning of the technical components of the PTF, while UC Davis will develop the operational models, and provide A&E services to oversee design and construction of conventional facilities. UC Davis will also take responsibility for arranging financing of the PTF, anticipated to come primarily from a private fund-raising campaign, already in its initial stages. The MOA sets the framework for collaboration towards development of the PTF. It calls for specific plans to be developed through Working Agreements, written and updated from time to time as appropriate, between the principals at LBL and UC Davis. For now, Dr. Jose Alonso (LBL) and Dr. James Goodnight (UC Davis) share this responsibility. Dr. Goodnight is the principal investigator on the current application signifying the switch in emphasis from LBL to UC Davis. There is at present an excellent working arrangement, with strong participation by both institutions to bring this project to fruition.

D. Year Two Progress

1. Year Two Progress - Technical Studies Progress

Following the goal of developing contacts with the private sector, our strategy in Year Two has revolved around the design of appropriate studies to commission of industrial firms. The intent, in addition to directly addressing the technical issues identified for study, is to stimulate interest and develop the expertise needed for effective participation by the private sector in the final design and construction of clinical proton therapy facilities. While several firms possess the expertise to design 250 MeV proton accelerators, it is quite clear that the most difficult element of a clinical facility is the successful integration of the accelerator with the treatment delivery and dosimetry control systems. At present there are no companies that have fabricated and delivered an entire proton-based therapy system. It is our belief that the most effective exercise in "technology transfer" that LBL can perform is to assist US industry in obtaining such a capability.

A second goal for Year Two has been to coordinate efforts with Massachusetts General Hospital to develop potential technical scenarios applicable at both UC Davis and MGH. The complementary strengths of both institutions has the potential for the development of superior plans. To date cooperation between LBL and MGH has been quite good. Several meetings have taken place to define and coordinate efforts, with notable progress in generating a set of clinical specifications for our proton therapy facilities. As will be seen below, these clinical specifications will play a key role in the continued design and subcontracting process.

To initiate contacts with the private sector, we (LBL and MGH jointly) published an advertisement in the Commerce Business Daily soliciting interest in participating in the proposed program of studies. We received responses from 17 firms, encompassing essentially all of the US industrial expertise in building accelerators suitable for our application, as well as several foreign vendors.

Early in the grant year a Joint Advisory Committee was formed by LBL and MGH advise us on the conduct of our preliminary design studies. Listed in the Table below, this Committee met in mid-January at LBL, and strongly encouraged us to focus our efforts on clearly-defined projects. Taking the Loma Linda facility as a base, we should carefully evaluate how to build a second-generation facility. The committee, although containing cyclotron and linac experts, suggested that more rapid and sure progress would be made by building on the Loma Linda synchrotron base than by conducting studies in other technologies that had no proven clinical

record. This Committee also urged us to carefully research the "organizational conflict of interest" (OCI) issue when we engage companies to perform preliminary design studies, lest these companies be summarily excluded from participation in the final design process.

Table IV.1 - MGH/LBL - UC Davis Advisory Committee

Name	Affiliation	Expertise	Appointed by
Dr. James Smathers,Chair	UCLA	Medical Physics	LBL
Dr. W. Kenneth Dawson	TRIUMF	Control systems	LBL
Dr. Thomas B. Kirk	Argonne Nat'l Lab	High energy physics	MGH
Dr. Edward Knapp	Santa Fe Institute	Linacs	LBL
Dr. Pierre Mandrillon	CAL, Nice France	Cyclotrons	MGH
Dr. J. Richard Orr	Fermilab (ret)	Accelerator systems	MGH
Dr. Ben Prichard	SSC	Systems Integration	LBL
Dr. Mary Austin-Seymour	U. Washington	Radiotherapy	MGH
Dr. Herman Winick	SLAC, Stanford	Synchrotron rad.	MGH

The OCI issue has emerged as a significant problem. There is in fact a real danger that a company participating in preliminary studies may be excluded from the final design process. This could be catastrophic to the project: as mentioned above all the firms with the requisite resources to design and build the proton therapy facility have expressed interest in participating in the preliminary studies. After extensive consultation with legal counsel and OCI experts, we have evolved a strategy that should allow us to proceed with our original plans. The preliminary design studies must focus on very narrowly- defined technical issues related to particular aspects of accelerator and beam delivery technology. The results of these studies will be published, fully open to any group that will be engaged in final design studies for this or any other proton therapy facility. Any inventions or patents resulting from the studies must be available to the ultimate designer on an appropriate licensing basis.

The selection of the final designer must be made based on specifications that were in no way determined or influenced by firms involved in the preliminary studies. The specifications that will be used for this selection will be centered around the UC Davis PTF clinical specifications which will be finalized before the industrial studies have finished. By thus separating the two processes, we have been assured that OCI issues will not play a role.

With this strategy decided upon, we then concentrated on the structure of the Year Two studies. As stated earlier, these studies will focus on narrowly defined technical issues identified in the Year One study, collected under the generic name of "critical technology" studies.

The importance of these studies cannot be overemphasized and a recapitulation of the findings from Year One is not out of order to stress this point. If we look at the technology base available today for options on which to design a proton therapy facility, several clearly limiting areas emerge. A walk through a design exercise will illustrate the above theme. If we ask for the most basic of criteria for a clinical HCP facility, most clinicians and physicians would agree that it should have the capability for isocentric beam delivery, should be reasonably sized and priced, and should be capable of conveniently incorporating upgrades from developments in treatment-delivery techniques that are bound to evolve over the 40-or-so year lifetime of the facility.

These very simple "specifications" place surprisingly tight constraints on the design choices for the technical system components. First of all, the gantry necessary for isocentric delivery of these beams is dauntingly large, even for the lightest of the "heavy" particles, the proton. A heavy-ion gantry (suitable for carbon or neon-ions) would be two to three times larger, is viewed by the medical community as beyond the reasonable state of the art. So, size and cost issues identify protons as the ion of choice for this generation of systems.

With regard to proton gantries themselves, the question of reducing the size from the "existence proof" Loma Linda design requires careful thought. The appeal of the "compact gantry" designs of PSI, IBA, Uppsala in reducing the size of the treatment room and possibly the overall cost of a gantry system must be offset by the potential loss of flexibility inherent in their design. The large Loma Linda gantry is a "separated function" design; that is the beam spreading system is contained entirely within the "nozzle" area after the last bending magnet, so any beam spreading system that will fit in a linear three meter space can be incorporated into this gantry design. The compact gantries of necessity integrate the beam spreading system into the magnetic bending system of the gantry and thereby reduce the options for spreading systems to those that in fact can be integrated. In this regard, scanning systems meet these criteria much more readily than scattering systems. Requiring a scanning system, however, can have an effect on the accelerator choices, which can then impact the flexibility requirement.

Effective use of a scanning system requires very stable performance from the accelerator, and a high level of control over the time- and intensity-structure of the beam. While cyclotrons can in principle offer this level of stability, these machines suffer from one major drawback, namely their inability to vary the energy of the beam. Adjusting the beam energy, hence the range of the beam in the patient, must be done with degraders between the accelerator and the patient. Such an energy-degrading system causes a significant degradation of beam quality, and produces background radiation and beam intensity loss. Although workable for present-day delivery technology, the loss of beam quality may hamper the performance of the overall facility when 3-D treatment capabilities are ultimately available. Synchrotrons, on the other hand, do have the ability to change the beam energy from pulse to pulse, and present to the beam-spreading system the highest-possible quality of beam. Synchrotrons, however, have two well-known problems. The first is that although designing the machine to deliver the required intensity is not difficult, actually achieving the desired intensity performance at Loma Linda has proven elusive. A more serious problem is achieving the beam stability. The resonant extraction process is prone to instabilities, and extreme care in the overall system design must be exercised to achieve the required performance. This includes attention to proper power supply filtering, feedback systems and dynamic control systems. Synchrotrons at different laboratories around the world have achieved such performance, but not without great care and attention to details.

So, synchrotrons offer ultimately more flexibility, but there is a significant risk in specifying a scanning system for use with a synchrotron until solutions to the beam control problems have been demonstrated. It is desirable, then, to have a fallback position of being able to start treating with a scattering system that is insensitive to the beam-structure problems encountered with poor synchrotron operation. A compact gantry that allows for use of a scattering system has some engineering difficulties, so a better choice then is the larger, separated function gantry.

By this chain of logic, we have arrived at exactly the parameter set for the Loma Linda facility. We should ask how we can progress from this starting point, or if in fact this does represent an optimal choice given today's technology. The key issues outlined above are: beam stability and control from a synchrotron, integration of a scattering system into a compact gantry; and to a lesser extent beam intensity from a synchrotron.

Should the cyclotron be considered a viable option, the problem to overcome is how to prevent loss of beam quality with a degrading system. Cyclotrons face another issue; currently operating machines in the 250 MeV energy range are very large and expensive. Compact designs have been proposed by IBA in Belgium and Michigan State University, but none have been built. Engineering and physics issues must be studied carefully before declaring that such designs are viable for clinical applications.

3-D scanning system development is important, but not critical for the parameter selection process described above. Currently-operating scanning systems are successfully treating patients in a 2-dimensional manner; upgrading these systems to 3-D capability is more of a control and

power supply issue than one of overall configuration design. A compact gantry with a 2-D system would meet the flexibility requirements for eventual upgrading to a 3-D system at the appropriate time.

The "critical technology" studies being undertaken in the current year are structured to address all of the above issues. Synchrotron and cyclotron studies, gantry and scanning system designs, and control system specifications have been identified. Results of these studies should provide valuable data to assist in assessing technological risks of moving ahead from the Loma Linda baseline.

We have broken the studies into several stages, with at least two "critical technology" RFPs to be issued as well as one or more focused studies to be directed to known experts who can best address specific topics in their field of specialization. The first RFP is almost ready for issue, it will be issued jointly by LBL and MGH. Topics 1, 2 and 3 of the list below are included in this RFP; the other topics will be released in a subsequent RFP, as they are ready. We anticipate the studies to be completed by this fall.

In all, we anticipate commissioning between 8 to 10 studies, for a contract fee of between $50K and $200K per study, for which LBL will perform oversight, coordination and management functions. In addition to the topics discussed below, we are hiring a consultant, an expert in the current status of cyclotron technology, to evaluate objectively the suitability of the compact cyclotron designs for clinical application.

Topics for the first "critical technology" RFP:

1. Achieving required intensity in a synchrotron-based 250 MeV proton treatment facility. Improving on the performance of the Loma Linda machine will require optimization of the injector design, as well as an analysis of possible changes in the synchrotron lattice and design. Beam loss mechanisms should be studied for improvements in overall system performance.

2. Study of rapid energy variation and beam stability for a synchrotron-based 250 MeV proton treatment facility. To ensure the most flexibility in treatment delivery, the system should have the capability of changing the beam range in the patient from one pulse to the next. This requires automatically setting the desired accelerator energy, extracting the beam at this energy, ensuring that all the beam transport magnets track this energy so it is delivered to the patient without having shifted from its central axis. Scanning systems require tight control over the beam intensity, and elimination of "beam structure" which is common of synchrotrons. All these tasks have been demonstrated as possible in modern accelerators, but developing the specifications to ensure this can be done requires careful study of all the elements of the accelerator and beam transport system.

3. Isocentric rotating gantry designs. As alluded to above, optimization of the beam delivery system offers great potential for cost savings and performance enhancement. Studies of "compact" versus "separated function" gantry designs will be performed, to include mechanical designs, integration of beam spreading systems, as well as mounting of dosimetry equipment and beam shaping systems.

Topics for subsequent "critical technology" RFPs:

4. Shielding studies: data compilation and computer codes. It was discovered during the design of the Loma Linda facility that there was no definitive source of data and computational tools to facilitate the specification of shielding walls. This information does exist, but even today is not conveniently available. The intent of this study is to collect in one place such tools, so that appropriate shielding calculations can be performed for any new clinical proton therapy facility.

5. Specifications for an integrated control system. A common failing of existing heavy charged particle treatment facilities is the lack of proper communication between the various control systems. This generally arises from a lack of understanding of the requirements and constraints on each system by the designer of the others. Accelerator control systems experts generally have little knowledge of dosimetry control and patient record keeping, and vice versa. As a result, the proper bandwidth for exchange of information between these control systems is inadequate. It is highly desirable, therefore, to have specifications established for an integrated control system by designers with an understanding of all parts of the therapy operation. A goal of the control system design should also be to minimize operations staffing requirements and facilitate maintenance. Specifications to achieve these ends should be developed.

Other topics for study are still being discussed and will be developed suitably for inclusion in subsequent RFPs. With these studies successfully completed, we feel we can move confidently into the final design stage, and from there into actual construction of the Proton Therapy Facility at UC Davis. The detailed strategies for undertaking the final designs of the building and technical components are outlined in Section V below.

2. Year Two Progress - Building Design Progress

The UC Davis Proton Therapy Task Force was created in October of 1991 as a resource and advisory board for the development of the Proton Therapy Facility. Membership includes key individuals from LBL and UC Davis who are responsible for overseeing the myriad steps involved in the development of the facility at UC Davis Medical Center. In the past year, the Task Force has reviewed and provided input on the following processes: the design phase for technical component of the Proton Therapy System; development of the Memorandum of Agreement between LBL and UCD; development of feasibility studies for UCD fund raising; and the development of Systems Specifications. Membership of this committee is included in Table IV.2.

Table IV.2 - Proton Therapy Task Force Committee

J. Goodnight,M.D.,Ph.D.(Chair)	UC Davis	Director, Cancer Center
J. Alonso, Ph.D	LBL	Sr. Physicist, Accelerator & Fusion Research
B. Anderson	UC Davis	Comm. Coord., Med. Sci. Relations
J. Barsalou, Ph.D.	UC Davis	Prin. Cont. Negotiator, Office of Research
E. Brennan	UC Davis	Admin. Analyst, Pat. & Admin. Services
J. Castro, M.D.	LBL/UCSF/UCD	Dir, Rad Onc/Prof & V. Chair Rad Onc
W. Chu, Ph.D.	LBL	Sr. Scientist, Life Science Division
L. King	UC Davis	Manager, Hosp. Public Affairs
G. Koppel	UC Davis	Assoc. Dir H&C, Pat & Admin Services
K. Lelevier	UC Davis	Acting Manager, Cancer Center
F. Loge	UC Davis	Director H&C, Hospital Administration
D. Martensen	UC Davis	Director, Med: News & Communications
B. Neidt	UC Davis	Exe. Dev. Officer, Med Sci Planning
P. Oddone, Ph.D.	LBL	Deputy Director
T.L. Phillips, M.D.	LBL/UCSF/UCD	Prof/Chair, Rad Onc/Chief, RadOnc
M. Rivas	UC Davis	Research Asst, Univ Rel and Development
T. Rush	UC Davis	Sr. Architect, Architects & Engineers
A. Smith, Ph.D.	UC Davis	Sr. Admin. Analyst, Med Sci Planning
L. Verhey, Ph.D.	UCSF/UCD	Assoc, Professor & Vice Chair, Physics
H. Williams, M.D.	UC Davis	Dean, School of Medicine

The "Proton Therapy Building Committee" was appointed to investigate parameters relevant to the design of the facility. While finalization of the facility design awaits completion of

the design of the proton accelerator and the beam delivery system, the Committee's tasks in Year Two are as follows:

1. To project the need for proton therapy in Northern California and the surrounding states;

2. To investigate the patient care spaces needed and their optimum adjacencies;

3. To translate the accelerator and beam transport system into a list of spaces and required adjacencies;

4. To coordinate site studies regarding location, orientation, and design of the PTF in relation to its immediate environment.

Table IV.3 - Proton Therapy Building Committee

G. Koppel - (Chair)	UC Davis
J. Alonso, Ph.D.	LBL
J. Castro, M.D.	UC Davis/UCSF/LBL
W. Chu, Ph.D.	LBL
J. Goodnight, M.D., Ph.D.	UC Davis
D. Kubo, Ph.D.	UC Davis
T. Rush	UC Davis
A. Smith, Ph.D.	UC Davis

Discussions have been held in the clinical subcommittee of the Proton Therapy Cooperative Oncology Group (M. Austin-Seymour, J.R. Castro, Co-chairs) at several PTCOG meetings regarding clinically promising new uses for proton therapy. Many tumor sites have not been treated as yet despite their potential due to lack of resources, beam time and other limitations in the laboratory accelerator facilities used at LBL and MGH. A. Smith, Medical Scientist Analyst and J.R. Castro, have begun an assessment of potentially advantageous tumor sites to be treated with proton therapy, based on the physical advantages of protons, the use of radiotherapy in the Northern California region, and an assessment of what percentage of these patients might be best suited for proton therapy. Refinement of these data will take place as further analysis is carried out in the PTF Building Committee deliberations. A summary of the patient resources available to the UCD PTF from the Sacramento area, the Bay Area and Northern California is shown in Table IV.4. In addition, patients are expected to be referred from Oregon and northwestern Nevada. A conservative estimate has been made of the number of patients who would need proton therapy, approximately 20% of patients referred for primary radiotherapy in the region.

The first draft of this epidemiological overview of cancer in California's Region 3 (Sacramento area) and in Northern California, generally (Regions 1, 2, 6, & 8) is included in Table IV.4. This overview focuses on both community need and demand in order to project the volumes that this facility should be designed to handle. In doing so, the following types of data were examined:

1. **Demographic Projections** — These were obtained from the local Population Research Center (as designated by the Bureau of the Census), and consisted of age and sex interval population projections for Northern California counties for the years 1995, 2000, and 2005.

2. **Current Incidence of Invasive Cancer** — Counts of invasive cancer were made available by the California Tumor Registry. These figures were sorted by site of malignancy and by patient residence in each of the five regions in Northern California, and all the counties of Region 3.

3. **Current Use of Beam Radiation** — Data also sorted by site of malignancy were also obtained on frequency of beam radiation for the regions of Northern California and the counties in Region 3.

4. **Estimates of Need for Proton Beam Radiotherapy** — Based on preliminary research experience of proton accelerators and anticipated results of future research, estimates were made of the percentage of patients needing proton therapy, by cancer sites.

Table IV.4 suggests that up to 500 patients per year will be referred for treatment upon commissioning of the facility, rising steadily as population growth and referral patterns grow. Even at this level, with the developing third-party reimbursement schedules in place at Loma Linda, MGH and LBL, this will make a material contribution to the operational costs of the PTF. We expect that Medicare and third-party reimbursements will continue. The costs of proton therapy for those patients who cannot be well treated with other modalities is modest compared to the cost of failure to cure the tumor, with its resultant subsequent medical care costs. In addition, it compares favorably with other modern, high tech cancer treatments such as bone marrow transplants, complex surgical techniques, Gamma Knife treatments and others.

PROTON THERAPY NEEDS
Calculations for Northern California

Statistic	Region 3 *				Surrounding Regions (1, 2, 6, 8)				Total			
	1988	1995	2000	2005	1988	1995	2000	2005	1988	1995	2000	2005
Population (1000s)	2,417	3,026	3,411	3,784	9,062	10,377	11,125	11,825	11,479	13,402	14,536	2,417
Cancer Rate	3.79	3.79	3.79	3.79	3.90	3.90	3.90	3.90	3.88	3.88	3.88	3.88
Cancer Cases	9,163	11,470	12,931	14,346	35,366	40,495	43,416	46,147	44,529	51,965	56,348	60,493
Beam Radiotherapy Rate	23.4%	23.4%	23.4%	23.4%	23.4%	23.4%	23.4%	23.4%	23.4%	23.4%	23.4%	23.4%
Beam Radiotherapy Cases	2,144	2,684	3,026	3,357	8,276	9,476	10,159	10,798	10,420	12,160	13,185	14,155
% Needing Proton Therapy	21%	21%	21%	21%	21%	21%	21%	21%	21%	21%	21%	21%
Cases Needing Proton Therapy	447	560	631	700	1,727	1,977	2,120	2,253	2,174	2,537	2,751	2,954
Referral Rate	0%	30%	50%	70%	0%	15%	25%	35%				
Realized Volume	0	168	316	490	0	297	530	789	0	465	846	1,279
Fractions @ 20/Case	0	3,360	6,314	9,807	0	5,932	10,600	15,774	0	9,293	16,914	25,581
Fractions/day @ 250	0	13	25	39	0	24	42	63	0	37	68	102

* Sacramento and surrounding counties

4-May-92

PRELIMINARY DRAFT

The Building committee also addressed facility configurations needs and requirements. Preliminary studies on configuration and programming have been carried out by the Committee with the assistance of the staff of LBL, radiation oncology personnel at UC Davis Cancer Center and the LLUMC Proton Beam Therapy Facility, UCDMC Medical Sciences Planning, and a consultant. These studies are identifying the necessary spaces and desired adjacencies, and then evaluating conceptual configurations for the facility.

These studies will result in the following products: (1) a list of spaces, with net assignable square footage, and a description of the functions for each; (2) the required adjacencies and separations of spaces; (3) conceptual layout (such as bubble diagrams) for the facility; (4) a rough estimate for gross square footage for the facility; and (5) a very preliminary estimate of building cost.

The site chosen for the PTF is in the UCDMC zone designated for ambulatory care facilities. The area is clear of other buildings except for the adjacent Cancer Center. UCDMC has also contracted with a campus master plan consultant to plan the layout of future buildings and circulation. The Committee will work with the consultant to determine (1) the optimal orientation of and access to the Proton Treatment Facility, and (2) the circulation between and amongst facilities. This will also include optimizing connections with the Cancer Center to utilize the center's services and resources.

To complete Building Design activities for Year Two, a recommendation on the exact site and orientation of the building will be made in conjunction with both the master plan consultant's report and the above facility configuration recommendation by September 30, 1992.

V. PTF DETAILED DESIGN PROCESS

A. Specific Aims for the Design Process

We propose to complete the design process for the UC Davis Medical Center Proton Therapy Facility (PTF) by April 1995. During the design process it will be important to maintain close relationships between the groups designing the System and the groups designing the Building. Overall responsibility for management of both designs will be in the purview of Dr. James Goodnight, Principal Investigator of the Project. He is aided by his administrative staff at the Cancer Center, Ms. Lelevier and the Analyst, and the committees set up for various functions. The Proton Task Force Committee, (Table IV.2) will serve as the forum to keep abreast of developments in both the System and Building design teams and coordinate and resolve any conflicts between the designs before they are finalized. Dr. Alonso, who heads the Systems design team and Mr. T. Rush and Dr. A. Smith, who are responsible for the Building and capital planning, are all on this committee reporting to Dr. Goodnight as Chair. In addition, the Building Committee (Table IV.3) and the Systems Committee (Table V.1) have members who sit on both committees and also the Task Force Committee. Given these overlaps of Committee membership, any potential design conflicts between the two design teams will have been brought up and resolved within the respective committees long before they become problems. The design for the machine will be completed by April 1994, with the building and environmental designs completed one year later. By April 1994, we anticipate full readiness to begin hardware acquisition for the PTF and, by May 1995, to select a contractor to begin building construction.

Specific tasks to be accomplished in the design process are:

1. **Finalize PTF clinical specifications.** This must be done before the start of the grant year to allow for timely selection of industrial participants in the final System design process.

2. **Complete technical component (System) designs.** Detailed design and costing for all the technical elements of the PTF will be carried out by an industrial firm to be selected early in the grant year by LBL and UC Davis. This firm will be fully qualified to build, install and commission all the technical components of the PTF. Upon Regental approval of the UC Davis Medical Center fund-raising program, the firm will receive a contract to complete these elements of the project.

3. **Obtain Approval for the PTF from the University of California Regents.** This step is essential prior to commencement of construction. Several steps must be completed prior to presentation of the project to the Regents, among which is the preparation of two documents by UC Davis Medical Center staff. The Detailed Project Program identifies the initial layout of the facility, incorporating space needs determined earlier (initiated as part of the Year Two studies), and shows the probable integration of the PTF with the existing Cancer Center. The Program Project Guide outlines the full scope of the project, ties it in with the overall Medical Center Zone-Utilization plan, and provides the arguments and justifications required to obtain regent approval. Input from the architectural design team is critical for this process.

4. **Complete architectural and building design plans.** Detailed layouts and drawings as well as costs will be produced by an architectural firm selected by UC Davis. As stated above, this firm will work closely with the Medical Center A&E office to coordinate the production of necessary documents. By April 1995, we anticipate having full working drawings, and design approval. Immediately thereafter, the contracting process can begin to select the construction firm. Critical in the timing of the project is that the Building architects and the System designer will be working together to ensure that requirements are met for utilities, space and

installation needs of the accelerator and beam delivery components. The proposed timetable meets this requirement quite adequately.

5. **Complete shielding specifications.** Based on studies performed in the current year, LBL will assemble detailed specifications for shielding requirements for the PTF, and work together with the design architect and a shielding consultant to ensure that proper wall thicknesses and labyrinth designs are incorporated into the final design.

6. **Complete strategies and steps to be taken to obtain necessary regulatory approval for operation of the PTF.** UC Davis Medical Center will hire consultants to assist with this task.

7. **Complete studies of operating budget and staff requirements.** This study will be coordinated by LBL and will draw on resources from the System designer, UCD Cancer Center and its consultants and LBL itself. The System designer will determine the staff required to operate and maintain the accelerator and beam delivery components, as well as costs for utilities and consumables and requirements for a spare parts inventory. LBL will specify operations requirements for the treatment area and any interface requirements between the accelerator and clinical operations. UC Davis will, with the assistance of a consultant provide input to this study of clinical operations experience at the Cancer Center and expected extension of existing operations to include the PTF.

8. **Complete development of a funding plan for PTF construction.** To be carried out by the UCDMC Development Office, this plan will rely principally on a large-scale fund-raising campaign. A feasibility study, being launched in May 1992, will determine the projected goal for this campaign. The Development Office will work closely with other project elements to ensure that sources of funds are available to cover the full anticipated construction costs of the PTF. A financial plan will be fully developed by May 1993, this is required as a part of the package presented to the Regents. NCI funds are not being used for Development Office work, as these studies are being funded by the Medical Center.

B. PTF Project Organization

As the proton studies move into the final design and construction stage, it is important that responsibility for the project be transferred from LBL to UC Davis. Nevertheless, the technical expertise to oversee the System design and fabrication remains at LBL. A management team has been assembled from UC Davis and LBL which builds on the strengths in each institution. Upper management at LBL and UC Davis have expressed confidence in this management structure to bring the PTF project to a successful conclusion.

The first important step has been to establish the framework for LBL and UC Davis to work together. The MOA previously mentioned and the mechanism for Working Agreements establishes this, and cements the relationship between the institutions.

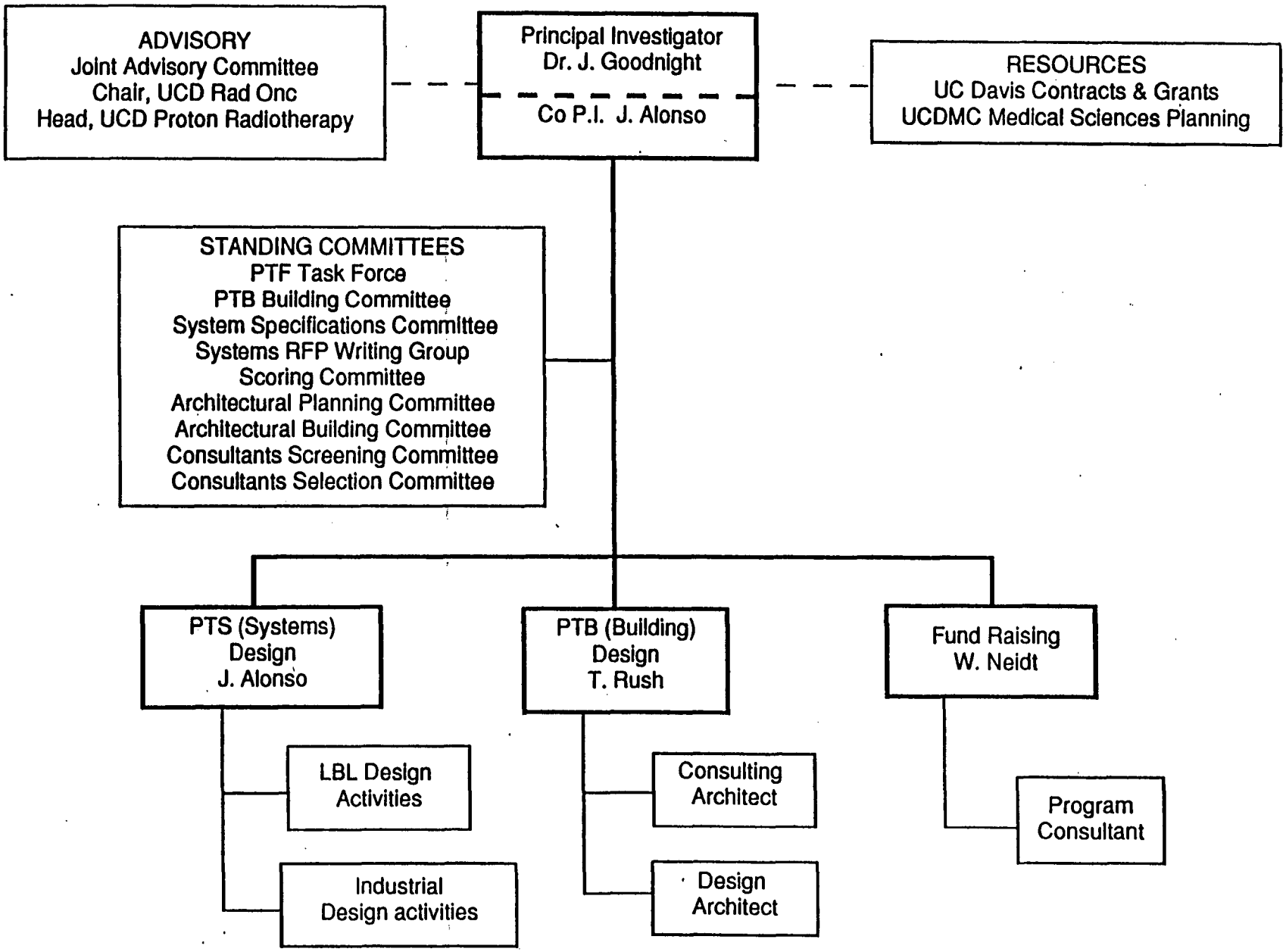
As seen in the Management chart on the next page, leadership of this project rests with Dr. Goodnight. Dr. Alonso as co-principal investigator provides the link with the preceding NCI studies as well as with LBL activities to be undertaken during the design process. Three main tasks must be undertaken: the System design will be headed by Dr. Alonso, the Building design will be headed by Mr. Rush, a senior project architect in the UC Davis Architectural and Engineering office and the fund raising initiative will be led by Mr. Neidt, head of the UCDMC Development Office.

Although a high level of integration of LBL and UC Davis personnel has been accomplished in this management structure, it is still important that line management responsibility lie entirely within one institution. As a result, a joint appointment is being sought for Dr. Alonso so that in his capacity as co-PI and leader of the System design effort, he will answer to UC Davis management.

Advisory groups from within the UC Davis organization, as well as the external Joint Advisory Committee, provide input into strategic decisions and project goals. The Joint Advisory Committee serves both UC Davis and the Massachusetts General Hospital and provides a basis for commonality in the two projects. Internal advisory bodies bring a perspective for the role of the PTF within the overall UC Davis community and specifically the Medical Center. Resource groups from within the UC Davis system provide support in contractual, managerial and logistical matters. The size and research nature of the PTF project make it well suited to the institutional support structure available as projects of this scope are not unusual within the University system.

The PTF project is aided by several Standing Committees listed on the chart and described throughout this proposal. These committees serve to keep all areas of the UC Davis management properly informed of the progress of the project and perform very valuable functions in establishing specifications, analyzing options and proposals and generally advising the project leadership on all matters pertaining to the project.

Project Management Organization
PTF Design



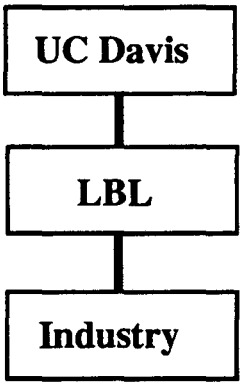
C. Design Process: Technical Components

1. Proton Therapy Systems Design

a. Description of the Design Process

Detailed design of the technical components of the PTF (such technical components are generically called the Proton Therapy System (PTS) or "System") will be a joint undertaking of the UC Davis Medical Center, LBL, and a firm from the private sector selected through a competitive bidding process. The Organization Chart shown below details the interrelationships between these three entities.

PTS Design Organization



In other words, responsibility for the conduct of the technical designs will be subcontracted to LBL. Funds to finance the industrial study, and to hire consultants that may be required for proper discharge of these responsibilities will be passed from UC Davis to LBL. LBL will, in turn, take responsibility for hiring the firm that will perform the actual detailed designs, through the competitive bidding process described below. This model was selected over one in which UC Davis would issue contracts to both LBL and the industrial firm. The selected model allows tighter LBL control over the design process, and offers better opportunities for technology transfer from LBL to the vendor, during the design phase of the project.

From the timeline shown in Section I, it shows that the technical design process is anticipated to require approximately eighteen months from the beginning of the grant year, with procurement of technical components starting April 1994. The formal completion of the technical design phase is scheduled approximately one year ahead of the completion of the detailed drawings for the building; however, as was detailed earlier in this application, this scheduling offers optimal meshing of the two components. Key decision points affecting both components occur concurrently; furthermore, accelerator component fabrication, testing and delivery generally requires more time than building construction.

It should be noted that the preliminary stages of the contractual process to select the design-build contractor have already started well before the beginning of the grant year. This effort is being supported from the current RO1 Grant funds: this work is entirely within the stated goals of the current Grant. The selection of the contractor and obligation of funds will not occur until after the start date of the new Grant and until NIH permission has been obtained. No unauthorized financial obligations are incurred by initiating the process early, and significant time savings can be effected without compromising the quality of the overall design.

The vendor selected is referred to as the "design-build" contractor, as it is the intention of UC Davis and LBL that the same firm selected to perform the design will also receive the contract

for procurement of the System components. This is required to avoid conflict of interest issues. The various points associated with this strategy are discussed at length in section (b.iii) below.

b. Coordination with the Massachusetts General Hospital

In the Year Two of the NCI-funded study process, LBL and MGH developed a collaborative relationship to further the efforts of both institutions. It is anticipated that this relationship will continue throughout the detailed design stage, with mutual benefit to all parties.

As stated in an earlier section, the rationale for this collaborative relationship is to provide the best chances for optimizing the design and operations models for our hospital-based proton therapy facilities. Both MGH and LBL have unique and in many ways complementary experience in the field of heavy-charged-particle therapy. By working together we can utilize the best ideas from each and prevent unnecessary duplication of effort. To best achieve this collaboration it is most important that effective communication mechanisms be in place.

Processes we have developed in the current Grant year are applicable, and will be further developed. As noted earlier, we have formed a Joint Advisory Committee which has served as an excellent vehicle for distillation of strategies and ideas. It has identified several problem areas that LBL and MGH individually had not thought of before, and provided fresh approaches to a number of known problems. We will continue to utilize this Committee to assist us in keeping to the course of highest productivity in the design process. Formal meetings between LBL and MGH team members, with travel by group members to one or the other site, or gatherings at conferences, have served as valuable points for interchange of information. With a frequency of about once every three to four months, these meetings have helped to effectively stimulate ideas on issues of importance to both design efforts. We have initiated periodic (on a roughly bi-weekly schedule, as the course of business dictates) telephone conferences between our groups, which we find allow for clarification of ideas, and helps in expediting projects of interest to both groups. We are looking into video conferencing possibilities for these discussions as hardware is available (though somewhat difficult to schedule) to both parties through Hepnet-installed facilities at Harvard and LBL. Over the next year, meetings in all of the formats discussed above will continue, with increasing participation by UC Davis personnel. On the whole, we anticipate good communications, and a high level of productivity as a result of our collaborative efforts.

One key decision in the collaborative process must be whether MGH and UC Davis/LBL should issue a joint "design-build" RFP (System RFP) or two separate ones. At this time, we believe it is in the best interest of both parties for each institution to issue its own System RFP. We do not feel that this decision in any way weakens the collaboration between our institutions. We fully expect very significant cooperation in the writing and review of these RFPs, and even see a high degree of likelihood that the same vendor may be selected by both parties.

c. Process for Selection of the "Design-Build" Contractor

i. Clinical Specifications

As stated earlier, clinical specifications will be used as the primary standards in the System RFP. A Specifications Committee has been formed to draw up a list of the parameters to be specified, and to identify appropriate values to set for these parameters. The table below identifies the individuals serving on this committee.

Table V.1 - Proton Therapy Systems Specifications Committee

J. Goodnight, M.D., Ph.D., (Chair)	UC Davis
J. Alonso, Ph.D.	LBL
J. Castro, M.D.	LBL/UCSF/UCD
W. Chu, Ph.D.	LBL

G. Koppel	UC Davis
D. Kubo, Ph.D.	UC Davis
K. Lelevier	UC Davis
B. Ludewigt, Ph.D.	LBL
T. Phillips, M.D.	LBL/UCSF/UCD
T. Renner, Ph.D.	LBL
L. Verhey, Ph.D.	UCSF/UCD

This committee has been charged by UC Davis management to generate a list of clinical specifications and selection criteria by July 1, 1992 that will be written into the System RFP.

Clinical specifications, as opposed to "machine parameters," are performance specifications measured at the treatment isocenter. Using such yardsticks allows us to cleanly separate the Year Two "critical technology" studies from the "design-build" process so as not to compromise (because of Organization Conflict of Interest) the opportunities for any of the industrial participants of the Year Two studies. Examples of items that will be included on the list of clinical specifications are: dose rate, field size, beam orientation around the patient, beam range in patient, dose uniformity, and edge (lateral and distal) definition.

It should be noted that the System RFP will not specify one accelerator technology to the exclusion of others. It is expected that proposals with conceptual designs based on synchrotrons and cyclotrons will be submitted, and although rather unlikely, it is possible that a linac-based system may be proposed. We are expecting that the relative technical risks associated with the leading technologies will have been adequately evaluated with the help of our "critical technology" studies. The results of these studies will be made available to the bidders before or during the time they are preparing their proposals, to assist them in addressing issues raised in these studies. The studies will also play a key role in the selection process in providing objective guidelines to assist in evaluating the technical aspects of the proposals that are submitted.

ii. Writing the System RFP

The actual writing of the System RFP will be the responsibility of a Writing Group, listed in Table V.2. Prime responsibility for generation of the RFP will reside with LBL, although input from UC Davis and a parallel MGH effort will solidify coordination with both RFPs.

Table V.2 - System RFP Writing Group

J. Alonso, Ph.D., (Chair)	LBL
R. Arri (advisor)	LBL Purchasing Department
J. Castro, Ph.D.	LBL/UCSF/UCD
W. Chu, Ph.D.	LBL
C. Fragiadakis (advisor)	LBL Technology Transfer Office
D. Gage (advisor)	UC Davis Purchasing Department
J. Goodnight, Jr., M.D., Ph.D.	UC Davis
J. Iler	LBL
D. Kubo, Ph.D.	UC Davis/UCSF
K. Lelevier	UC Davis
B. Ludewigt, Ph.D.	LBL
T. Renner, Ph.D.	LBL
J. Staples, Ph.D.	LBL

Certain key points will be emphasized in the writing of the System RFP. First, LBL feels very strongly that one of its principal contributions to the design process lies in its body of knowledge and experience with accelerators and therapy systems. As a result, LBL has a strong desire to establish the most effective links possible to ensure transfer of this experience and technology into the final design of the System. Successfully implementing "technology transfer"

will require experts who understand the subtle nuances of this process, and writing the correct language into the System RFP and subsequent contract to effect this goal will require much care. Again, very fortunately, resources to enhance the success of this effort are at our disposal at LBL.

A second point to be written into the RFP is that it is expected that part of the design process may include the fabrication of prototype hardware elements that will assist in verifying design parameters and fabrication costs for critical elements of the system design. An example might be a synchrotron dipole magnet, as often measurements of the magnetic field map, most critical in synchrotron performance, may not come out exactly as predicted, and a modification of the design will be needed to ensure that the accelerator performs properly.

A third point to be stressed is that an important end-product of the design will be a comprehensive model for operating costs for the facility. The contractor will be expected to provide manpower, maintenance and utilities needs for operation of the System.

After LBL and the System vendor have successfully presented UC Davis with the final System design it is the intention of UC Davis, after all approvals for the PTF construction are obtained, to award the contract for acquisition of System components to the successful bidder of this System RFP. This is necessary to avoid having to issue a separate RFP for procurement, which because of conflict-of-interest regulations would exclude the design contractor from participating in fabrication of the components it had designed. While perhaps desirable in the architectural and building arena, such a procedure would not produce optimal results in the accelerator acquisition area. Note, however, that an escape mechanism will be included in the RFP and in subsequent contracts, which allows severance of relations with the design contractor should it be impossible to arrive at a suitable procurement contract. In this case, a procurement RFP would need to be issued, from which the design contractor would in fact be excluded from participating.

A critical issue to be addressed is whether or not the System RFP will specify that the proposals must include a fixed-price quotation for the full design and construction process. At this time we feel it best to ask for a fixed-price bid for the design phase only, but that contracting for the construction costs is not appropriate at this stage. First of all, LBL will be negotiating the design contract, while UC Davis will be responsible for the actual procurement contract, and even though they will be issued to the same corporation, they must be independently negotiated. In addition, locking in a construction cost prior to the detailed design will hamper the design optimization process. Another reason is that the first-stage configuration of the PTF will not be known at the time the System RFP is written. As seen below this configuration will be determined by the outcome of financing studies now in process, and which will not be completed until after the design contract has been let. Thus, configuration and decisions must be made at the conclusion of the final design process.

The obvious advantage available by asking for fixed-price contracts at a time when open competitive bidding is taking place is not taken advantage of under this scenario. The logical question then is how to preserve competitiveness in the costs generated in the final design process by a single vendor who has been essentially guaranteed a follow-on procurement contract. Tight oversight of the contractor, requirements for justifications of quoted prices, and ultimately the threat of invoking the above-mentioned escape clause are all mechanisms for keeping prices in line. It is believed these will be sufficient to assure fairness in the overall process. Furthermore, requiring a fixed-price contract before detailed designs are completed will probably induce bidders to include a larger-than-normal contingency because of uncertainties that may arise during the final design process. Thus, we believe that our proposed procedures for acquiring the system designer/builder will best meet the needs for flexibility, cost and open competition.

Perhaps the most difficult task for the Writing Group will be the determination of the selection criteria on which the proposals submitted will be evaluated. These criteria must be written into the System RFP, so that all bidders are aware of the rules under which their proposals

will be judged. Criteria must be objective, fair, and comprehensive enough to ensure that the best proposal can stand out unambiguously in an evaluation based on impersonal numerical scoring. Again, LBL and UC Davis are fortunate in having resources in their Purchasing, Contracts and Grants, and Technology Transfer offices capable of providing invaluable assistance in this process. Furthermore, we will have gained experience in the process through selections for the "critical technology" studies in Year Two. The results of these studies will of their own right contribute to the selection process by providing a firm basis on which to assess proposed technical scenarios.

We already have a fairly good idea of the basic selection criteria that will be employed. In addition to the degree to which the clinical specifications are met, each proposal will be scored on several other very important considerations: overall system safety, availability and maintainability of the system design, efficiency of design, and flexibility of the overall system to accommodate technological improvements that may emerge over the useful lifetime (projected to be 30 to 40 years) of the Facility.

Once the System RFP has been written, we intend to seek input from the Joint Advisory Committee, and we will submit this System RFP to NCI for concurrence with its form and content. If deemed appropriate by management at LBL and UC Davis, other consultations and reviews may be scheduled as well.

iii. Selection Process

After publication of the System RFP, firms will be given a reasonable time to submit proposals. We anticipate this time to be around three months. Following receipt of the proposals, the selection process must take place. Evaluation of the proposals on a basis of the selection criteria published in the System RFP will be conducted by the Scoring Committee, whose membership is listed in Table V.3.

Table V.3 - Scoring Committee, to Evaluate System "Design-Build" proposals

J. Goodnight (Chair)	UC Davis
J. Alonso	LBL
R. Arri (advisor)	LBL Purchasing Department
J. Castro	LBL/UCSF/UC Davis
W. Chu	LBL
D. Gage (advisor)	UC Davis Purchasing Department
G. Koppel	UC Davis
D. Kubo	UC Davis/UCSF
B. Ludewigt	LBL
T. Phillips	UC Davis/UCSF/LBL
T. Renner	LBL
A. Smith	UC Davis
J. Staples	LBL

Although LBL has prime responsibility for issuance of the design contract, UC Davis must play a key role in the selection process. As stated above, a commitment must be made to the successful bidder that if the project proceeds beyond the design stage this vendor will receive the procurement contract. As this commitment is made by UC Davis, and not by LBL, it is critical that the vendor be acceptable to UC Davis management. Again, though, it should be noted that evaluation of the proposals is based on the selection criteria published with the RFP; consequently it is imperative that these criteria be designed as carefully as possible, and reflect the true priorities of both institutions.

As was the case at other stages of the project, the Joint Advisory Committee will be consulted prior to making the final contracting decision.

The generation of the contract to cover the design phase of the System will be handled through the LBL Purchasing Department, a group well experienced in this process. Contracting for System procurement, when the project reaches this stage, will be handled through the UC Davis Purchasing Department.

iv. Implications of this Process for MGH-LBL Collaboration

As mentioned above, the current decision is that UC Davis/LBL and MGH will issue independent System RFPs for selection of the "design-build" contractor. There are several excellent reasons for this. Among them is the fact that the constraints on each project are different, and that issues such as institutional priorities, specific site conditions and differences in management philosophy may play a more important role in the ultimate selection process than purely technical considerations.

Given this independence of selection process, it might be worthwhile exploring possible alternative paths which our collaborative efforts may take. Because the number of qualified vendors in the field is quite limited, a good chance exists that MGH and UC Davis/LBL may independently select the same vendor who may be proposing essentially identical facilities for each site. In many ways this would be the most desirable scenario, as definite cost savings could be effected in design and fabrication by sharing tooling, shop drawings, and other economies of scale. Should this happen, we anticipate that the "technology transfer" aspects of the UC Davis/LBL contract could have a significant impact on the MGH design.

Even in the event that different vendors are selected by UC Davis/LBL and MGH, it is likely that certain elements of the proposed designs may exhibit similarities that would benefit from a combined design effort to effect the desired economies of scale for at least some subsystems of the overall facility. Groundwork for such a possibility should be laid by ensuring that appropriate communications channels are in place between LBL and MGH purchasing departments at the time contracts with the successful bidders are being made up to ensure that appropriate language is included in the respective contracts for cross-collaboration. In all this, the assumption is being made that the timing for issuance of System RFPs and selection of successful bidders is close enough to contemplate such coordinated activities.

d. Supervision of the Design Process

Once the design contract is in place, LBL physicists and engineers expect to work closely with the contractor to make available the experience gathered from many years of medical and accelerator developments at LBL. Some of the areas where we anticipate technology transfer will occur are detailed in Table V.4 below.

Table V.4 - Areas where Technology Transfer are expected to occur

Accelerator design	Beam spreading systems
Beam transport optics	Field definition hardware
Magnet design	Patient support, immobilization
Beam diagnostic instrumentation	Control system integration
Nozzle design	Safety systems designs
Dosimetry instrumentation	Safety, QA analyses for overall system design
	Shielding design

Various techniques are envisioned for enabling the transfer of this technology, such as direct communication with the firm's design team and assistance with the detailed designs;

assistance with establishment of detailed specifications for individual components; conducting design reviews; and evaluation and feedback on fabrication techniques for critical components. Close interaction with the design firm will ensure that the needs and expectations of the UC Davis Medical Center are best met by the final results of the design process. Optimization of designs will be carried out through iteration in specifications and configurations that will be facilitated by such interactions.

Interactions also will be required with the Building design Architect to ensure space and environmental requirements for the System components are properly provided for. System parameter input will be with the overall design process. It is expected that these interactions will carry through to the preparation of the final design report. Input into this report will ensure that material is presented in the most useful manner for UC Davis management to prepare for the construction phase of the project, and will also serve as a vehicle for cost-containment.

e. Final Design Report

The format for the Final Design Report will feature presentation of design information organized in a modular fashion, with detailed designs, performance specifications and costs for each major subsystem listed as a stand-alone entity. Such major subsystems will include the accelerator, beam transport lines, a fully equipped gantry treatment room and a fixed-beam room. The rationale for this approach is that the final configuration of the PTF will depend on the budget established for the project, and as this number can be significantly enhanced by a successful private fund-raising campaign, the full extent of the resources available for PTF construction will not be known until close to the end of the design process. By presenting UC Davis management with a "catalog" of components, a decision can be made as to which components to specify for construction, and which might be left for a later enhancement should additional resources be required to complete the intended scope of the project.

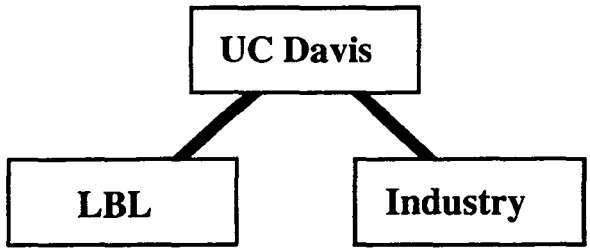
The submission of the Final Design Report will present an opportunity for convening the Joint Advisory Committee to review the progress made and to provide recommendations for the correct manner of proceeding with the construction phases. Assuming concurrent design phasing with MGH, this Committee could evaluate both designs, with the possibility of suggesting fine design adjustments prior to commencement of construction and hardware acquisition.

f. Follow-on Activities

Although beyond the scope of this Grant, we can foresee the subsequent actions that will result from the submission of the Final Design Report. A study group will be formed to evaluate the report and analyze the matching of possible PTF configurations with near-term and long-range goals of the UC Davis Medical Center, and with the availability of financial resources for the project. Following this, and after all the proper approvals for the project have been obtained from the UC Regents and appropriate regulatory agencies, UC Davis management will decide on a given configuration, and the UC Davis purchasing department will initiate the contracting process with the design firm.

During the hardware acquisition phase, LBL is expected to play a significant role in oversight of the contractor, providing QA services to UC Davis throughout the construction, installation and commissioning of the System components. Organizationally, both LBL and the contractor report directly to UC Davis, as outlined in the figure below.

PTS Procurement Organization



2. Shielding Design

a. Organization of Work Effort

Responsibility for specifications of shielding thickness and materials requirements will be held by LBL, headed by Dr. Bernhard Ludewigt. He will work closely with Antony Smith from UC Davis, who will be determining regulations of allowed radiation levels around the PTF. Actual calculations of attenuation factors for detailed shielding designs will be carried out by a consultant hired for this purpose. Throughout the process, interactions will occur with UC Davis A&E staff and the selected Executive Architectural firm to ensure that the designed shielding configurations produces the required attenuation of projected radiation levels generated by the System.

b. Assessment of Tools Available

One of the Year Two "critical technology" studies concentrate on collecting and analyzing available shielding data for 250 MeV protons. Although accelerators for 250 MeV protons have been around for many years, designers of the Loma Linda facility found that there was no comprehensive collection of shielding information available for beams from such machines. Although they devoted significant resources to addressing this problem, the shielding designs for Loma Linda were still governed by a large degree of conservatism based on the lack of fully adequate neutron flux and attenuation information. As conservatism often leads to over-design and increased costs, we felt it wise to invest in an effort to collect the best available data and shielding design codes that might constitute tools for optimizing the PTF shielding design. These tools will have been collected at the start of the grant year. However, it is not likely that they will be immediately available in a form suitable to perform PTF shielding designs.

A first step must be an evaluation of the accuracy and usefulness of the tools acquired. LBL will engage a consultant to perform this evaluation, quite possibly the same firm that performed the Year Two shielding, study assuming a satisfactory conclusion of this first phase. In addition, considerable radiation protection expertise is available in the LBL Environmental, Health and Safety Division (EH&S). We intend to involve these experts in an assessment of the quality of work performed by our consultant.

The actual evaluation will be performed by testing shielding transport and design codes against actual data. If need be, some experimental measurements may be performed, perhaps using the Loma Linda facility as a source of 250 MeV protons. Critical, though, will be a determination that the design codes reproduce accurately the actual radiation levels measured for a given shielding configuration. Without this modeling accuracy, obtaining optimized shielding designs will be very difficult.

c. Determination of Required Radiation Levels

UC Davis Medical Sciences Planning (MSP) staff, under Dr. Antony Smith, will be responsible for determining the regulatory requirements relevant to radiation levels in different areas of the PTF. Different requirements will be specified for areas, depending on the occupancy

factors and on the type of personnel in these areas. Areas to be occupied only by designated radiation workers will be treated differently than those accessible to the general public. Relevant NCRP documents will serve as references; however, further State of California regulations must be met before approval of the PTF plans is obtained from regulating state agencies. Note that one important set of regulations deal with allowed radiation emanations into the environment outside the entire PTF. Specifically, we must consider at least possible ground-water contamination, and site-boundary radiation.

Regulations that pertain to the PTF will be collected by MSP and conveyed to LBL, the shielding consultant and the design architects.

d. Shielding Calculations

Once the required radiation levels are known by the consultant, he will perform shielding thickness calculations for different areas of the PTF. He will fold into these calculations best-estimate evaluations of the source term, that is, the proton flux that will be lost in a given area, either in tuning, normal clinical operation, in machine development periods, or in anticipated failure modes of the PTS. Included in the source-term determination is the neutron production (quantity, energy spectrum and angular distribution) from protons stopping in various substances: steel (magnets), aluminum (vacuum chambers), copper (magnet coils), graphite (beam dump), water (phantoms), tissue (patient), lead or cerrobend (collimators), plastic (compensators). Data for these determinations should be part of the data set collected in the Year Two study.

Basic output of these calculations will be determinations of the required thicknesses of different types of materials to provide the necessary attenuation of radiation levels. Materials to be studied include concrete, both light (150#) and heavy (225#), steel, and an optimized combination of different materials. These thicknesses will be given to the design architect for incorporation into the detailed design.

Calculation of radiation emanating from various labyrinth designs must also be performed. By providing the architect with several acceptable labyrinth designs, a good first-pass design will be possible. These straw-man designs will be determined from existing designs at LBL, Loma Linda and other facilities, as well as from practical experience of LBL and the consultant.

e. Iteration to Final Building Layout

From thickness and material requirements generated by the consultant, the design architect will produce a first-pass layout of the areas where radiation will be produced. Along with this layout, occupancy factors will be assessed by MSP for the various areas adjacent to these radiation-producing areas. The consultant will then evaluate the radiation fields emanating from the shielding and labyrinth designs, and assess compliance with the specified regulations. Important in this will be an assessment of neutron flux penetrating to the outside of the building, for possible ground-water contamination.

Any soft areas must be redesigned; the consultant and LBL staff may suggest remediation measures, which will be passed on to the architect so that he can modify the building design. Such design changes generated by the architect will receive further attention from the consultant, for possible new shielding calculations. The process will be repeated until satisfactory performance of the shielding design is achieved. At this point, the architect will incorporate the design of the shielding walls into the detailed building drawings.

3. Operating Manpower and Cost Studies

a. Organization of Work Effort

Assessing the costs of operation of the PTF will be an important ingredient in planning for integration of the PTF into the ongoing operations of the entire UC Davis Medical Center. As one of the stated goals in the design process is to minimize operating costs, an analysis of the factors contributing to these costs is an important input into optimizing the overall design of the PTF. Preliminary work will have been done by LBL and UC Davis staff in Year Two to assess needs for operations, based on studies of operations at the Bevalac, Loma Linda, and the UC Davis Cancer Center. These studies will provide a valuable baseline for the more detailed studies to be performed in this portion of the Grant.

LBL will assume prime responsibility for the conduct of these new studies. Dr. William Chu will lead the study team, coordinating efforts by LBL physicists and engineers, UC Davis staff members and their operation analysis consultants, and appropriate staff from the System design contractor. LBL will develop the user support models; the contractor will develop models for accelerator operations, maintenance needs, utilities, and required spare parts and the UC Davis consultants will develop models of clinical operations needs.

In addition, LBL and the design contractor will develop models for the "pre-ops" and commissioning phases of the PTF, to ensure that suitable budget plans are made for these activities. The end product of these studies will be an Operations Analysis Report (OAR), which will be submitted to UC Davis at the conclusion of the Detailed Design phase of the project.

b. Establishment of Accelerator Operations and Maintenance Needs

The System design contractor will develop models for operations needs for the accelerator and other components he is designing. As the goal is to minimize operating costs, the designer is encouraged to include features in the design which reduce reliance on human operators, and expedite maintenance and repair functions. Thus, a highly automated control system, excellent reproducibility of parameter sets, self-diagnosis of faults, and extremely high reliability are all desirable attributes of the final design.

From the design that is developed, the contractor will evaluate the number of operators needed for the projected operating schedule, most likely a 15-shift per week scenario. Maintenance staff will also be assessed, including engineers, technicians, computer scientists. A suitable inventory of spare parts and other consumables will be specified, arriving at a cost for "supplies." For the given operating scenario, a reasonable estimate of power consumption and water usage will be generated to arrive at utility costs. Working with LBL, this information will be collected for input to the OAR.

c. Establishment of Research Coordination and Facility Development Groups

As the PTF will be a cancer research center, it must be prepared to support the broad base of different research programs that will be conducted on-site. While most of this research will involve treatment of human cancer and a search for ways of improving the effectiveness of the treatments, some biological and physics research will be done as well. A new Research Coordination Group will be formed to provide effective liaison between these research programs and the PTF.

A key part of the PTF operations organization must be the Facility Development Group which will assume responsibility for development and improvement activities for enhancement of the performance of the System itself. Over the projected 40-year lifetime of the System, there will most likely be significant advances in the state of the art for proton therapy. The System must be

positioned to take advantage of these developments and to stay current in the field. The only way to achieve this is to have an active, adequately funded, and highly-talented group of scientists who are motivated towards the above-stated goal.

Extensive experience has been collected at the Bevalac in the needs of a varied research community. As a consequence, LBL is uniquely qualified to generate a model for the user support needs of the PTF. In generating this model, the LBL group will draw heavily from its own Bevalac experience, as well as from operations at the Harvard Cyclotron, and Loma Linda. This group will first define user support needs for the projected programs. It will also assess the needs for continuing development of System performance improvements. It will then determine from these requirements the most appropriate size and composition of the PTF Research Coordination and Facility Development Groups. It may be possible to obtain external funding to support a part of these groups through independent research activities of their own. It will be important to estimate the level of such possible support, as this represents a reduction in "base-program" funding requirements. The above model is based on the existing biomedical operations group at the Bevalac, which indeed shares funding from the Bevalac base program as well as having its own grant support.

d. Establishment of Clinical Operations Models

UC Davis Cancer Center staff, led by Drs. J. Castro and D. Kubo, will work with the operations analysis consultants to develop a model for clinical operations of the PTF. Drawing from experience gained at LBL and Loma Linda, the size and composition of a suitable staff will be determined. It will be necessary to evaluate any further requirements that may arise from the research nature of the PTF operations. Funding of the staff necessary for clinical operation of the PTF must also be studied, again to determine how much of this group can be funded out of ongoing research grants, and how much must be included in the base program. In this context, the availability of revenue from patient billing of accepted treatments must be assessed to assist with base-program costs. An important goal of this study will be to assess the overall impact of the projected clinical research program on the base-program costs for the operation of the PTF. This will be an important section of the OAR.

e. Compilation of "Steady-State" Operating Costs

From the various studies outlined above, LBL will collect and compile an overall picture of manpower needs and base-program costs for operation of the PTF. It is most likely that in the first pass through this exercise, we will find the projected manpower needs and costs to be well in excess of expected figures, and an iterative process will have to be undertaken to pare the operating staff of the PTF down to an acceptable level. UCDMC personnel will play a key role in this iterative process.

f. Analysis of Pre-operations and Commissioning Needs

LBL will work with the System design contractor to develop pre-ops and commissioning models. Pre-operations work must begin about a full year prior to the beginning of commissioning of the facility. Working through staff requirements and detailed assignments for each staff member, development of operating procedures for all elements of the facility, and eventually recruiting and hiring the staff members of the operating teams all require significant effort that must be planned for and budgeted. While installation and commissioning costs are usually included as part of the overall procurement contract, such pre-operational activities require coordination with UCDMC and LBL staff that also must be thought through and budgeted for.

The models for pre-ops and commissioning will include details of the scope of work that be included in the budget, and a time-line for this work to ensure that everything flows smoothly

within the overall projected time schedule. From this scope of work, staff levels and costs will be ascertained for inclusion in the OAR.

g. Publication of the Operations Analysis Report (OAR)

LBL will assume responsibility for producing the OAR, combining the "steady-state" models and the pre-ops and commissioning data. The OAR will be presented to UCDMC for its analysis and evaluation. If the process has worked as projected, UCDMC will have already had ample opportunity for input into the operating models and budget projections, so UCDMC management should feel comfortable with the overall operating scenarios proposed.

The completion of the OAR will be correlated with the end of the detailed design phase of the project, so that all costs can be made available to UCDMC concurrently. It is suggested that this report be reviewed by the Advisory Committee, which is likely to have very substantive comments on the models developed.

D. Design Process: Building Components:

1. Overall Process Description

The University of California Davis Medical Center's planning, design and construction processes are governed by University policy and the Public Contracts Code of the State of California. The process begins with program definition in the form of a Project Planning Guide (PPG), which describes the spaces, functions, and relationships required for the project. The PPG includes a financial feasibility analysis, a project budget, and a project schedule. The PPG is approved by the Regents of the University of California.

Following approval of the PPG, an Executive Architect is selected to prepare construction documents for the project. The Executive Architect will be responsible for designing a building which meets all requirements of the PPG. The Building design process will include significant coordination with the selected System vendor for the PTS. The coordinated efforts of the Executive Architect and the System vendor will fully integrate the technical and operational requirements of the System into the building design.

A number of reviews are required at each phase of the Building design process. All review procedures required by NCI under the grant and by the Regents, will be accomplished. Required reviews are for technical aspects of the project, conformance to the approved program as described in the PPG, and conformance to budget. Environmental analysis and review is also completed during the Building design phases. Since funds are requested from NIH to defray partially the construction costs for research facilities, the NIH will also be consulted at each stage of the pre-construction process prior to commitment of funds. Upon completion of Construction Documents and after receipt of all required regulatory approvals, construction bids are publicly solicited.

2. Design Process Administration

a. Committees

An Architectural Planning Committee will be appointed by the Hospital Director. The committee will consist of building users and Medical Sciences Planning staff, and will be chaired by an Associate Director of the Hospital. The Office of Architects and Engineers will assign a Project Manager who will provide staff support to the committee. The committee's task is to develop the space program and budget for the project. A Planning Architect will be hired to assist in this effort, and will produce a Detailed Program Plan (DPP). Medical Sciences Planning will use the DPP as an aid to produce a Project Planning Guide (PPG), which will be approved by the Regents of the University of California.

Upon completion of the DPP, an Architectural Building Committee will be appointed by the Vice Chancellor for Facilities. The Building Committee membership will be the same as the Planning Committee. The Building Committee will periodically review and approve the progress of the building design as it is developed.

b. Staffing

Staff support for the project will include a Project Manager from the office of Architects and Engineers. Additional support will be provided for specific tasks by planners and engineers in the office of Architects and Engineers, and by Medical Sciences Planning staff. Clerical support will be provided by the Cancer Center and by the office of Architects and Engineers.

3. Research Into Existing and Planned Facilities

The Planning Committee, Project Manager, Medical Sciences Planning, and DPP consultant will all conduct research into existing and planned proton therapy facilities. The existing facility at Loma Linda University has agreed to provide detailed information into the costs and construction methods used for their completed facility. There will be continued collaboration between UCD Medical Center (UCDMC) and Massachusetts General Hospital (MGH) as the System and Building designs progress.

4. Consultant Selection Process

Consultant selection at UCDMC is governed by University of California policy. For all consultant selections where the expected fee is in excess of $50,000, consultant services are publicly solicited. The advertisement for services will describe the proposed scope of work, services expected of the consultant, and a brief description of the selection process, including a description of the criteria by which the selection will be made.

Written proposals for consultant services will be reviewed by a Consultants' Screening Committee composed of UCDMC staff and the UCDMC Project Manager. A short list of firms to be interviewed will be approved by the Vice Chancellor for Facilities (VCF). Interviews will be conducted by a Consultants' Selection Committee appointed by the VCF. The consultant selected will be approved by the VCF.

5. Supervision of Building Design Process

a. Design and Planning Criteria

Design criteria to be given to the Executive Architect will include the DPP and PPG documents, along with the UCDMC Long Range Development Plan, other urban design studies, and any environmental review documents prepared for the project. The consultant will sign an Executive Agreement with the University which describes the expected scope of services, fees and schedule for the project. The Executive Agreement requires the consultant to design the building to be in compliance will all applicable local, state, and federal codes and regulations. The Executive Agreement will also describe the required design review process, including reviews by external agencies.

b. Integration of System Design Requirements

The vendor selected for design and construction of the System will provide technical and operational requirements to the Planning and Executive Architect firms. These requirements will be used in the preparation of the DPP, PPG and development of the building design. Both the Executive Architect and the System vendor will be required to coordinate their respective efforts throughout the Building design process in order to fully integrate the System into the building design.

c. Design Review

A number of reviews are required at each phase of the design process, including Schematic Design, Design Development, 50% Construction Documents, and 100% Construction Documents. For new construction with a value in excess of $5,000,000, the building exterior design and site improvements must be approved by the Regents. Other required reviews are for technical aspects of the project, conformance to the approved program as described in the PPG, and conformance to budget. Typical review submittals include site plans, floor plans, elevations, sections, details, written specifications and cost estimates as appropriate to the stage of design. Environmental analysis and review is also completed during the Building design phases. Also, NIH approval will be obtained at each critical review stage. Funds are requested in the budget to cover trips to Philadelphia as part of the review and approval process.

d. Cost Control

Cost estimates will be provided broken down by CSI format. As the design progresses, more detailed estimates will be required. Backup information will include quantity take-offs and unit prices, as well as breakdowns of general requirements, contractor overhead and profit, and design contingencies. Cost estimates provided by the Executive Architecture firm will be reviewed by UCDMC staff. As necessary, independent cost estimates will be commissioned by UCDMC in order to verify cost estimates. Other costs for the project, such as consultant fees, internal fees, and surveys and tests, will be tracked by the UCDMC Project Manager. All new cost information received will be compared to previous estimates in order to track progress on individual cost items as well as overall project costs.

e. Schedule Control

Schedules for the building design process will be developed and tracked both by the Executive Architecture firm and by the UCDMC Project Manager. The schedule will include a detailed breakdown of the tasks required and appropriate milestones for reviews and financial approvals. The UCDMC schedule will be prepared and monitored using Timeline Version 4 software. Typical hardline copies will be in Grant format. Critical items will be identified in the Status column of the display. Schedule updates will be prepared periodically.

6. Deliverables

a. Detailed Project Program (DPP)

The DPP will be prepared by the planning architect. It will contain a detailed listing of required spaces, along with specific requirements for equipment or special services for each space. The DPP will also analyze building design and site development issues, including recommendations for exterior and interior finishes, mechanical and electrical systems, and internal and external circulation. Functional relationships between spaces will be described. The integration of the System into the building design will be fully described. A conceptual cost estimate for the building will be prepared.

b. Program Planning Guide (PPG)

The PPG comprises the precise summary of the project as approved either by the Regents of the University of California, or by their designee. The PPG will also be submitted to NIH for review and approval. The PPG contains at least these six essential components: (1) rationale, need statement, objectives, use projections and discussion of alternatives considered; (2) a description of the project, including the programs to be accommodated, the list of spaces and key adjacencies, and relationship to site and to other projects in UCDMC's Capital Plan; (3) the design and construction schedule; (4) a cost estimate; (5) the financing plan; and (6) an environmental

impact classification statement. The PPG provides the description of the project and its budget which cannot be substantially altered without approval by the Regents, University President or Campus Chancellor, and NIH as appropriate.

c. Schematic Design Documents

The Executive Architecture firm will submit schematic design documents for review. These will consist of drawings and outline specifications which describe the general proposed design characteristics of the project, including the following:

Site issues, such as building location, access and egress, pedestrian and vehicular circulation, parking and landscape elements.

Building issues, such as space layouts for each floor, relationships of functional elements, circulation, massing, roof elements, aesthetic expression, exterior wall materials and fenestration patterns.

Structural issues, such as type of foundation, vertical support, horizontal support, and seismic resistance.

Mechanical issues, such as type of heating and cooling systems, energy conservation measures, and locations of major equipment.

Electrical issues, such as service entry point and locations of major equipment.

d. Design Development Documents

The Executive Architecture firm will submit design development documents for review. These will consist of drawings and specifications which describe the proposed design characteristics of the project as approved for schematic design and expand and detail elements of the project including the following:

Site issues, such as types of materials, specific selections for landscaping, and identification of curbs, walks, driveways, drainage patterns, and site furnishings.

Building issues, such as development of wall sections, waterproofing, insulation, partition types, casework, and exit pathways.

Structural issues, such as soil type and bearing capacity, foundation system, vertical and horizontal live and dead loading, locations for lateral resistance elements, and preliminary sizing of columns, beams, purlins and slabs.

Mechanical issues, such as number and location of fixtures, descriptions of special systems for piped gases and lab wastes, number and location of floor and roof drains, sizing of heating and air conditioning ductwork, and fire protection systems.

Electrical issues, such as electrical distribution system, number and location of panels, expected loads, and descriptions of special systems for telecommunications, data, and fire alarm.

e. Construction Documents

The Executive Architecture firm will submit 50% and 100% construction documents for review. These will consist of drawings and detailed specifications which describe the proposed

design characteristics of the project as approved for design development, and expand and completely detail all elements of the project, including the following:

General project information, including code summaries, administrative information, drawing index, location map, vicinity map, and contractor access and staging areas.

General coordination between all disciplines, including coordination of architectural, structural, mechanical and electrical systems.

Site issues, such as grading elevations, invert elevations, irrigation systems, and details for all site improvements.

Building issues, such as large scale, fully dimensioned floor and roof plans, wall sections and details, casework details, stair sections and details, reflected ceiling plans, interior elevations, and specification of all interior finishes.

Structural issues, such as framing plans, member schedules, connection details, and support details for all fixed equipment.

Mechanical issues, such as equipment schedules, riser diagrams, air flow calculations, control diagrams, and mounting, support and attachment details for all equipment.

Electrical issues, such as location and size of switches, circuiting layouts, panel and equipment schedules, one-line power diagrams, and identification and specification of special and emergency power and receptacles.

f. Periodic Cost Estimates

The Executive Architecture firm shall submit a cost estimate at each design phase, formatted as described in paragraph 5.e above. Each design review will also include review of the cost estimate for conformance with the approved budget.

g. Environmental Impact Report

A review of environmental impacts will be conducted concurrently with the Schematic and Design Development phases. All impacts associated with the project will be identified. These impacts will be coordinated with the Environmental Impact Report (EIR) which was prepared for the UCDMC Long Range Development Plan (LRDP), and with the mitigating measures approved for the LRDP. If it is determined that the impacts of the project exceed or differ substantially from those identified in the LRDP EIR, a supplemental EIR will be prepared and approved as required by the California Environmental Quality Act. All NEPA requirements will also be complied with.

LAWRENCE BERKELEY LABORATORY
UNIVERSITY OF CALIFORNIA
TECHNICAL INFORMATION DEPARTMENT
BERKELEY, CALIFORNIA 94720