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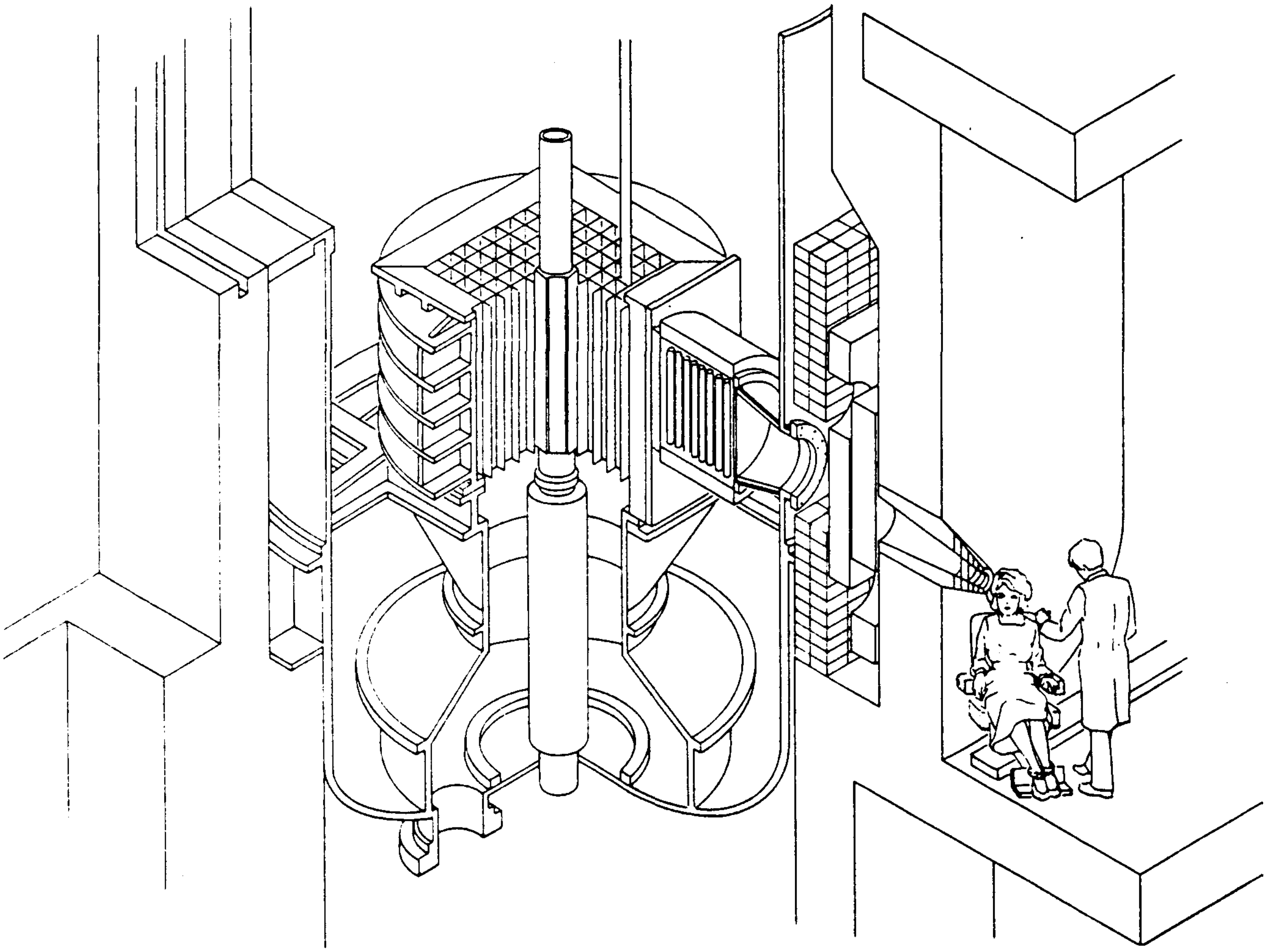
PBF/BNCT Program for Cancer Treatment

Volume 3, No. 2



Bulletin

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PRINCIPAL INVESTIGATOR'S HIGHLIGHTS

Highlights of the PBF/BNCT Program during January include progress within the areas of:

1. Project 1: Supporting Technology Development

Task 1: Gross Boron Analysis in Tissue Blood and Urine - Large numbers of biological samples continue to be analyzed.

Task 2: Analytical Methodologies Development for BSH (Sodium Borocaptate) Purity Determination - Problems continue with poor stability and short lifetimes of the HPLC columns. Work continues to solve the problems and procedures used by researchers at Shionogi Chemical in Japan may provide answers.

Task 4: Boron Microscopic (Subcellular) Analytical Development - Refinement of tissue acquisition techniques was the main focus of work. Samples to-date have shown signs of extensive cellular damage. Dr. David Miller (INEL) visisted Cornell University to coordinate and review the research program.

Task 5: Noninvasive Boron Quantification Determination - General Electric has agreed to a 90-day extension of the MRI research software agreement, allowing continuation of hardware and software development. A permanent agreement will hopefully be in place soon.

Task 6: Dosimetry - Dosimetry data analysis of the phantom and dog experiments at BMRR in January continue. Dosimetry data from the first dose-tolerance studies have been obtained and analysis of neutron spectrum data from the BMRR Al_2O_3 filter continues. Much of this work, and the fit to the modeling, is being prepared for the upcoming conference on thermal/epithermal neutron physics and sources at MIT.

Task 7: Analytical Radiation Transport and Interaction Modeling for BNCT - Considerable work being performed to prepare for the MIT conference. Much of the requested results from the modeling, to be presented at the conference, is given in this bulletin in tabular and graphic form.

Project 2: Large Animal Model Studies - The ongoing, normal-tissue toler-work at BMRR continued. Pharmacokinetic studies continued with the brain tumor dog admitted late in January. Initial blood-brain-barrier analysis will soon be available on the BMRR experimental animals.

Project 5: Neutron Source and Facility Preparation - Comprehensive design work on the neutron filter is continuing, including the filter itself, filter cooling system, and filter shutter system.

Core A: Administration and Common Support - A Biomedical Advisory Committee meeting is scheduled for April 20-21. Work in support of a number of PBF/BNCT presentations is outlined in this month's bulletin.

Core B: PBF Operations - The considerable effort necessary to maintain PBF in appropriate status is reviewed, including preventive maintenance, safety, and training.

Ronald V. Dorn III, M.D.
Principal Investigator
PBF/BNCT Program

ACRONYMS

ASME	American Society of Mechanical Engineers
BMRR	Brookhaven Medical Research Reactor
BNL	Brookhaven National Laboratory
BNCT	Boron Neutron Capture Therapy
BSH	Sodium Borocaptate
CSF	Cerebrospinal Fluid
CT	Computed Tomography
DOE	Department of Energy
DOE-ID	Department of Energy-Idaho Operations Office
EDF	Engineering Design File
EIRMC	Eastern Idaho Regional Medical Center
GE	General Electric
HMPAO	Hexamethyl-propylene-amineoxime
HPLC	High Performance Liquid Chromatography
IAEA	International Atomic Energy Agency
ICP/AES	Inductively-Coupled Plasma Spectroscopy/Atomic Emission Spectroscopy
INEL	Idaho National Engineering Laboratory
LOFT	Loss-of-Fluid Test Facility
MIT	Massachusetts Institute of Technology
MRI	Magnetic Resonance Imaging
PBF	Power Burst Facility
PDARS	Patient Data Acquisition and Retrieval System
PET	Positron Emission Tomography
RBE	Relative Biological Effectiveness
SIMS	Secondary Ion Mass Spectroscopy

ACRONYMS (CONTINUED)

TLD	Thermoluminescent Dosimeter
TTAF	Test Train and Assembly Facility
UofU	University of Utah
UofW	University of Washington
WSU	Washington State University

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PBF/BNCT PROGRAM MONTHLY BULLETIN

PROJECT 1: SUPPORTING TECHNOLOGY DEVELOPMENT

TASK 1: Gross Boron Analysis in Tissue, Blood, and Urine

Approximately 300 biological samples were processed and analyzed for boron utilizing the Inductively Coupled Plasma-Atomic Emission Spectroscopy (ICP-AES) technique this month. This is slightly below last month's total. The decrease resulted from reanalyzing a group of samples to confirm initial values as part of our data Q/A process. Additional work was also performed to determine if direct injection into the ICP could be used to analyze high-boron content urine samples. These data are still being evaluated. If applicable, the use of direct injection would decrease the amount of analysis time needed for each sample and increase sample throughput.

TASK 2: Analytical Methodologies Development for BSH (Sodium Borocaptate) Purity Determination

Work was hampered this month by the lack of high-performance liquid chromatography (HPLC) columns. As reported last month, the stability of the HPLC columns is variable and the lifetimes are short. Columns were ordered to perform additional experiments. These additional experiments will include the use of a saturation column prior to the analytical column to prolong column lifetime. Experiments are also planned to examine the effect of buffering the eluant system used in the separation. The pH of the eluant is within the range the HPLC columns will tolerate, but it is on the high end of the range. Buffering with an appropriate material will lower the pH closer to the midrange of the column tolerance.

Dr. Albert Soloway of Ohio State University recently visited Japan and spoke with researchers at Shionogi Chemical Company. These researchers say they have developed an HPLC technique which does not suffer from column degradation. The column in use by Shionogi researchers is a Nucleosil C18. This column is equivalent to those used in Idaho National Engineering Laboratory (INEL) research, but the column is made by a different vendor. From information provided by Dr. Soloway (over the phone), the procedures used by Shionogi researchers appear unchanged from procedures presented at the first international BNCT meeting several years ago. The reported Shionogi procedures formed the basis of initial INEL attempts to use HPLC for QA/QC analysis. The initial paper did not detail the exact conditions used. Shionogi researchers plan to present additional data at a December meeting in Hawaii, but were kind enough to give Dr. Soloway a preprint of their paper and permission to discuss their work with selected researchers in the U.S. BNCT community. Dr. Soloway is sending a copy of the paper to the INEL for review. Revisions to INEL procedures will be made, if necessary, based on the Shionogi paper.

TASK 3: Analytical Methodologies Development for Active Form Identification

This task is presently unfunded.

TASK 4: Boron Microscopic (Subcellular) Analytical Development

Ion-microscopic analysis of various canine tissues obtained by Washington State University (WSU) staff using three methods of sample acquisition all showed high sodium concentrations relative to potassium; an indication of extensive cellular damage, possibly a result of the sampling procedure. In addition, while boron was detected in the tissue samples, it was evenly distributed throughout the tissue with no observable localization. A number of tissue collection and handling factors are being evaluated as potential contributors to the problem. It is possible that the cells warmed at some point before the freeze-drying procedure was completed. The ideal procedure calls for approximately instantaneous deep-freezing of living tissue, and maintaining low temperature (liquid nitrogen temperature) until freeze-drying is complete. The mass of tissue that can be adequately frozen, with the available tools, is unknown. It is possible that the tissue samples obtained were too massive for the tool heat sink. Warming of the tissue will result in the formation of large ice crystals, erroneous concentration gradients, or, in the worst case, disruption of the in-vivo representation of the ion distributions. In an effort to eliminate possible sampling-procedure-induced artifacts, Dr. Constance DeHaan from WSU visited Cornell on February 27 to observe successful "slam-freeze" tissue excising methods and to discuss other possible sampling and transport problems.

Much of the work this month involved fabrication of the devices used to prepare samples for analysis and emphasized development of alternatives to the labor-intensive, time-consuming procedures presently employed. Indium-on-silicon sample mounting surfaces were prepared (a multi-step, vapor deposition on foil procedure). These mounting surfaces provided the planarity, conductivity, and adhesion required for ion microscopy. Sample holders for the ultracryomicrotoming procedure are being machined into a new shape to streamline the microtoming procedure. Additional work is being conducted to evaluate the need for the rigorous ultracryomicrotome procedures presently used relative to the more conventional cryostat/cemented sample. The two procedures result in section thickness of 0.75 microns and 2 microns, respectively. The difference in tissue thickness may cause sample electrostatic charging which interferes in ion microscope analyses.

On February 15, Dr. David L. Miller (INEL) visited Cornell to review research progress and discuss future plans. During this visit, images of canine tissue samples (collected at WSU) were reviewed and the interpretation of the results discussed. Discussions were also held regarding acquisition of some human tumor cell lines (glioblastoma, if possible) to use in future cell culture experiments.

TASK 5: Noninvasive Boron Quantification Determination

General Electric (GE) has agreed to a 90-day extension (commencing February 21, 1989) of the previous magnetic resonance imaging (MRI) software agreement allowing the use of spectroscopy software at the Eastern Idaho Regional Medical Center (EIRMC). In addition, GE has indicated an interest in discussing a research agreement whereby they would be active participants in the research being conducted. GE/INEL staff discussions were held at the Society of Magnetic Resonance Imaging Conference February 28 in Los Angeles. This preliminary meeting will be followed by a more comprehensive meeting at either GE Medical Systems in Milwaukee or at the INEL. It is anticipated that a research agreement could be in place before the current 90-day extension expires.

Some of the signal-to-noise difficulties experienced (and reported last month) with the ^{10}B and ^{11}B signal comparisons were found to originate with the University of Washington's (UofW) CSI-II Imager/Spectrometer and not with the radiofrequency coils. At lower frequencies, there is a discrepancy between the CSI-II display and output frequency. This causes invalid signal-to-noise measurements. Future comparisons will correct for this problem.

TASK 6: Dosimetry

Analysis of the Brookhaven Medical Research Reactor (BMRR) dosimetry data obtained during the January, 1989 experiments is in progress. These data are from wires and thermo-luminescent dosimeters (TLDs) implanted in the dog phantom and in two dogs, and will be used for validation of the analytical, predictive tool.

The first of the large-animal, dose-tolerance studies were begun during February. Four dogs were given right-hemisphere irradiation at BMRR using a ^{6}Li hydroxide-loaded polyethylene mask (50-mm thickness) having an aperture of 50 mm x 100 mm. Three dogs were irradiated to a total, calculated blood-volume dose (gamma plus neutron plus charged- particle) of 1000 cGy and one to 2000 cGy. These dogs will be followed for response determination. Foil activation measurements used gold-copper foils to evaluate neutron fluence at various external locations. TLDs were used at the same locations to evaluate gamma dose. Eight locations were used on each dog: (1-2) left and right eyes, (3) rear of skull, (4) trachea (inside mouth), (5) external throat at the thyroid, (6) chest at the heart, (7) on the spine at the shoulder, and (8) at the testicles. Analysis of the data has begun. For the 1000 cGy dogs, irradiations were of 42-48 minutes duration (varying with boron concentration), and the 2000 cGy irradiation was for 90 minutes. Gamma doses for the shorter irradiations ranged typically from 8 cGy at the testicle to about 120 cGy in the trachea. For the longer irradiation time, the values at these same locations were 17 and 229 cGy, respectively.

The December, 1988 neutron spectrum data from the Al_2O_3 filter at BMRR is being analyzed. The FERRET least-squares-adjustment code system is being used to provide a detailed multigroup characterization of the neutron spectrum. This analysis includes:

1. Generation of a 620-group spectrum-weighting function and 44-group input-guess spectrum (both based on the DOT-17 transport calculations),

2. Processing of the relevant 620-group ENDF/B-V dosimeter cross sections into the 44-group structure,

3. Processing of the covariance matrices for the dosimeter cross sections,

4. Computation of dosimeter cross-section, self-shielding factors based on P-factors calculated with a Monte Carlo code,

5. Detailed analysis of the uncertainty estimates for the measured integral reaction rates, and

6. Some initial computer runs with the FERRET code.

To achieve best fit consistency between the measured and calculated reaction rates, the FERRET computation adjusted the input-guess spectrum by: (1) downward adjustment of 20-50% in group flux values between 6 keV and 0.5 eV, (2) upward adjustment of 25-60% in group flux values between 3 keV and 100 keV, and (3) upward adjustment of 60-100% in group flux values above 100 keV. These analyses indicate that use of the unadjusted neutron spectrum obtained from the DOT-17 transport calculation leads to an underprediction of the neutron dose KERMA by as much as a factor of 2. FERRET analysis will be completed in March and a detailed presentation of the results will be prepared for the upcoming conference on neutron beams at the Massachusetts Institute of Technology (MIT).

TASK 7: Analytical Radiation Transport and Interaction Modeling for BNCT

Contract negotiations with the University of Utah (UofU) are still in progress. The problem with liability indemnification was solved by including UofU on the EG&G Idaho insurance policy. An issue was then raised by UofU regarding the definition of "restricted rights" in the proposed license agreement and how this would apply to the hybrid version of Alpha-1 that would be developed for Task 7d by UofU. This (along with a few other points) has resulted in delays in obtaining agreement on a contract. On February 28 written confirmation was received from the UofU that included contract terms and conditions agreeable to both parties.

In support of the upcoming Department of Energy (DOE)/MIT Neutron Beam Design Workshop, dose distributions were predicted for a brain-tissue-equivalent cylinder exposed to the "as-built", Al_2O_3 filtered, BMRR epithermal neutron beam. The analyses used a two-dimensional DOT model of the 18-cm diameter by 23-cm cylindrical phantom. Workshop, comparative-analyses, specified conditions were evaluated including: (1) a tumor-boron concentration of 30 ppm, (2) healthy-tissue equivalent boron concentrations of zero and 3 ppm, and (3) neutron beam diameters of 4.6, 10, and 20 cm. Data processing and graphic displays utilized auxiliary codes developed at INEL in support of this task. Results will be presented at the DOE/MIT workshop the end of March. Requested for the workshop were: (1) advantage depth, or the depth at which the total tumor dose equals the maximum healthy-tissue dose, (2) advantage dose rate, or dose rate at the advantage depth, (3) advantage ratio, or centerline integral of tumor dose to healthy tissue dose from zero to the advantage depth, and (4) the relative percentages of high-LET, low-LET and ^{10}B contribution to the advantage ratio.

Tables 1-3 show the detailed results of phantom calculations for the as-built Al_2O_3 filter in BMRR at 1 MW power. Figures 1-9 show centerline plots (1 MW) of dose components, RBE dose components, and elemental contributors. The RBEs were specified for the workshop as 1.6 for fast neutron and ^{14}N protons and 2.3 for the ^{10}B capture fragments. Figures 10-18 show isocontours of thermal flux, background dose and total gamma dose.

Table 1. BMRR 4.6-cm Beam With 18x23 Phantom

	Healthy Tissue Boron Concentration			
	Without RBE		With RBE	
	0	3 ppm	0	3 ppm
advantage depth (cm)	5.750E+00	5.135E+00	6.675E+00	5.818E+00
*advantage dose rate	3.525E-01	4.447E-01	4.447E-01	6.386E-01
advantage ratio	3.508E+00	2.824E+00	5.923E+00	3.979E+00
Dose Distribution				
% low-LET	1.816E+01	1.774E+01	9.292E+00	9.186E+00
% high-LET	1.035E+01	1.050E+01	7.590E+00	7.626E+00
% ^{10}B at 30 ppm	7.149E+01	7.176E+01	8.312E+01	8.319E+01
*max. ^{10}B dose rate (30 ppm)	9.576E-01		2.202E+00	
location (cm)	1.125E+00		1.125E+00	

	Maximums	Locations (cm)
*Total dose rate w/3ppm	4.447E-01	1.125E+00
*Neutron dose rate	2.595E-01	3.750E-01
*Gamma dose rate	2.080E-01	1.625E+00
Thermal Flux (n/cm^2•s•MW)	6.566E+07	1.125E+00

* NOTE: All dose rates have units of cGy/(MW•min)

Table 2. BMRR 10-cm Beam With 18x23 Phantom

	Healthy Tissue Boron Concentration			
	Without RBE		With RBE	
	0	3 ppm	0	3 ppm
advantage depth (cm)	6.750E+00	6.144E+00	8.009E+00	6.928E+00
*advantage dose rate	2.456E+00	3.037E+00	2.721E+00	4.129E+00
advantage ratio	3.228E+00	2.661E+00	5.536E+00	3.834E+00
Dose Distribution				
% low-LET	2.272E+01	2.230E+01	1.198E+01	1.175E+01
% high-LET	8.253E+00	8.343E+00	6.080E+00	6.118E+00
% ^{10}B at 30 ppm	6.902E+01	6.936E+01	8.194E+01	8.213E+01
*max. ^{10}B dose rate (30 ppm)	6.118E+00		1.407E+01	
location (cm)	1.625E+00		1.625E+00	

	Maximums	Locations (cm)
*Total dose rate w/3ppm	3.037E+00	1.875E+00
*Neutron dose rate	1.323E+00	1.375E+00
*Gamma dose rate	1.750E+00	2.125E+00
Thermal Flux ($n/cm^2 \cdot s \cdot MW$)	4.118E+08	1.625E+00

* NOTE: All dose rates in units of cGy/(MW•min)

Table 3. BMRR 20-cm Beam With 18x23 Phantom

	Healthy Tissue Boron Concentration			
	Without RBE		With RBE	
	0	3 ppm	0	3 ppm
advantage depth (cm)	7.250E+00	6.634E+00	8.577E+00	7.508E+00
*advantage dose rate	6.669E+00	8.068E+00	7.271E+00	1.058E+01
advantage ratio	2.922E+00	2.473E+00	4.982E+00	3.591E+00
Dose Distribution				
% low-LET	2.670E+01	2.622E+01	1.442E+01	1.415E+01
% high-LET	7.517E+00	7.595E+00	5.649E+00	5.683E+00
% ^{10}B at 30 ppm	6.578E+01	6.619E+01	7.993E+01	8.017E+01
*max. ^{10}B dose rate (30 ppm)	1.441E+01		3.314E+01	
location (cm)	1.875E+00		1.875E+00	

	Maximums	Locations (cm)
*Total dose rate w/3ppm	8.068E+00	2.125E+00
*Neutron dose rate	3.022E+00	1.625E+00
*Gamma dose rate	5.125E+00	2.375E+00
Thermal Flux ($n/cm^2 \cdot s \cdot MW$)	9.596E+08	1.875E+00

* NOTE: All dose rates are cGy/(MW•min)

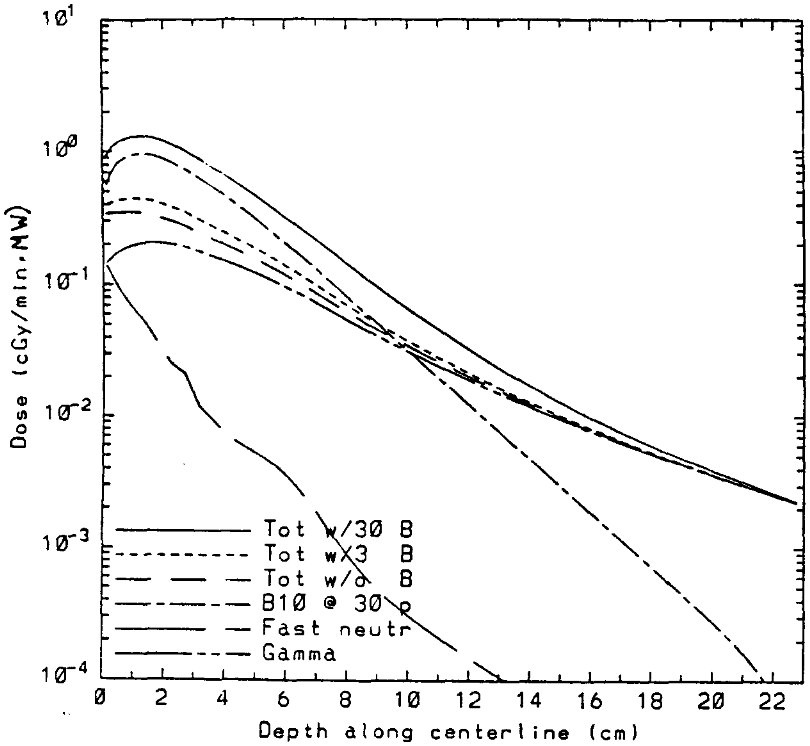

Figure 1. BMRR 4.6-cm beam with 18x23 phantom - axial distribution.

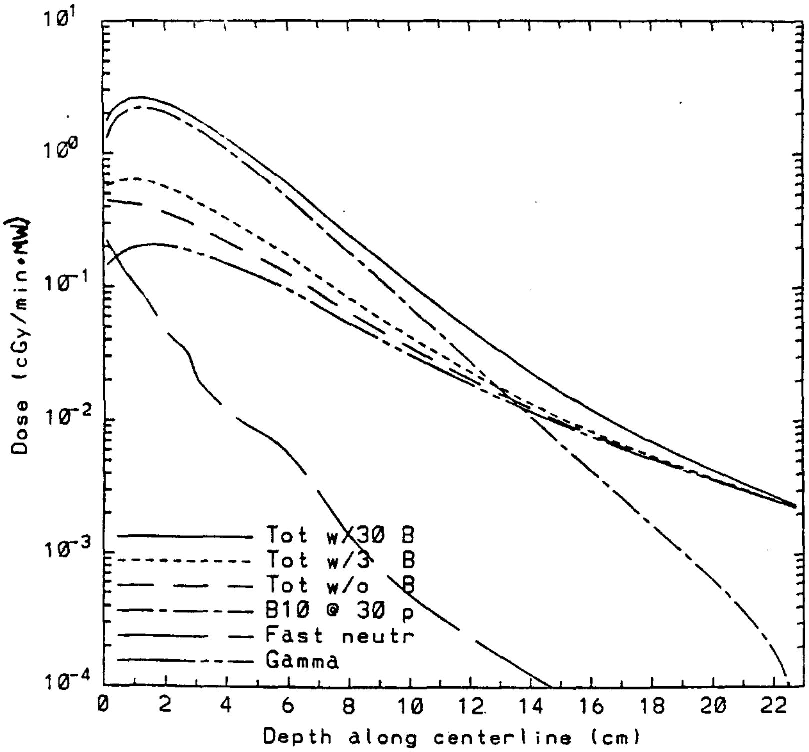

Figure 2. BMRR 4.6-cm beam with 18x 23 phantom - axial distribution with RBE factors.

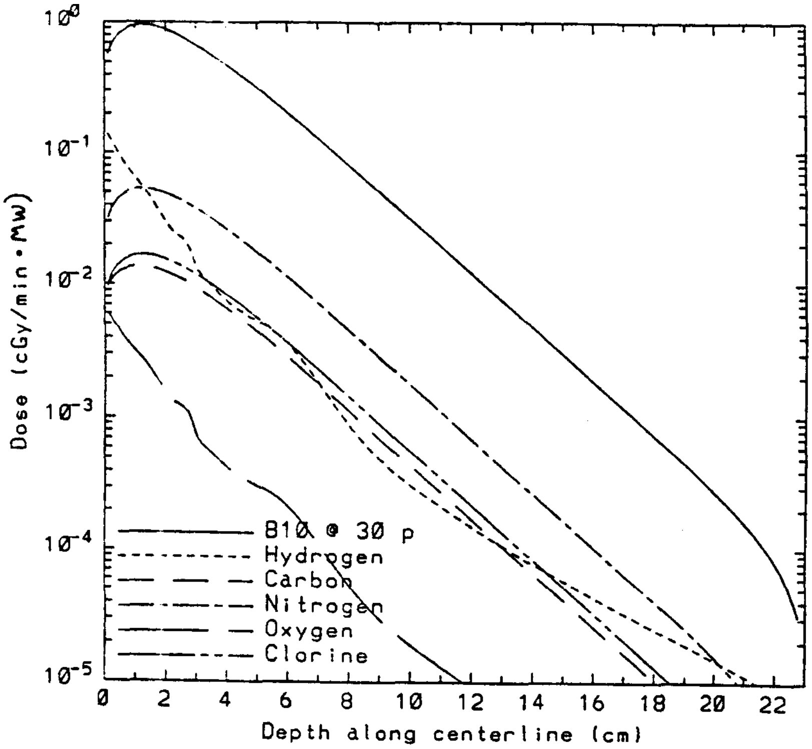

Figure 3. BMRR 4.6-cm beam with 18x23 phantom - axial distribution by element.

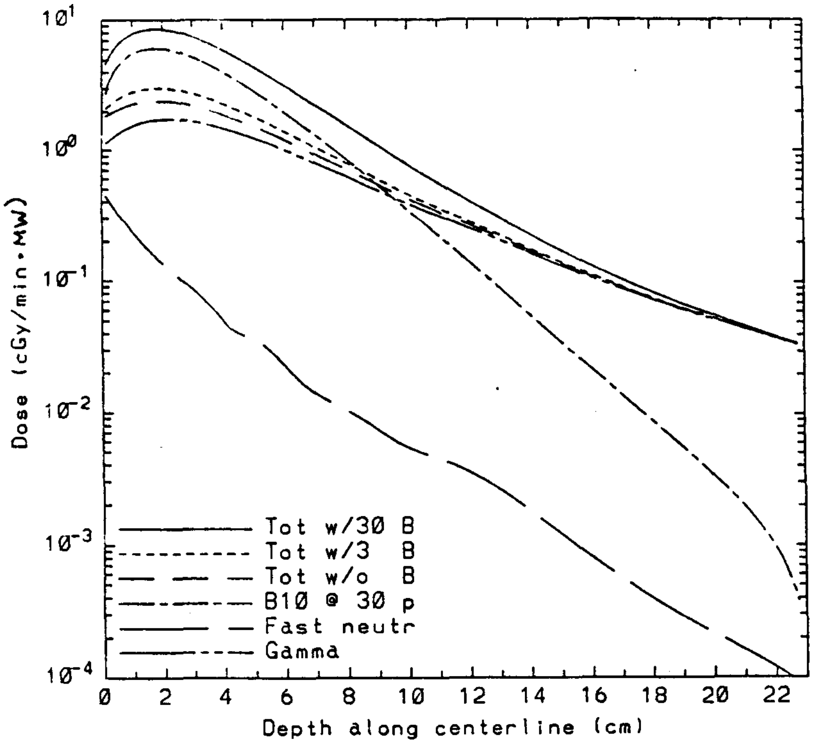

Figure 4. BMRR 10-cm beam with 18x23 phantom - axial distribution.

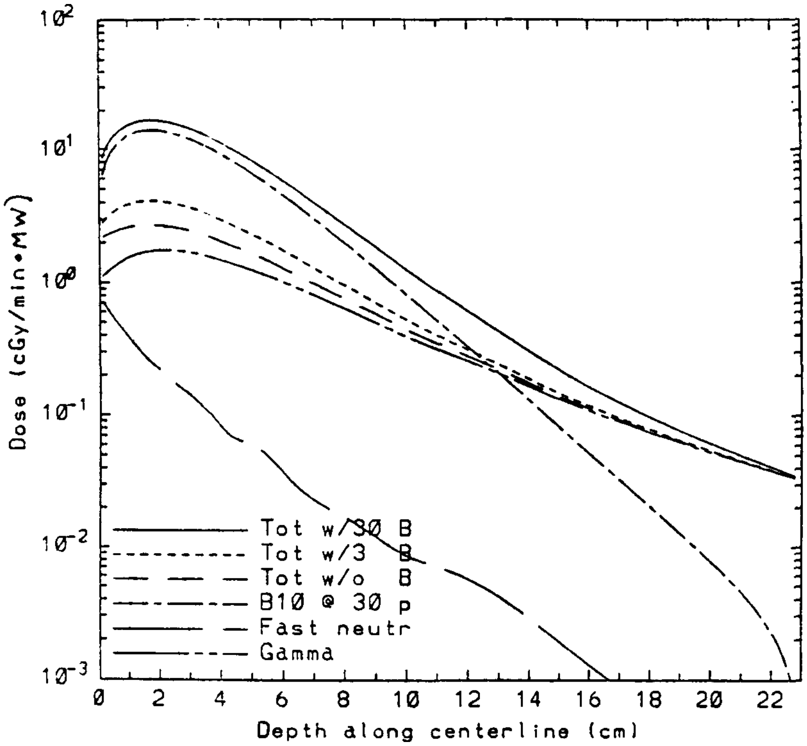

Figure 5. BMRR 10-cm beam with 18x23 phantom - axial distribution with RBE factors.

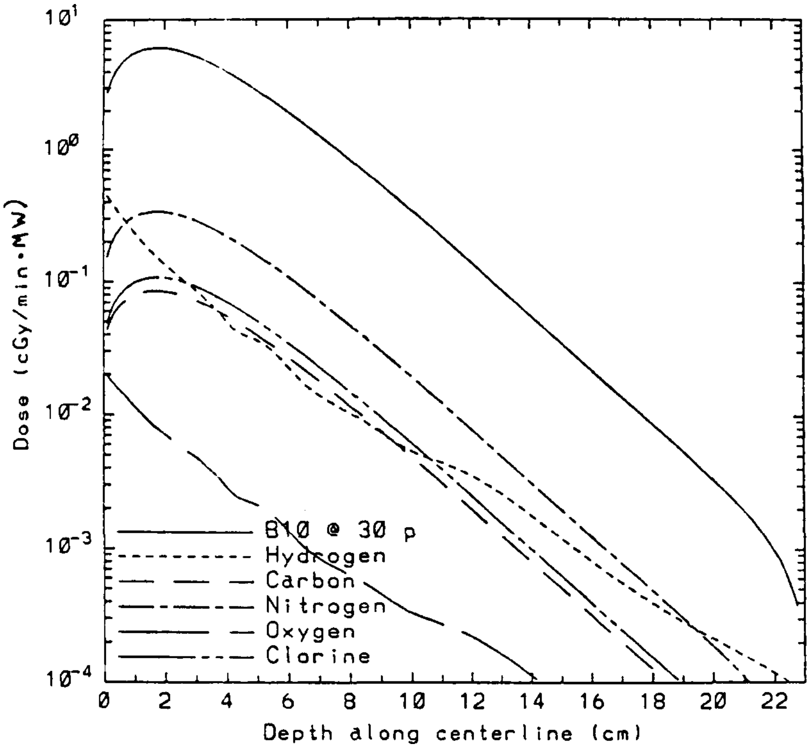

Figure 6. BMRR 10-cm beam with 18x23 phantom - axial distribution by element.

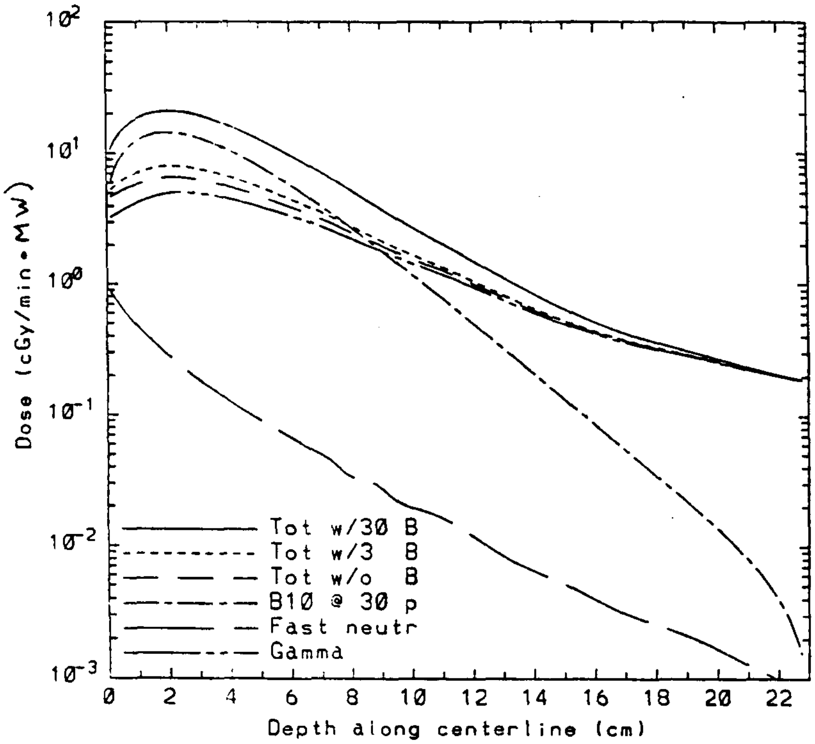

Figure 7. BMRR 20-cm beam with 18x23 phantom - axial distribution.

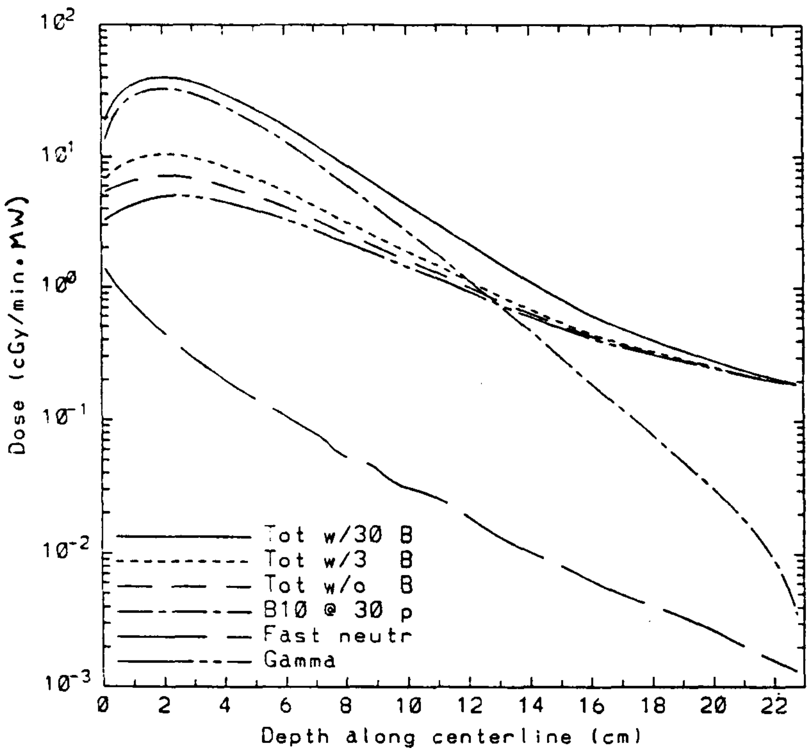

Figure 8. BMRR 20-cm beam with 18x23 phantom - axial distribution with RBE factors.

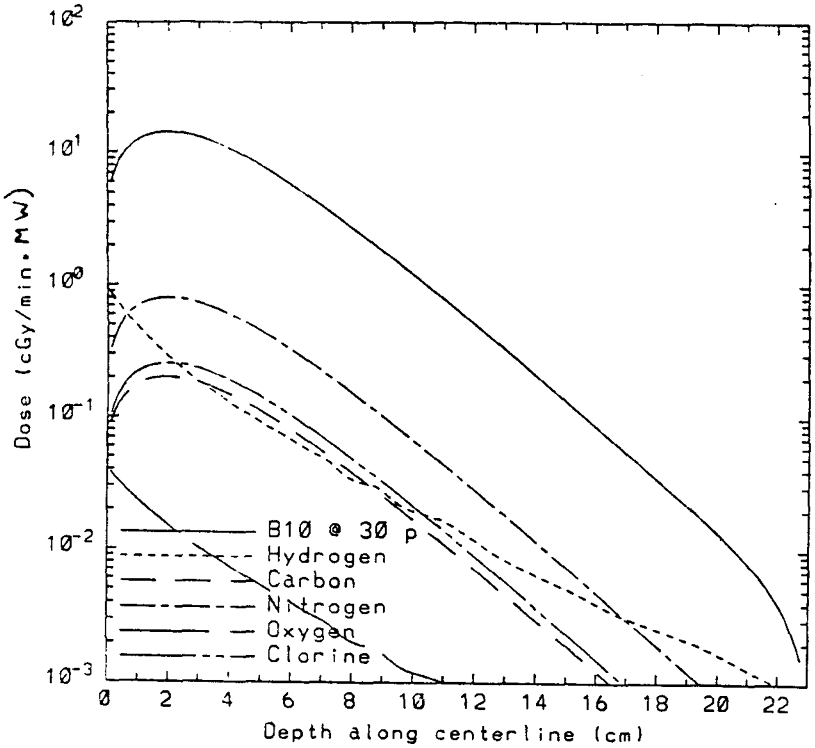

Figure 9. BMRR 20-cm beam with 18x23 phantom - axial distribution by element.

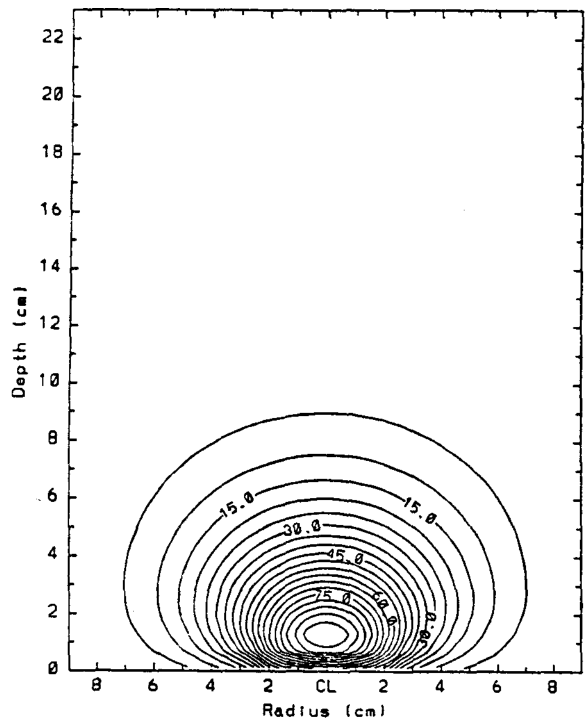

Figure 10. BMRR 4.6-cm beam with 18x23 phantom - thermal flux contours (max = 6.57E+07).

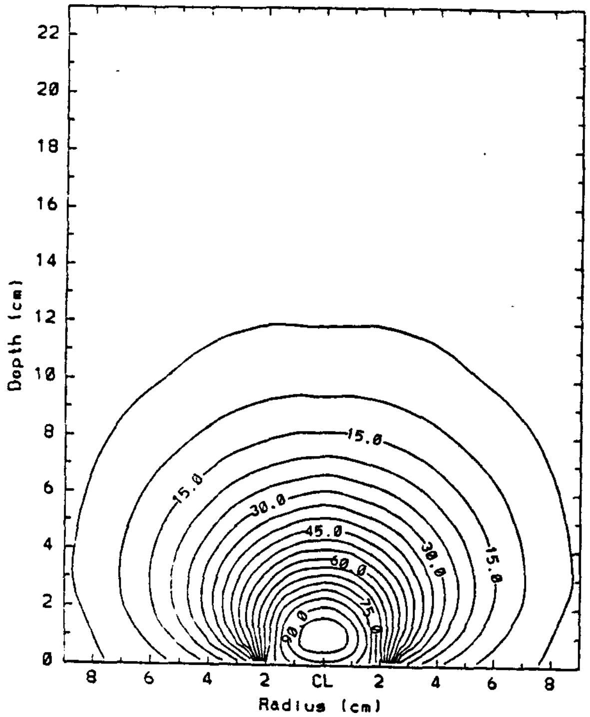

Figure 11. BMRR 4.6-cm beam with 18x23 phantom - total background dose with 3 ppm ^{10}B (max = 4.45E-01).

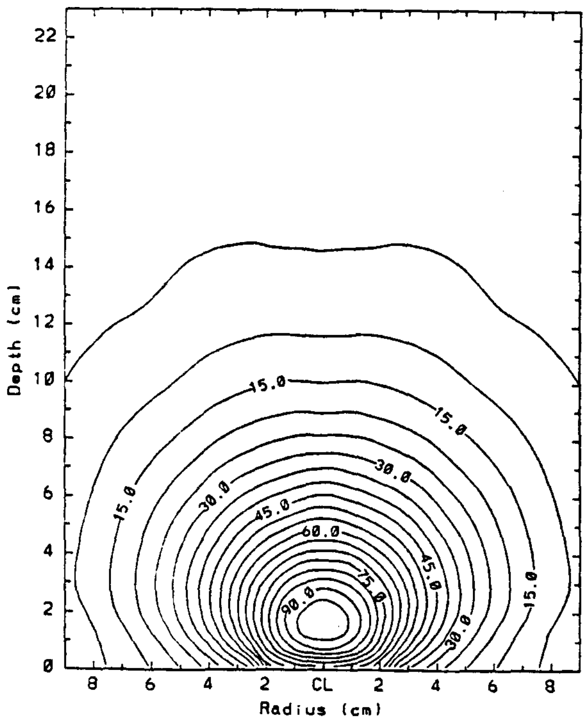

Figure 12. BMRR 4.6-cm beam with 18x23 phantom - total gamma dose (max = 2.08E-01).

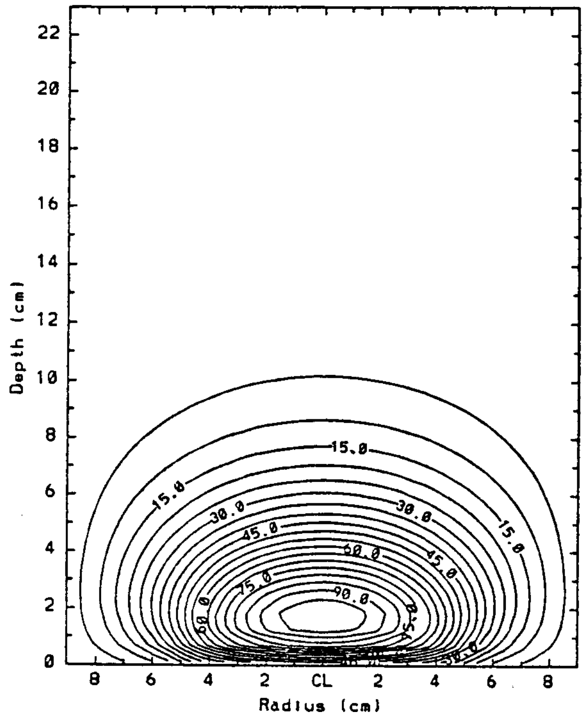

Figure 13. BMRR 10-cm beam with 18x23 phantom - thermal flux contours (max = 4.38E+08).

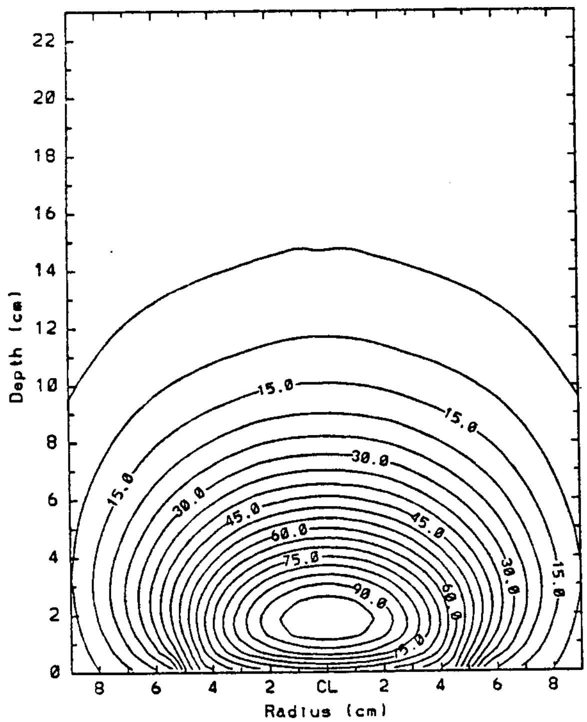

Figure 14. BMRR 10-cm beam with 18x23 phantom - total background dose with 3 ppm ^{10}B (max = 3.23E+00).

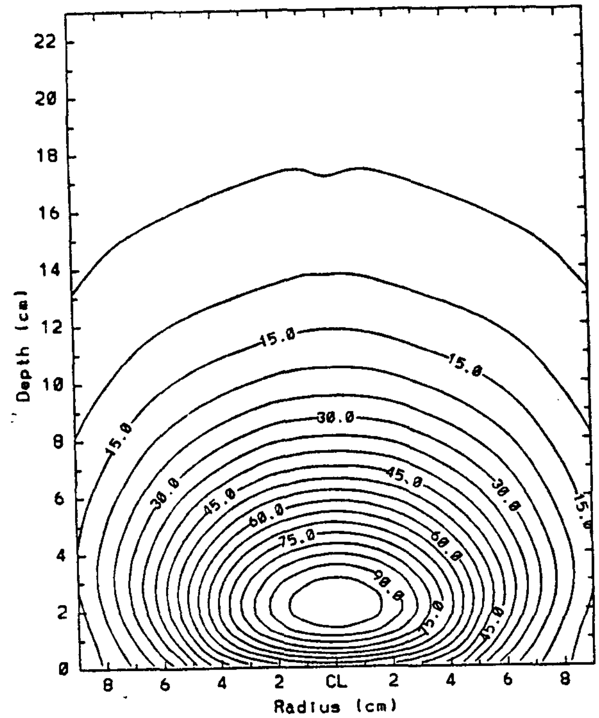

Figure 15. BMRR 10-cm beam with 18x23 phantom - total gamma dose (max = 1.86E+00).

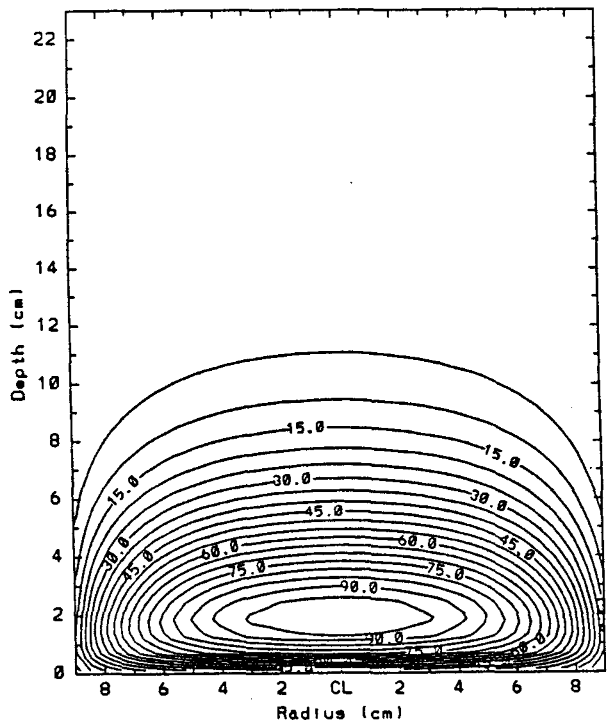

Figure 16. BMRR 20-cm beam with 18x23 phantom thermal flux contours (max = 1.15E+09).

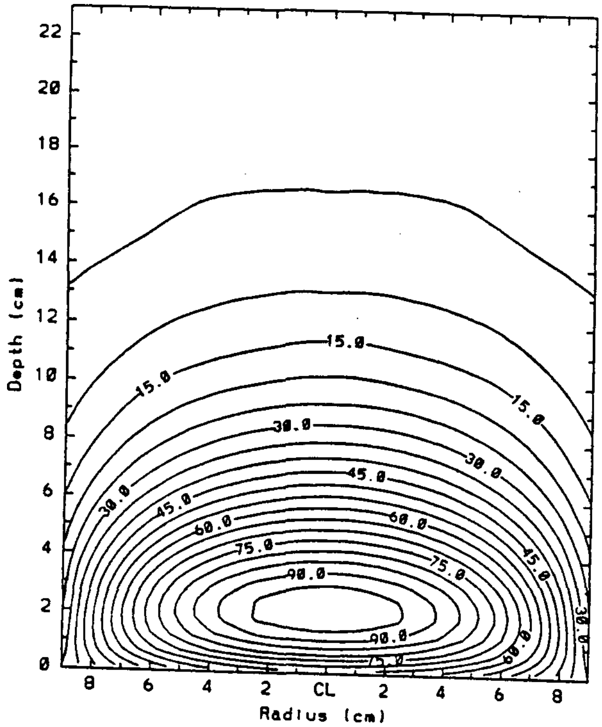

Figure 17. BMRR 20-cm beam with 18x23 phantom - total background dose with 3 ppm ^{10}B (max = 9.68E+00).

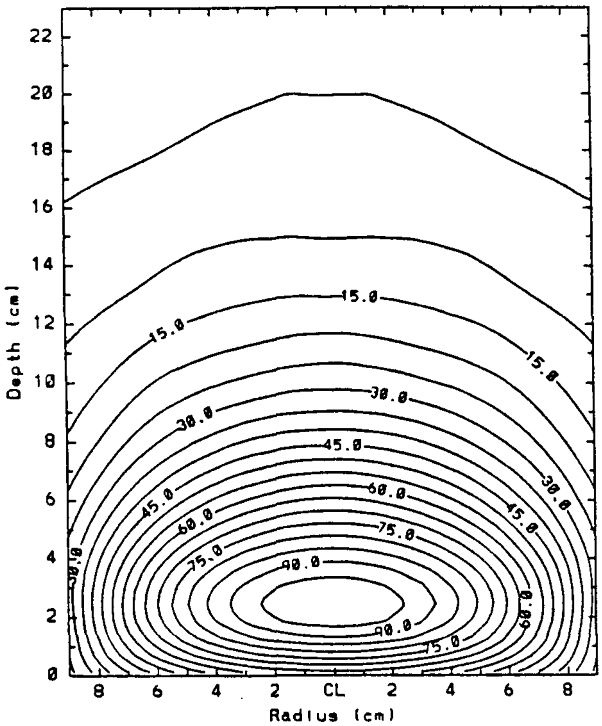

Figure 18. BMRR 20-cm beam with 18x23 phantom - total gamma dose (max = 6.15E+00).

PROJECT 2: LARGE ANIMAL MODEL STUDIES

Work was completed on the brain tumor dog admitted in the latter part of January, 1989. A hexamethyl-propylene-amineoxime (HMPAO) cerebral blood-flow nuclear scan was performed and the results are being analyzed. The computed tomography (CT) and MRI scans demonstrated an enhancing right cerebromedullary mass. Infusion, euthanasia, and necropsy were performed on February 7. Boron infusion (55 mg/kg) was administered and the routine blood and urine samples were collected over 500 minutes with plasmapheresis and plasma exchange at 360 minutes. Euthanasia was performed 500 minutes after start of infusion and necropsy confirmed the presence of the mass. Results of this sampling and histology are pending.

The baseline MRI, HMPAO cerebral blood-flow scans and neurometric analysis (brain mapping) were completed on all of the normal laboratory dogs to be used in the BMRR dose ranging study. Positron emission tomography (PET) scans were performed on two dogs at UofW in Seattle February 20-24. These dogs are scheduled to receive 2000 cGy February 28-March 2.

The first irradiations of normal laboratory dogs were completed February 8-10. Three dogs received 1000 cGy to the right hemisphere and the fourth dog received 2000 cGy to the right hemisphere. Three hours prior to irradiation, potassium penicillin was administered at a dose of 10,000 units/pound. Cerebrospinal fluid (CSF) was collected immediately prior to the irradiation via atlanto occipital puncture. On the day following irradiation, potassium penicillin was again administered at a dose of 10,000 units/pound. Three hours post administration, CSF was again collected. Penicillin normally should not cross the blood-brain-barrier; if it is found in the CSF following irradiation a break in the blood-brain-barrier is likely. Penicillin levels have not yet been determined. To-date, no acute reactions have been observed in any of the dogs. The two-week, post-irradiation CT scans have been completed on two dogs and are normal. CT scans on the other two dogs will be completed by month end. Post-irradiation cerebral blood-flow scan studies have been completed, but the results have not yet been analyzed. MRI scans are scheduled for March 5. Brain mapping is scheduled for February 27-March 5.

The second group of healthy dog irradiations will begin February 28. Two dogs will receive 2000 cGy to the right hemisphere and two dogs will receive 3000 cGy to the right hemisphere. A fission chamber and counting system have been prepared for on-line flux measurements within the oral cavity during this set of irradiations. The on-line fission chamber output will be correlated with dog-head phantom dosimetry.

The latest information on large animal model experiments is summarized on Pages 23-26.

WSU CANINE PHARMACOKINETIC STUDY
SUMMARY OF PATIENT DATA AVAILABLE FROM PBF/BNCT CENTRAL PROGRAM FILES

ANIMAL	NAME OF DOG	EUTHANASIA DATE	EUTHANASIA MIN*	CASE SUMMARY	PATHOLOGY DIAGNOSIS	BLOOD SERUM AND URINE ANALYSIS	TISSUE ANALYSIS	CT UNENH.	CT ENH	MRI UNENH.	MRI ENH
35447-1	"Muffy" Klugh	3/23/87	660	Yes	Pituitary adenoma	Yes	Yes	Yes	Yes	Yes	Yes
35447-2	"Stashi" Christensen	5/18/87	750	Yes	No tumor/positive boron control	Yes	Yes	N/P	N/P	No	No
35447-3	"King" Henry	5/18/87	Control	Yes	No tumor/negative boron control	Control	Yes	N/P	N/P	No	No
35447-14	"Marsha" Despain	6/30/87	780	Yes	Invasive Adenocarcinoma	Yes	Yes	Yes	Yes	Yes	Yes
36085	"Amos" Vallangdigham	8/3/87	780	Yes	Invasive nasal carcinoma	Yes	Yes	Yes	Yes	Yes	Yes
35447-18	"Slim" Pozzobon	9/14/87	770	Yes	Invasive nasal adenocarcinoma	Yes	Yes	Yes	Yes	Yes	Yes
35447-20	"Mischief" Scott	11/2/87	90	Yes	Meningioma	Yes	Yes	Yes	Yes	Yes	Yes
35447-23	"Rocky" Christensen	11/13/87	770	Yes	Pituitary adenoma	Yes	Yes	Yes	Yes	Yes	Yes
35447-24	"Mariah" May	11/24/87	410	Yes	Nonenhancing lesion	Yes	Yes	Yes	Yes	Yes	Yes
36845-25	"Sandy" Frazier	1/26/88	770	Yes	Meningioma	Yes	Yes	Yes	Yes	Yes	Yes
35447-28	"Boots" Belisle	2/22/88	125	Yes	Nonenhancing right cerebellar mass	Yes	Yes	Yes	Yes	Yes	Yes
35447-30	"Sunny" Seeley	3/1/88	420	Yes	Extraaxial lesion	Yes	Yes	Yes	Yes	Yes	Yes
35447-32	"Pip" Hahn	2/26/88	410	Yes	Pituitary/thalamic tumor	Yes	Yes	Yes	Yes	Yes	Yes
35447-33	"Coco" Pechtel	3/23/88	420	Yes	Nasal adeno carcinoma	Yes	Yes	Yes	Yes	Yes	Yes
35447-37	"Tucker" Reeves	4/14/88	420	Yes	No tumor/positive boron control	Yes	Yes	N/P	N/P	No	No
35447-39	"Fritts" Coglan	5/2/88	110	Yes	Meningioma	Yes	Yes	Yes	Yes	Yes	Yes
35447-40	"Rocky" Underwood	5/3/88	420	Yes	Fungal Granuloma	Yes	Yes	Yes	Yes	Yes	Yes
35447-43	"Blue" Archer	5/23/88	420	Yes	Diffuse cortical astrocytoma	Yes	Yes	N/P	N/P	Yes	Yes
35447-49	"Jenny" Nelson	6/29/88	420	Yes	Glial cell infiltrate	(P)	Yes	Yes	Yes	Yes	Yes

* Euthanasia time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.

(P) Partial results
N/A Not applicable
N/P Not Performed

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WSU CANINE PHARMACOKINETIC STUDY
SUMMARY OF PATIENT DATA AVAILABLE FROM PBF/BNCT CENTRAL PROGRAM FILES

ANIMAL	NAME OF DOG	EUTHANASIA DATE	EUTHANASIA MIN*	CASE SUMMARY	PATHOLOGY DIAGNOSIS	BLOOD SERUM AND URINE ANALYSIS	TISSUE ANALYSIS	CT UNENH.	CT ENH	MRI UNENH.	MRI ENH
35447-50	"Caesar" Chenoweth	7/13/88	420	Yes	Meningioma	(P)	Yes	Yes	Yes	Yes	Yes
35447-54	"Licorice" Meyers	8/3/88	410	Yes	No Tumor/Positive boron Control	(P)	Yes	Yes	Yes	Yes	Yes
35447-55	"Kelley" Langsston	8/17/88	410	Yes	Diffuse Astrocytoma	(P)	(P)	No	No	Yes	Yes
35447-57	"Rafferty" Reber	9/1/88	420	Yes	Meningioma	(P)	(P)	No	Yes	Yes	Yes
35447-59	"Heidi" Boyer	9/12/88	180	Yes	Meningioma	Yes	(P)	No	Yes	Yes	Yes
35447-62	"Chester" Scott	10/9/88	180	Yes	Meningioma	(P)	(P)	No	Yes	Yes	Yes
35447-67	"Muffet" Hammel	11/1/88	180	Yes	Astrocytoma	(P)	(P)	No	Yes	N/P	N/P
35447-70	"Mac" Meyers	11/15/88	180	Yes	Fibrillary Astrocytoma	(P)	No	No	Yes	Yes	Yes
35447-71	"Jake" Brede	1/4/89	180	Yes	Choroid Plexus Papilloma	Yes	Yes	Yes	Yes	N/P	N/P

* Euthanasia time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.

(P) Partial results
N/A Not applicable
N/P Not Performed

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WSU CANINE PLASMAPHERESIS STUDY

GROUP	ANIMAL	SEX	PLASMA EXCHANGE DATE	FIRST MIN.	SECOND MIN.	THIRD MIN.	EUTHANASIA (MIN.)	BLOOD SERUM & URINE ANALYSIS	TISSUE ANALYSIS
1	2095	M	6/8/88	360*	---	---	430	Yes	Yes
1	2084	M	6/9/88	360*	---	---	445	Yes	Yes
1	2109	F	6/10/88	360*	---	---	410	Yes	Yes
2	2097	M	6/14/88	360	---	---	413	Yes	Yes
2	2074	M	6/15/88	360	---	---	410	Yes	Yes
2	2092	F	6/16/88	360	---	---	400	Yes	Yes
3	2103	M	6/20/88	360	---	---	755	(P)	Yes
3	2081	M	6/22/88	360	---	---	755	Yes	Yes
3	2089	F	6/24/88	365	---	---	Yes	Yes	
4	2096	M	6/27/88	360	470	600	640	(P)	Yes
4	2104	M	6/28/88	360	480	600	660	(P)	Yes
4	2098	F	6/29/88	375	555	695	785	(P)	Yes
	2091								
	2073								
	2090								
	2078								
	2093								
	2086								
	2068								
	2082								

* Control Group (reinfused same boronated plasma that had just been extracted).

WSU ACUTE CANINE DOSE STUDY

		IRRADIATION							
ANIMAL	SEX	DATE	START TIME	MIN.	CALCULATED DOSE (cGy)	^{10}B EST. AVG.	EUTHANASIA DATE	BLOOD SERUM & URINE ANALYSIS	TISSUE ANALYSIS
1592*	M	1/11/89	345	58	1000	31.1	1/11/89	Yes	Yes
1587*	M	1/12/89	210	36	1000	57.8	1/12/89	Yes	Yes
966	M	2/8/89	235	48	1000	(?)	---	---	---
1588	M	2/9/89	220	49	1000	38.5	---	---	---
995	M	2/9/89	238	42	1000	47.8	---	---	---
1591	M	2/10/89	194	90	2000	45.5	---	---	---

* Dosimeter animals euthanized after irradiation.

PROJECT 3: HUMAN STUDIES

This project is currently not funded.

PROJECT 4: STABILITY, PHARMACOLOGY, AND TOXICOLOGY OF DRUGS

This project is currently funded by a grant from the State of Idaho. There was no reportable progress during December.

PROJECT 5: NEUTRON SOURCE AND FACILITY PREPARATION

The PBF-BNCT Quality Program Plan, Revision M was released for internal use and sent to DOE-ID for review and approval.

PBF Core and Physics Design Analysis

Analysis

PBF Core and Physics Design Analysis - The documentation and refinement of the CRAY version of PDQ-7 and the engineering design file (EDF) documenting the results of the depletion modeling of the PBF core were not completed as predicted in last month's report. This work was temporarily suspended during the reporting period to apply resources to New Production Reactor work at INEL.

Design

The drawings for the Reactor Vessel Nozzle and Closure Flange were signed and released. The action items from the final design review were resolved and a closure letter was released. These actions complete the design activity on the Reactor Vessel Nozzle and Closure Flange for FY-1989.

Design activity on the Neutron Filter components during the reporting period included producing drawings of the aluminum filter plates, plate separating pins, D_2O coolant connection fittings, the flange connecting the Neutron Filter to the reactor vessel nozzle and a plan and elevation drawing showing the neutron filter installation. These drawings are being reviewed by the design engineer.

Sketches showing the stainless steel diaphragm sandwiched between the aluminum neutron filter end plates have been completed. Sketches of the seal for the connection between the neutron filter shell and the nozzle flange have also been completed. These sketches will be used in discussions with diaphragm, bellows, and o-ring seal suppliers.

The cost of lithiated aluminum for the neutron filter led the designers to a design using pure aluminum plate. The only positive response from a supplier for lithiated aluminum involved contracting for a mill run of the required composition. The cost of a mill run was too high and for too large a quantity when compared to costs for other acceptable, but less desirable, designs. Efforts to maintain contact with material suppliers to identify opportunities to piggyback an order for lithiated aluminum for PBF/BNCT onto a larger order will continue.

The neutron filter support design required minor modification as a result of the stress analysis. The stress analysis revealed stresses uncomfortably close to the American Society of Mechanical Engineers (ASME) Boiler and Pressure Vessel Code Section III allowables for Class 2 components. The attachment of the beamline support to the reactor vessel wall was redesigned to a solid block welded to the vessel. The stresses were then within acceptable limits and EDF PBF-BNCT-120 was released documenting the results.

The resolution of comments from the final design review of the neutron filter cooling system continues. A system hydraulic evaluation was performed to compare pump performance with system requirements (under varied flow conditions). The results of this evaluation are documented in EDF PBF-BNCT-122 Rev. 1 and confirm the need for a flow control valve with an equal percentage flow characteristic and a flow coefficient (C_v) of 28. Documentation of the overpressure protection analysis and review of the consequence of loss of D_2O through venting and pressure relief is proceeding. The analysis is being performed to the requirements of the ASME Boiler and Pressure Vessel Code, Section III, Subsection ND-7000. Completion of system documentation and drawings for the neutron filter cooling and air purge system is scheduled for mid-April, 1989.

Design of the dummy inpile tube to replace the pressure tube is conceptualized as an 8-inch aluminum tube with a 1-inch wall thickness. A round bar will be attached inside the tube to provide a 0.92 aluminum volume fraction. A 10-inch diameter by 1/2-inch thick donut will be welded to the top of the 8-inch aluminum tube to provide bolted attachment points for the filler piece.

Work on the neutron filter shutter system mechanical design was resumed in mid-February, 1989. Efforts are being directed toward drawing completion and documentation of design criteria and analysis. A final mechanical design review of this system is scheduled for April 28, 1989, with completion of system documentation and drawings scheduled for mid-July, 1989. Electrical design work on the neutron beam shutter control system is continuing. Opening and closing the shutter will be accomplished by the use of a hydraulic pump. A control system will be designed to control and monitor operation of the shutters and the hydraulic system. The shutter control system will receive a permissive signal from the reactor control system if all plant operating systems are ready. Receipt of this signal will permit opening the shutter to begin treatment. The control system will also close the shutter if the reactor shuts down or, if the shutter fails to close on command, the shutter control system will shut the reactor down. Provision will be made for operation of the shutter for maintenance when the reactor is not operating. Included in the shutter control system design is the Patient Data Acquisition and Retrieval System (PDARS). This system will receive data on the patient's neutron dose from the Neutron Beam Nuclear Instrumentation System and on the plant's status from the Reactor Control System, Neutron Monitoring System, Neutron Nozzle/Core Filter System, and Radiation Monitoring System. This data acquisition system will provide on-line display of the current plant status, neutron filter status, shutter status, neutron flux, and patient dose. The current design philosophy is to make the shutter control system computer controlled with control parameters specified by the person in charge of treatment.

Design of a replacement system for the Reactor Building Temperature Monitoring System was started in late January, 1989 and is continuing. The system currently used for measuring temperatures will be replaced because it requires frequent repair and has become undependable. A system obtained from the decommissioned Loss-of-Fluid Test Facility (LOFT) will be used to replace the existing system. The preliminary design of the system was completed this month.

The design of the modifications to the plant annunciator system was started late in January, 1989. Annunciators in the plant are to be relocated and grouped together according to function and system. Annunciators not required for BNCT operation are to be removed and the space used for systems installed for BNCT. Relocation and removal design is expected to be completed by the end of March, 1989.

A short form data sheet for a Research and Analysis Laboratory for PBF-BNCT was completed by incorporating DOE-Idaho Operations Office (ID) comments and was transmitted to DOE-ID Plans and Budgets Branch. The estimated cost for this laboratory was $7.7 million.

The extended synopsis for a paper proposed for the International Atomic Energy Agency (IAEA) conference in Chalk River in October received patent clearance and will be sent to DOE-ID for review and submittal to IAEA with other proposed papers.

CORE A: ADMINISTRATION AND COMMON SUPPORT

Programmatic/Administrative

It has come to the editor's attention that certain pages are missing from previously issued bulletins. This was due to a paper jam in the INEL printing department and if you would please notify me at the address on the back cover of this bulletin, or telephone me at (208) 526-9264, letting me know which page(s) you need, I will forward the missing page(s) on to you. Please accept our apologies for any inconvenience this may have caused you, but, even if the best of situations, accidents can happen.

Dr. Patrick R. Gavin (WSU) made a presentation to the Brookhaven National Laboratory (BNL) Medical Department on the BNCT large animal irradiation program.

A Biomedical Advisory Committee review meeting has been set for April 20-21, 1989 at the EIRMC auditorium. The purpose of the meeting is to obtain Advisory Committee recommendations on the progress to date with the brain tumor program and an evaluation of the proposed melanoma treatment expansion. A copy of the proposed melanoma treatment expansion has been sent to all Advisory Committee members as well as the major researchers in the program with the request that they review and prepare comments and suggestions for presentation at the meeting.

INEL, EIRMC, and Idaho Falls medical personnel met at EIRMC on March 2, 1989 to discuss organization of an Animal Care and Use Committee needed to review and approve animal, boron-imaging experiments planned in support of near-term development of MRI at EIRMC.

Five grams of cesium borocaptate (BSH) have been received, from a potential new supplier, for purity analysis. If it proves to be of good quality, we will know that the potential supplier can make the compound to our specifications. Competitive bid process can then be instituted for future boron salt orders.

BNL Support:

A contract has been negotiated with Babcock and Wilcox for the construction of six new fuel elements for the BMRR. The funding for this fuel, through a work-for-others contract with BNL, is waiting final approval at BNL before being sent to EG&G Idaho. The one, new, excess University of Michigan fuel element, located by EG&G Idaho, was loaded into the BMRR. All reactivity measurements were completed and the reactor is now back in operation.

Meetings, Conferences, and Proceedings

Visual aids in support of Dr. Ronald V. Dorn's lectures at ONCOVAIL '89 in Vail, CO, February 26-March 4, 1989, were prepared and delivered to Dr. Dorn.

Two papers, with visuals, were prepared for presentation at the Workshop on Beam Design, Development, and Performance for Neutron Capture Therapy, to be held at Massachusetts Institute of Technology, Cambridge, MA on March 30-31, 1989. Floyd Wheeler will present "Physics Design for the Brookhaven Medical Research Reactor (BMRR) Epithermal Neutron Source," and William A. Neuman will present "Neutron Beam Studies for a Medical Therapy Reactor."

Ken Bradshaw (INEL), Dr. Todd Richards (UofW), and Dr. David Madden (EIRMC) attended an MRI meeting in Los Angeles February 24-March 1, 1989.

CORE B: PBF OPERATIONS

Revision of the Plant Operating Manual to delete those sections that would not be applicable to the BNCT program continued through the month of February.

Comments were received on the draft revision to the Test Train and Assembly Facility (TTAF) revised Safety Analysis. These comments are currently being incorporated into the document and evaluated as to whether additional seismic analysis will be required for the canal area.

Procedures for replacement of the ion-exchange column in the TTAF canal were issued. The ion-exchange column is being replaced due to its depletion after approximately ten years of use in the canal. The procedures for the eight-year interval inspection of the fuel racks in the TTAF canal were written and are out for review.

The monthly, routine, safety walkthrough of the PBF plant was completed. Safety deficiencies identified during walkthroughs are corrected as they are reported.

Preventive maintenance performed in the plant included: (1) secondary system chemical treatment pumps, (2) auxiliary air compressor, (3) gas stack monitor, (4) constant air monitors, (5) utility cooling water pump, (6) hot waste storage transfer pump, (7) air dryer prefilter, (8) plant air valves and piping, (9) heating and ventilation electrical heaters and supply fans, (10) jib crane, (11) control center furnaces, (12) overhead truck doors, and (13) annual silver zeolite efficiency test.

An engineering evaluation was completed on the wear areas on the 5/15-ton crane bridge trolly rails. This evaluation determined that the existing wear on the rails did not warrant any weld repair, but recommended that limit switches be installed at a later date to preclude running the trolly against the rail stops. Administrative controls were put into effect to limit the travel within one foot of the stops. The 5/15 crane was subsequently released and a load test was completed on the crane.

Training conducted during the month of February consisted of training of the emergency bus drivers and performance of the biannual recertification and qualification review committee examination for an Experimental Power Reactor Operator.

A request for approximately $20.5K of capital equipment funds is being prepared for purchase of an additional radiation portal monitor for the PBF reactor building. This monitor is required for full compliance with DOE Order 5480.11 to preclude contaminated personnel from entering the reactor building eating area.

Inventory of Boron Salt and Standards

BNCT	8	$Na_2{}^{10}B_{12}H_{11}SH$	3 gms
	9	$Na_2{}^{10}B_{12}H_{11}SH$	4 gms
	10	$Na_2{}^{10}B_{12}H_{11}SH$	1 gm
	11	$Na_2{}^{10}B_{12}H_{11}SH$	.75 gms
	13	$Na_2{}^{10}B_{12}H_{11}SH$	~2 gms
	107	$Cs_2{}^{10}B_{12}H_{11}SH$	5 gms
BNCT	12	$Na_2B_{12}H_{11}SH$	500 mg
	15	$Na_2B_{12}H_{11}SH$	.140 gms
	14	$Na_2B_{12}H_{11}SH$	~ 2 gms
		(this represents some BNCT 27 returned by Cornell)	
	23	$Na_2B_{12}H_{11}SH$	1.5 gms
	24	$Na_2B_{12}H_{11}SH$	.3 gms
	27a	$Na_2B_{12}H_{11}SH$	500 mg
		(this represents some BNCT 14 returned by Cornell)	
	22	$Na_2B_{12}H_{11}SH$	~ 6 gms
BNCT	17	$CsB_{12}H_{11}SCN(CH_3)(CH_2)_3CH_2$	100 mg
	27	$CsB_{12}H_{11}SCN(CH_3)(CH_2)_3CH_2$	100 mg
	30	$CsB_{12}H_{11}SCN(CH_3)(CH_2)_3CH_2$	1 gm
BNCT	19	$Cs_4B_{12}H_{11}SSB_{12}H_{11}$	500 mg
	25	$Cs_4B_{12}H_{11}SSB_{12}H_{11}$	400 mg
	29	$Cs_4B_{12}H_{11}SSB_{12}H_{11}$	1 gm
	31	$Cs_4B_{12}H_{11}SSB_{12}H_{11}$	200 mg
	108	$Cs_4B_{12}H_{11}SSB_{12}H_{11}$	200 mg
BNCT	26	$Na_4B_{12}H_{11}SOSB_{12}H_{11}$	400 mg
		(opened 12/29/88 - removed 29.3 mg)	
	28	$Na_4B_{12}H_{11}SOSB_{12}H_{11}$	1 gm
		(opened 12/7/88)	
BNCT	16	$CH_3(CH_2)_2N(CH_3)CS$	5 gm
	18	$LiB_{12}H_{11}XH_2O$	1 gm
BNCT	32	$Na_2B_{12}H_{11}SH$	1 gm
		(opened 12/13/88 - removed 100 mg)	
		(opened 12/19/88 - removed 42.6 mg)	
	33	$Na_2B_{12}H_{11}SH$	1 gm
	34	$Na_2B_{12}H_{11}SH$	1 gm
	35	$Na_2B_{12}H_{11}SH$	1 gm
	36	$Na_2B_{12}H_{11}SH$	1 gm
	37	$Na_2B_{12}H_{11}SH$	1 gm

<u>Inventory of Boron Salt and Standards (continued)</u>

BNCT 38	$Na_2B_{12}H_{11}SH$	1 gm
39	$Na_2B_{12}H_{11}SH$	1 gm
40	$Na_2B_{12}H_{11}SH$	1 gm
41	$Na_2B_{12}H_{11}SH$	1 gm
BNCT 42	$Na_2B_{12}H_{11}SH$	1 gm
43	$Na_2B_{12}H_{11}SH$	1 gm
44	$Na_2B_{12}H_{11}SH$	1 gm
45	$Na_2B_{12}H_{11}SH$	1 gm
46	$Na_2B_{12}H_{11}SH$	1 gm
47	$Na_2B_{12}H_{11}SH$	1 gm
48	$Na_2B_{12}H_{11}SH$	1 gm
49	$Na_2B_{12}H_{11}SH$ (opened 12/6/88)	1 gm
50	$Na_2B_{12}H_{11}SH$	1 gm
51	$Na_2B_{12}H_{11}SH$	1 gm
52	$Na_2B_{12}H_{11}SH$	1 gm
53	$Na_2B_{12}H_{11}SH$	1 gm
54	$Na_2B_{12}H_{11}SH$	1 gm
55	$Na_2B_{12}H_{11}SH$	1 gm
56	$Na_2B_{12}H_{11}SH$	1 gm
BNCT 57	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
58	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
59	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
60	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
61	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
62	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
63	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
64	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
65	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
66	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/4/89)	1 gm
67	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/4/89)	1 gm
68	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
69	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/4/89)	1 gm
70	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/4/89)	1 gm
71	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/4/89)	1 gm
72	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
73	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/4/89)	1 gm
74	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
75	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
76	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm
77	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/4/89)	1 gm
78	$Na_2{}^{10}B_{12}H_{11}SH$ (sent to WSU 1/31/89)	1 gm

Inventory of Boron Salt and Standards (continued)

BNCT 79	$Na_2{}^{10}B_{12}H_{11}SH$	(sent to WSU 1/31/89)	1 gm
80	$Na_2{}^{10}B_{12}H_{11}SH$	(sent to WSU 1/4/89)	1 gm
81	$Na_2{}^{10}B_{12}H_{11}SH$	(sent to WSU 1/31/89)	1 gm
82	$Na_2{}^{10}B_{12}H_{11}SH$	(sent to WSU 1/4/89)	1 gm
83	$Na_2{}^{10}B_{12}H_{11}SH$	(sent to WSU 1/31/89)	1 gm
84	$Na_2{}^{10}B_{12}H_{11}SH$	(sent to WSU 1/4/89)	1 gm
85	$Na_2{}^{10}B_{12}H_{11}SH$	(sent to WSU 1/31/89)	1 gm
86	$Na_2{}^{10}B_{12}H_{11}SH$	(sent to WSU 1/31/89)	1 gm
87	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
88	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
89	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
90	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
91	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
92	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
93	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
94	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
95	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
96	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
97	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
98	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
99	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
100	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
101	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
102	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
103	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
104	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
105	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm
106	$Na_2{}^{10}B_{12}H_{11}SH$		1 gm

Major Upcoming Events

Feb 23-Mar 4, 1989	**ONCOVAIL'89 - Three-dimensional Treatment Planning and Execution**, Vale, CO
March 10-11, 1989	**Cancer Management Course**, Lubbock, TX. Sponsored by Commission on Cancer, American College of Surgeons and St. Mary of the Plains Hospital. Contact: Dr. David Close, Cancer Department, American College of Surgeons, 55 E. Erie Street, Chicago, IL 60611 (312) 664-4050.
March 11-17, 1989	**Advances in Clinical Oncology**, Snowbird, UT. Contact: Mary Humphrey, Arizona Cancer Center, Tucson, AX 85724 (602) 626-2276.
March 16-17, 1989	**The Workshop on Biomedical and Space Related Research with Heavy Ions at the BEVELAC**, Berkeley, CA
March 16-18, 1989	**Advances in Cancer Treatment Research and Autologous Bone Marrow Transplantation Symposium**, Grand Hyatt Hotel, New York City. Contact: Office of Continuing Medical Education, Albert Einstein College of Medicine, Montefiore Medical Center, 3301 Bainbridge Avenue, Bronx, NY 10467 (212) 920-6674.
March 18-23, 1989	**Radiation Research Society and North American Hyperthermia Group**, Seattle, WA. Annual meeting. Contact: Radiation Research Society, 1101 Market Street, 14th Floor, Philadelphia, PA 19107 (215) 574-3153.
March 18-24, 1989	**American Society of Neuroradiology**, Orlando, FL
March 20-21, 1989	**American Society of Preventive Oncology**, Hyatt Regency, Bethesda, MD. Contact: Dr. Richard Love, American Society of Preventive Oncology, 1300 University Avenue, 7C, Madison, WI 53706 (608) 263-6919.
March 22, 1989	**Advances in Cancer Control**, Guest Quarters Hotel, Bethesda, MD. Contact: Linda Morgan, Division of Cancer Control, Fox Chase Cancer Center, 7701 Burholme Avenue, Philadelphia, PA 19111 (215) 728-2986.

Major Upcoming Events (continued)

March 27-April 3, 1989	**Molecular Mechanisms in DNA Replication and Recombination**, Keystone, CO. Contact: UCLA Symposia, 2032 Armacost Avenue, Los Angeles, CA 90025 (213) 207-5042.
March 29-April 1, 1989	**Association of Community Cancer Centers**, Washington, D.C. 15th National Meeting. Contact: Carol Johnson, ACCC, 11600 Nebel Street, Suite 201, Rockville, MD 20852 (301) 984-9496.
March 30-31, 1989	**Workshop on Neutron Beam Design, Development, and Performance for Neutron Capture Therapy**, Massachusetts Institute of Technology, Cambridge, MA
April 4-5, 1989	**Computers in Diagnostic Radiology (IPSM)**, Newcastle-upon-Tyne, UK. Contact: Mr. K. Faulkner, Chairman of the Diagnostic Radiology Topic Group, Regional Medical Phyics Department, Newcastle General Hospital, Newcaste-upon-Tyne, UK.
April 4-5, 1989	**In-Vitro Toxicology: New Directions**, Johns Hopkins School of Hygiene and Public Health, Baltimore, MD. Contact: Program Coordinator, Office of Continuing Education, Turner 22, 720 Rutland Avenue, Baltimore, MD 21205 (301) 955-2959.
April 5-7, 1989	**Portal Imaging (AAPM)**, Las Vegas, NV. Contact: Dr. N. A. Baily, Department of Radiology, M-010, University of California at San Diego, LaJolla, CA 92093.
April 11-15, 1989	**15th L.H. Gray Conference on the Radiobiology of Human Cells and Tissues**, Canterbury, England. Contact: Dr. G. G. Steel, Radiotherapy Research Unit, The Institute of Cancer Research, Clifton Avenue, Sutton, Surrey SM2 5PX, UK.
April 12-15, 1989	**Strategies in Cancer Medical Therapy: Biological Bases and Clinical Implications**, Rimini, Italy. Contact: Dr. Ruggero Ridolfi, Oncology Department, Ospedale Pierantoni, Via Forlanini, 47100 Forli, Italy.

Major Upcoming Events (continued)

April 14-15, 1989	**National Melanoma Conference**, Sir Francis Drake Hotel, San Francisco, CA. Contact: Northern California Cancer Center and the Melanoma Foundation. (415)595-2704: within California, (800) 222-8882: outside California.
April 15-19, 1989	**American Radium Society**, Stouffer Grand Beach Resort, St. Thomas, U.S. Virgin Islands. Contact: Suzanne Bohn, Administrative Director, American Radium Society, 1101 Market Street, 14th Floor, Philadelphia, PA 19107 (215) 574-3179.
April 17-19, 1989	**Oral Complications of Cancer Therapies: Diagnosis, Prevention, and Treatment**, NIH Clinical Center, Bethesda, MD. NIH Consensus Development Converence. Contact: Kathleen Edmunds, Prospect Associates, Suite 500, 1801 Rockville Pike, Rockville, MD 20852 (301) 468-MEET.
April 18-21, 1989	**International Symposium on Tissue Characterization in MRI**, Wiesbaden, German. Contact: Dr. G. Bielken, Tissue Characterization in MRI, Deutsche Klinik fur Diagnostik, Ankammallee 33, D-6200 Wiesbaden, F.R.G.
April 20-21, 1989	PBF/BNCT Advisory Committee meeting to review Brain Tumor Program status and Melanoma Program expansion, Idaho Falls, ID
April 21-22, 1989	**Cancer Management Course**, Virginia Mason Medical Center, Seattle, WA. Contact: Phillip Jolly, M.D., F.A.C.S., Cancer Department, American College of Surgeons, 55 E. Erie Street, Chicago, IL 60611 (312) 664-4050.
April 30-May 10, 1989	**Molecular Basis of Cell Growth Regulation**, Mallorca, Spain. Contact: Dr. Mariano Barbacid, Department of Molecular Biology, Squibb Institute for Medical Research, P.O. Box 400, Princeton, NJ 08543.
May 7-10, 1989	**7th International Symposium: Radionuclides in Nephro-Urology**, Sponsored by the International Society of Nephrology and American Society of Hypertension), Williamsburg, VA

Major Upcoming Events (continued)

May 8-12, 1989	**Nuclear Medicine Computers - Advanced**, Amsterdam, The Netherlands. Contact: Ms. E. Busemann-Sokole, Department of Nuclear Medicine, Amsterdam Academic Medical Center, Meibergdreit 9, 1105A2, Amsterdam Zuidoost, The Netherlands.
May 15-17, 1989	**Noninvasive Vascular Diagnostic Techniques**, Southampton, UK. Contact: Mr. K. N. Humphries, Medical Ultrasound Courses, 10 Swale Drive, Woodland, park, Chandler's Ford, Hants, UK.
May 16-17, 1989	**Frontiers in Cancer Research**, New York. Contact: Julie Beaver, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, NY 10021 (212) 639-3573.
May 19-24, 1989	**American Society of Neuroradiology**, Orlando, FL
May 21-23, 1989	**Molecular Events in Mutation and Cancer**, Tiburon, CA. Third AACR Special Conference in Cancer Research. Participation is by application only. March 15 is the deadline for applications. For copies of the application form, contact AACR, 530 Walnut Street, 10th Floor, Philadelphia, PA 19106 (215) 440-9300.
May 21-26, 1989	10th **Symposium on Microdosimetry**, Rome, Italy. Contact: Dr. J. Booz, Institut fur Medizin, Kernforschungsaniage Julich, Postfach 1913, D-5170 Julich 1, F.R.G.
May 24, 1989	**Nuclear Medicine: Work in Progress**, London, England. Contact: Professor P. J. Eli, Institute of Nuclear Medicine, Middlesex Hospital, Mortimer Street, London, W1, UK.
May 24-27, 1989	**American Association for Cancer Research (AACR) Annual Meeting**, San Francisco, CA. Advance Registration available until March 31. Contact: AACR, 530 Walnut Street, 10th Floor, Philadelphia, PA 19106 (215) 440-9300.

Major Upcoming Events (continued)

May 28-31, 1989	**Molecular Aspects of Growth Control: Joint AACR/Japanese Cancer Association Meeting**, Sheraton Waikiki Hotel, Honolulu, HI. Contact: AACR, 530 Walnut Street, 10th Floor, Philadelphia, PA 19106 (215) 440-9300.
Jun 13-16, 1989	**36th Annual Meeting Society of Nuclear Medicine**, New Orleans, LA. Contact: The Society of Nuclear Medicine, Education and Meetings Department, 136 Madison Avenue, New York, NY 10016-6760.
Jun 20-23, 1989	**International Symposium on In-Vivo Body Composition Studies**, Toronto, Canada. Contact: Dr. J. E. Harrison or Dr. K. G. McNeill, Room 7326, Medical Sciences Building, University of Toronto, Toronto, Ontario M55 1A8, Canada
June 27-July 1, 1989	**Oncogenes**, Frederick, MD. Fifth annual meeting on oncogenes sponsored by Foundation for Advanced Cancer Studies. Contact: Margaret Fanning, FACS, P.O. Box 249, Libertytown, MD 21762 (301) 898-9266.
June 25-28, 1989	**CAR '89 Computer Assisted Radiology**, Berlin. Contact: CAR '89, Heinze U. Lemke, Institute for Technical Computer Science, Technical University, Berlin, Sekr. CG/FR 3-3, Franlinstr. 28-29, D-1000, Berlin 10, F.R.G.
July 1-4, 1989	**International Congress on Radiation Oncology**, Paris, France. Contact: American Society for Therapeutic Radiology and Oncology, 1101 Market Street, 14th Floor, Philadelphia, PA 19107-2990.
July 18-20, 1989	**Third Conference on Image Processing and Its Applications (IEE)**, Warwick, UK. Contact: IEE Secretariat, The Institution of Electrical Engineers, Savoy Place,London WC2R OBL, UK.
Jul 23-27, 1989	**Joint Meeting of the American Association of Physicists in Medicine (AAPM) with the Radiological Society of North America**, Memphis, TN

Major Upcoming Events (continued)

Aug 29-1 Sep 1989	**Vth Mediterranean Conference on Medical and Biological Engineering**, Patras, Greece. Contact: Dr. G. Nikiforidis, Department of Medical Physics, University of Patras, 26500 Patras, Greece.
October 1-6, 1989	**American Society for Therapeutic Radiology and Oncology**, San Francisco, CA. Contact: ASTRO, 1101 Market Street, 14th Floor, Philadelphia, PA 19107-2990.
October 16-21, 1989	**31st Annual Meeting American Society for Therapeutic Radiology and Oncology**, Los Angeles, CA. Contact: ASTRO, 925 Chestnut Street, Philadelphia, PA 19107.
October 19-20, 1989	**Midwest Regional Oncology Conference**, Kansas City, MO. Contact: Beth Paul (800) 451-3182.
Oct. 30-Nov. 1, 1989	**International Conference on Nuclear Technology in Medicine (INE)**, Stratford upon Avon, UK. Contact: Conference Secretary, Institution of Nuclear Engineers, Allan House, 1 Penerley Road, London 5E6 2LQ, UK.
October, 1989	**Western Society of Neuroradiology**, (date and place to be determined)
November 5-8, 1989	**13th Annual Symposium on Computer Applications in Medical Care**, Washington, D.C. Contact: The George Washington University Medical Center, Office of Continuing Education, 2300 K Street NW, Washington, D.C.
November 12-15, 1989	**New Approaches to Problems in Radiation Oncology: Applications of Molecular Biology**, Tucson, AZ. Deadline for poster session abstracts is August 15. Contact: Mary Humphrey, Conference Coordinator, Arizona Cancer Center (602) 626-2276.
November 12-17, 1989	**Joint Meeting (AAPM) Rad. Society of North America**, Chicago, IL. Contact: AAPM Executive Officer, 335 East 45th Street, New York, NY 10017.

Major Upcoming Events (continued)

April 8-12, 1990	**38th Annual Meeting Radiation Research Society**, New Orleans, LA. Contact: Ms. M. Keiser, Radiation Research Society, 1101 Market Street, 14th Floor, Philadelphia, PA 19107.
Jul 7-12, 1990	**9th International Congress of Radiation Research**, Toronto, Canada. Contact: Ms. M. Keiser, Radiation Research Society, 1101 market Street, 14th Floor, Philadelphia, PA 19107.
Aug 5-9, 1990	**32nd Annual Meeting (AAPM)**, St. Louis, MO. Contact: AAPM Executive Officer, 335 East 45th Street, New York, NY 10017.
Aug 27-31, 1990	**V World Congress, World Federation of Nuclear Medicine and Biology**, Montreal, Canada
November 4-7, 1990	**14th Symposium on Computer Applications in Medical Care**, Washington, D.C. Contact: The George Washington University Medical Center, Office of Continuing Education, 2300 K Street NW, Washington, D.C.