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INEL BNCT PROGRAM

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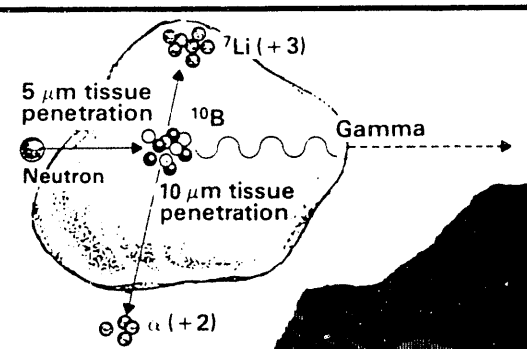

BULLETIN

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Bulletin

Published by the INEL BNCT Program - Arlene L. Ackermann, Editor

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Introduction

This Bulletin presents a summary of accomplishments and highlights in the Idaho National Engineering Laboratory's (INEL) Boron Neutron Capture Therapy (BNCT) Program for August 1991. This bulletin includes information on the brain tumor and melanoma research programs, Power Burst Facility (PBF) technical support and modifications, PBF operations, and updates to the animal data charts.

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1. Project 1: Supporting Technology Development

Task 1: Gross Boron Analysis

Both INEL ICP-AES instruments are now fully operational and the backlog of samples for analysis has been considerably reduced.

Task 2: Borocaptate Sodium (BSH) Purity Determination

A recent shipment of natural BSH from Callery Chemical was found to contain a relatively high weight percent of BSSO. It was decided the compound could still be used for terminal case studies in the canine project.

Task 3: Active Form Identification

Experiments are ongoing to confirm previous BSH to albumin binding data using equilibrium dialysis. ICP-AES analytical results for these experiments are under analysis.

Task 4: Subcellular Analytical Development

Cellulose nitrate films from the EC-BNCT and older types of cellulose nitrate films are being analyzed for use in determining the distribution of boron in the dog brain.

Task 5: Noninvasive Boron Quantification

The MRI system at the UofU is now fully functional for boron imaging. Two boron imaging studies have been completed. Calibration studies will take place shortly and progress is being made to overlay the boron image with the proton image. Permission to conduct pharmacokinetic studies at NWI should be received in September 1991. Boron MRI phantom studies at Sanford show there is an approximate linear relationship between the MR signal and the boron concentration above 100 ppm.

Task 6: Measurement Dosimetry

Dosimetry support was provided for eight dog irradiations at BMRR during August 1991. Preliminary analysis on the neutron characterization measurements made by INEL researchers at HB11 in Petten, The Netherlands, shows a total neutron flux at full reactor power at approximately one-third of what was initially expected. Preliminary data on peak thermal flux and maximum gamma dose rate at Petten have also been produced.

Evaluation of the ORSU reactor thermal column continues. Attempts are being made to reduce gamma fields by a factor of 10 using lead shielding.

Task 7: Analytical Dosimetry

The bnct_edit module was used to reconstruct a three-dimensional model of a human Glioblastoma patient directly for medical images. The software capability to easily position the beam at any angle and distance from the patient was shown. Results will be presented in Petten.

Sterility tests of the microbeam facility at PNL have been conducted, successfully identifying the source of the contamination problems in the open culture vessels. Researchers at PNL are also actively refining cell culture growth techniques for the transformed endothelial cell line (SVEC4-10) provided by Dr. James O'Rear at UCLA. A frozen ampoule of bovine endothelial cells was also provided by WSU researchers.

2. Project 2: Treatment Protocol Development
Task 1: Large Animal Studies

Several new dogs with spontaneously-occurring brain tumors have been entered into the project. Updates on those dogs already in the project are provided within this Bulletin. Four dogs without boron, two dogs with 50 ppm of boron, and one dog with 100 ppm of boron were irradiated at BMRR during the month.

Task 2: Pituitary Tumor Treatment Evaluation Studies

Preparations continue in preparing the reactor facilities at ORSU for planned *in-vitro* studies. Preliminary binding studies carried out on AtT-20 cell membrane preps suggest that an excellent immunogen for the production of monoclonal antibodies against the CRH receptor in BALB/C mice has been produced.

3. Project 3: Human Pharmacokinetics

The first successful MRI of the brain of a dog infused with natural BSH has been completed by INEL and UofU researchers (see Project 1, Task 5).

4. Project 4: Drug Interaction and Toxicity

This contract is still in negotiation with ISU.

B. MELANOMA RESEARCH

1. Project 1: Boron Localization Screening

   Liposome BNCT compounds screening has begun with 48 BDF mice at WSU. Tissue samples from multiple time points will be sent to INEL for boron analysis.

2. Project 2: Biodistribution, Pharmacology, and Toxicity of Boron Delivery Agents

   No reportable activity this month.

3. Project 3: Large Animal Model Studies

   Patients for these studies are being identified.

4. Project 4: Melanoma Detection and Boron Quantification by Scintigraphy

   Large animal studies are on hold pending results from small animal studies.

5. Project 5: Boronated Low Density Lipoproteins and Amino Acid Development and Evaluation

   Prompt gamma analyses have permitted further detailed studies of low-density lipoprotein samples from UCSF. Unexpected problems have developed in the ICP-AES analytical process of low-density lipoproteins and direct comparison with prompt gamma results is not yet possible. Good progress has been made in stereospecific carboranyl alanine synthesis.

6. Project 6: Boronated Liposome Development and Evaluation

   Researchers at UCLA have successfully encapsulated $Na_4B_{20}H_{17}OH \cdot 3H_2O$ into liposomes. This compound was sent to researchers at WSU for murine experiments using a melanoma tumor line (see Project 1).

C. ADMINISTRATION

A memo of understanding has been signed by the Vice-President of Interdisciplinary Programs for GIT. The memo provides the basis for GIT and INEL engaging in a joint endeavor to evaluate BNCT using the GTRR.

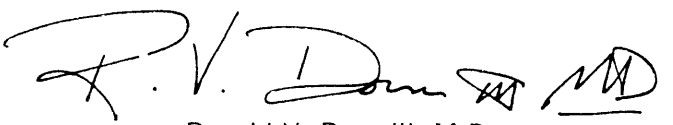
The U. S. Department of Commerce, Export Control Division, has approved the release of the dose-planning software requested by the EC-BNCT.

The DOE-ER peer review of the INEL BNCT Program, scheduled for September 11-12, 1991, was "postponed" pending "major program redirection."

Several INEL BNCT Program researchers will present papers at the International Workshop and Plenary Meeting of the ECBNCT, "Towards Clinical Trials of Glioma with BNCT, September 18-20, 1991, at Petten, The Netherlands.

D. PBF TECHNICAL SUPPORT AND OPERATIONS

Selection of work packages for completion that are applicable to both inactivation and the BNCT Program has begun.



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

A. BRAIN TUMOR RESEARCH

Project 1: Supporting Technology Development

Task 1: Gross Boron Analysis

Samples received	377
Samples prepared for analysis	~210
Samples analyzed	~564
Backlog:	
Awaiting preparation	~335
Prepared, awaiting analysis	~202

Both INEL inductively coupled plasma-atomic emission spectrometer (ICP-AES) instruments are now fully operational. Samples, received from Washington State University (WSU) from mice injected with boron-containing liposomes during the month, are undergoing analysis. Samples analyzed were from Project 1, Task 3 and dogs from the studies at WSU.

Task 2: Borocaptate Sodium (BSH) Purity Determination

The shipment of 30 grams natural BSH (BNCT-320) from Callery Chemical was analyzed and found to have a relatively high oxidized dimer (BSSO) content at 0.56 weight percent (wt%) (specification is < 0.4%). The dimer (BSS) content was only 0.23 wt% (specification is < 2%). It was concluded that the compound could still be used for terminal case studies in the canine program.

Task 3: Biochemistry of BSH and Its Oxidation Products

Experiments to confirm the previous BSH to albumin binding data using equilibrium dialysis were continued using whole-dog plasma and BSH to determine the major binding protein fractions. ICP-AES analytical results for many of the experiments have been received and data reduction and analysis are proceeding. High performance liquid chromatography (HPLC) procedures to separate the major molecular weight fractions of serum proteins are being set up to determine the fractions of these proteins with associated boron compounds. Some new nuclear magnetic resonance (NMR) data was also obtained concerning competitive binding of BSH and other anions with serum albumin.

Task 4: Subcellular Analytical Development

Task 4A: Secondary Ion Mass Spectrometry (SIMS)

No samples were submitted for analysis this month.

Task 4B: Sputter-Initiated Resonance Ionization Spectroscopy (SIRIS)

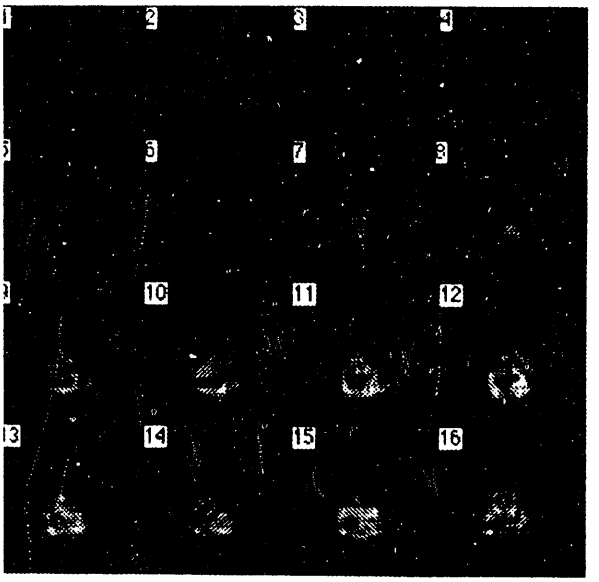
No samples were submitted for analysis this month.

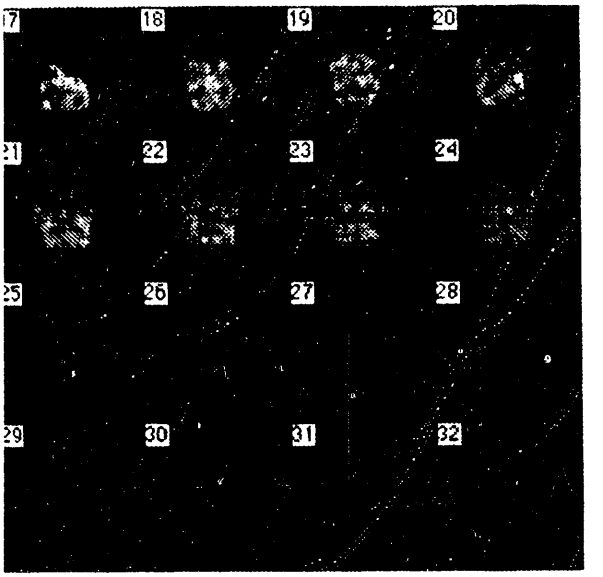
Task 4C: Alpha Track-Etch

Cellulose nitrate films from the European Collaboration on Boron Neutron Capture Therapy (ECBNCT) and dog brain from WSU have been received by Idaho State University (ISU) researchers. These films, as well as older types of cellulose nitrate films, are being analyzed for use in determining the distribution of boron in the dog brain.

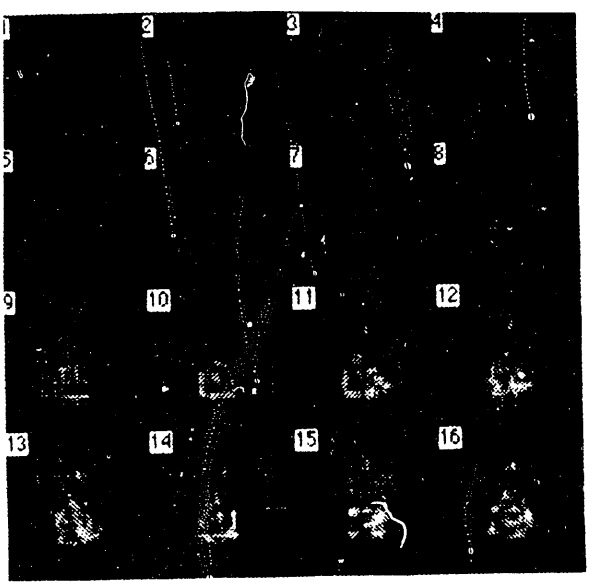
Task 5: Noninvasive Boron Quantification

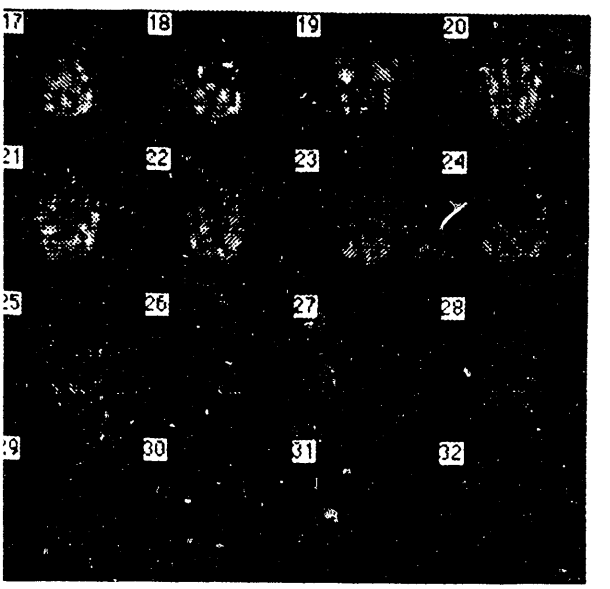
University of Utah (UofU): The magnetic resonance imaging (MRI) system at UofU is now fully functional for boron imaging. Two boron imaging studies have been completed. The first study, utilizing BSH/bovine serum albumin (BSA) phantoms, was used to check the performance of the system. Four BSH/BSA phantoms, varying from 100-500 ppm, were all visible. The second study was conducted with this configuration on a 19-kg, nontumor dog. An infusion of 100 mg boron/kg through the saphenous vein was performed over a one-hour period. When the boron MR signal peaked (five minutes after the termination of the infusion), a projection reconstruction scan was performed (Figures 1a and 1b). Another series was obtained 30 minutes later. In both cases, 32 slices of a 32 x 32 pixel matrix were acquired over a field of view of 24 cm. Scanning time was 8 minutes and 28 seconds (Figures 2a and 2b).





Figures 1a and 1b. Scans taken 10 minutes after end of IV infusion (0.75 cm voxel size).





Figures 2a and 2b. Second scans taken 30 minutes after Figures 1a and 1b.

The second study was conducted primarily to check the ability to coordinate efforts between university animal services, the MRI center, Project 3 researchers, and Project 1 Task 2 researchers. A complete pharmacokinetic study was not performed on this dog. Further studies will concentrate on calibrating MR data with absolute measurement of boron in tissue obtained by ICP-AES. Progress is also being made to overlay the boron image with a proton image.

Northwest Imaging, Inc. (NWI): The process of obtaining permission from GE to turn spectroscopy on at the NWI site requires additional guarantees, imposed by the Food and Drug Administration (FDA), be negotiated. This has slowed the expected initiation of spectroscopy, but the requirements are being met and permission to conduct pharmacokinetic studies should be received from GE in September 1991.

Stanford University: The projection reconstruction scanning techniques developed at Stanford were used to conduct a boron phantom study on Stanford's MRI system. A series of phantoms containing a mixture of different BSH concentrations and 4% by weight bovine serum albumin (BSA) were used to show there is an approximate linear relationship between the MR signal and the boron concentration above 100 ppm. Below 100 ppm, the binding characteristic between BSH and BSA is not linear, but is continuous and predictable (Figure 3). These results are being submitted in a paper to *The Journal of Magnetic Resonance in Imaging*.

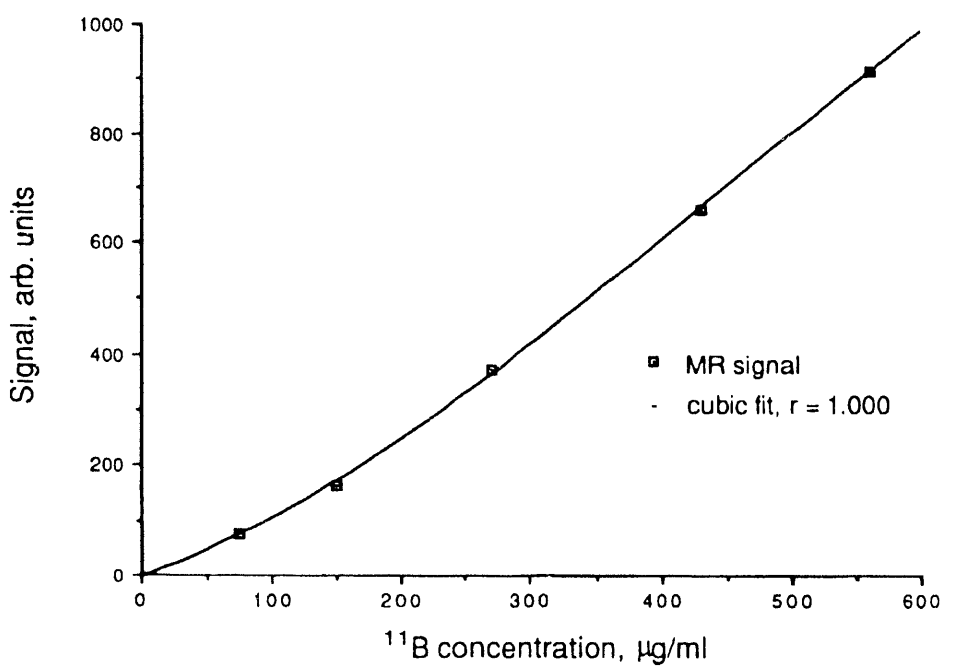


Figure 3. Binding characteristics between BSH and BSA.

Task 6: Measurement Dosimetry

Dosimetry support was provided for: (1) four dog irradiations (three dose-tolerance, one spontaneous tumor) August 8-9, 1991, and (2) four dose-tolerance dog irradiations August 22-23, 1991 at the Brookhaven Medical Research Reactor (BMRR). A fifth dose-tolerance dog was scheduled for August 8-9, 1991, but because of reactor time limitations the irradiation could not be accommodated. The fifth dog was again scheduled for August 22-23, 1991, but could not be completed as BMRR was shut down because of a problem in the secondary cooling system.

ECBNCT/Petten. A preliminary analysis has been performed on the neutron characterization measurements made on July 1-5, 1991 by INEL researchers at the HB11 epithermal-neutron beam at the High Flux Reactor (HFR) in Petten, The Netherlands. The total neutron flux at full reactor power (45 MW) is $4.3E+08$ n/cm^2 • sec. This is approximately one-third of what the Petten staff had expected. The fast-neutron dose rate from the INEL measurements is 1.65 Gy/hr at this power. This fast-neutron dose is consistent with the proton-recoil measurements reported by AEA Technology, Harwell, UK. The measured values are about 80% of the expected dose, based on the design calculations performed by the ECBNCT staff.

As mentioned last month, the beagle phantom results at HB11 indicate a peak thermal flux of about 70% of the BMRR results in the same phantom with the 7.6-cm circular beam aperture. Similarly, the HB11 peak thermal flux is approximately 50% that of the BMRR value for the cylindrical phantom.

The readout of the thermoluminescent dosimeters (TLDs) irradiated at Petten have been completed. These results indicate that at full power the maximum gamma dose rate is 210 cGy/hr in the beagle phantom and 260 cGy/hr in the cylindrical phantom. The comparable BMRR values using the 7.6-cm circular aperture are 420 and 400 cGy/hr, respectively. Some difficulties have been encountered in getting p-factors for the boron spheres (with copper foils) used in the Petten measurements. The p-factors for the other irradiations were completed earlier. It is expected that the problems connected with the boron spheres will be overcome during the next two reporting periods. A report has been sent to Petten for review.

Oregon State University (ORSU): The ORSU reactor thermal column is being evaluated for performing cell culture irradiations to support the BNCT research at Oregon Health Sciences University (OHSU). In June 1991, INEL personnel performed fast-neutron flux measurements at this reactor and the results were provided in the June report. As a followup, TLD-400 measurements were made on July 1, 1991 to confirm earlier TLD measurements made by ORSU. The results for the TLD-400 gamma measurements have now been obtained and are consistent with those obtained by ORSU. The thermal column gamma fields fall off exponentially as a function of distance from the core. The values range from 15 Gy/hour at 2.5 cm from the inside end, to 1.8 Gy/hr at 125 cm. ORSU is continuing to make TLD measurements using TLD-400, TLD-600, and TLD-700 dosimeters. They are attempting to reduce gamma fields by a factor of ten using lead shielding. So far, the gamma fields have been reduced by a factor of about 2, using 10 cm of Pb at the innermost position in the thermal column.

Task 7: Analytical Dosimetry

Task 7A: Dosimetry Software/Alpha 1 Software Development:

The bnct_edit module was used to reconstruct a three-dimensional model of a human Glioblastoma patient directly from medical images. The rtt_MC module was then used to determine detailed flux and dose patterns for two beams, one nearly isotropic and one forward peaked. This was an academic exercise to validate the treatment planning software. After some software modifications, the capability to easily position the beam at any angle and distance from the patient was achieved, a necessary feature for clinical applications. The three-dimensional distributions (i.e., therapeutic gain in the tumor) demonstrated the advantage of the forward-peaked beam and an oblique beam. Results will be presented at the upcoming International Workshop and Plenary Meeting of the ECBNCT in Petten, The Netherlands.

Conversion of the bnct_edit software to X-windows, in collaboration with Montana State University (MSU), is proceeding. Menu and image display systems have been converted and work is currently

proceeding on entering control points into the images. No obstacles to the successful completion of this task have been encountered.

Task 7B: Canine Dosimetry Analysis

Calculations were performed for the tumor dog ("Bessie" #35447-155) that was irradiated August 9, 1991 at BMRR.

Task 7C: Database Management System

Further work on the database tables and data entry screens continues and canine data is being entered. The INFORMIX database management software upgrade for the HP 9000/720 has been installed and the database successfully transferred from the HP 9000/425 to the HP 9000/720 at WSU. Networking between INEL, WSU, MSU, and JRC-Petten is operational and in regular use.

Task 7D: Biophysics/Stochastic Model Development

Sterility Test of Microbeam Facility: Pacific Northwest Laboratories (PNL) researchers conducted an extensive effort to identify sources of contamination associated with the use of open culture vessels in and around the microbeam irradiation apparatus. These efforts demonstrated that the problems occur on the scaffold platform in Building 3746B, rather than with the apparatus itself. A large number of plates were placed both inside and outside the light-tight chamber with their lids removed. The plates were then exposed for extended period (30 minutes to 4½ hours of open exposure), during which time personnel were moving about, the heating/ventilating blowers moved dust around the room, and the doors to the light-tight chamber were briskiy opened and closed. After 14 days incubation (which is adequate to allow most contaminants (fungus and yeasts) to demonstrate their presence) no contamination of any kind was apparent. Subsequently, all plates were exposed to confirm that the medium used was not toxic and that it would indeed successfully support the growth of such fungus and yeast.

PNL researchers have been in contact with Dr. James O'Rear at University of California/Los Angeles (UCLA), and were provided with a sample of the transformed endothelial cell line, SVEC4-10. The samples (not frozen) arrived safely at PNL and were subcultured immediately as directed by Dr. O'Rear. These cells had been maintained in RPMI-1640 medium, a relatively complex medium frequently used for a variety of cell lines. PNL researchers passed the cells in some outdated RPMI-1640 (fresh stock was not available at the time). This was complete medium (i.e., supplemented with serum and antibiotics) and, although it supported the cells, their growth indicated shortcomings that were assumed associated with the medium's age. The cells would grow well if numbers were sufficient, but when they reached confluence they would die and slough off almost immediately, generally within a day or two. Fresh RPMI-1640 powdered medium was prepared and used for the next passage. The growth was not remarkably different. Fortunately, the cultures received from Dr. O'Rear contained adequate numbers of cells, as sufficient numbers had not yet been generated at PNL to freeze reserves; however, the numbers of cells were getting critically low. Two other media were tested and prepared - a basal minimum medium developed by Eagle (BME), which appears to work well with many transformed lines (WSU researchers have been using BMR for similar cultures), and Dulbeccos modification of Eagles minimum essential medium (DMEM), an old favorite that often seems to work when others fail. Although a somewhat hazardous thing to do, the level of antibiotics was also reduced. It was felt that part of the problem might be sensitivity to streptomycin of penicillin. With this passage, the SVEC4-10 cells in DMEM are doing fine. Interestingly, the BMR medium does not appear to support growth of this line at all, even in plates begun at high densities. When growth is adequate, a number of ampoules will be prepared for freezing and a stock reserved to work with.

PNL researchers were provided a frozen ampoule of bovine endothelial cells from WSU researchers. The ampoule arrived intact and was immediately put into the liquid nitrogen storage dewar. These cells represent another endothelial cell line that will be characterized at a later time. WSU researchers attempted to obtain the glioma or glioblastoma cells, but none are currently available. It appears that the individuals working with these cells had merely ordered fresh stock from the American Type Culture Collection (ATCC) as needed and do not reserve their own stock in liquid nitrogen. There are several lines available from ATCC and acquisition of one or more of these is in progress.

Task 7E: Neutron Source Analysis

There was no activity to report this month.

Task 7F: Georgia Institute of Technology Research Reactor (GTRR) Physics Feasibility Study

Dr. David W. Nigg (INEL) has been invited to coauthor a paper with the Dr. Ratib Karam on the proposed GTRR epithermal-beam facility at an International University Reactor Technical Meeting in Indonesia during November 1991.

Project 2: Treatment Protocol Development

Task 1: Large Animal Studies

Spontaneously-Occurring Brain Tumors: "Licorice" Jewkes (#35447-159), a 12-year old female black Dachshund/Cocker cross, was entered into the Program on August 12, 1991 with a history of seizures beginning in December 1990. At four years of age, she had a diagnosis of encephalitis and became blind at that time.

"Niki" Woods (#35447-158), a five-year old female spayed Samoyed, was entered into the Program on August 1, 1991 with a history of seizures. Computed tomography (CT) and MRI evaluation were consistent with a cystic, space-occupying lesion in the left olfactory lobe extending caudally from the region of the cribriform plate. She underwent surgery and the cyst was aspirated for culture and a section taken for histopathology. The diagnosis of both was a granulomatous inflammation. She was placed on antibiotic therapy for a duration of 6-8 weeks and sent home with her owners. She is scheduled for a followup MRI the first two weeks of September 1991.

"Maggie" Peterson (#35447-157), a 10-year old female spayed Border Collie, was entered into the Program on July 17, 1991 with a history of seizure activity. An enchancing mass was observed on CT and MRI scans in the area of the olfactory lobe. The mass appears to extend from the region of the cribriform plate or rostral to the cribriform plate caudally to the region of the optic chiasm. Surgery was performed, but she died of unknown causes the following morning. Histological samples were collected during surgery and the tumor was identified as a meningioma.

"Bessie" Blish (#35447-155), a 12-year old female Retriever cross, was first entered into the Program on June 10, 1991 with a history of sudden onset of seizures. Her owners decided on BCNT and she was treated at BMRR on August 9, 1991. She died three days following treatment. Cause of death was not evident based on gross necropsy or histopathology of major organs. Histological examination of the brain is pending.

"Dudley" Fiset (#35447-151), a six-year old castrated male Golden Retriever, had his six-month checkup at University of California/Davis and passed with flying colors. The CT and MRI did not show any enhancing tumor. The only complaint found was his weight.

"Sugar" Ellsworth (#35447-142), a seven-year old female spayed Boxer, was euthanized last month because of declining neurological status. The histologic findings of the nonbrain tissues were relatively mild and primarily reflect aging changes. Brain histological results are pending.

"Muffy" Lower (#35447-140), a four-year old female spayed Terrier cross, had her six-month checkup. The CT and MRI revealed that the tumor has not changed in size, but she is clinically normal. She has also been taken off prednisone.

"Too Wide" Marshall (#35447-129), a four-year old female Newfoundland cross, has lost a lot of weight and is beginning to snap at people, although she is still running and playing. She is currently under observation for behavioral changes before any further decisions are made.

"Brandy" Hoff (#35447-94), a seven-year old female Golden Retriever, is still doing great.

Normal Tissue Tolerance (Neutron Irradiation): Baseline data collection is completed on the control dogs. Four dogs without boron have undergone epithermal-neutron irradiation at BMRR with a dose of 12.5 Gy. There has been a drop in platelet count and lymphocytes with these dogs, resulting

in a mild thrombocytopenia and lymphopenia. Two dogs with 50 ppm boron were irradiated to a dose of 27 Gy, and one dog with 100 ppm boron was irradiated to a dose of 27 Gy. Arrangements are being made to kennel dogs at Stoneybrook, NY.

Additional BSH (on order, expected September 6) must be received before continuation of the dose-tolerance studies.

Pharmacokinetics:

Samples from "Maggie" Peterson (#35447-157) were sent to INEL for boron analysis. This dog was originally a tumor dog that died following surgery.

The latest changes in the animal chart data from Project 2, Task 1 Large Animal Studies is summarized in Appendix A.

Task 2: Pituitary Tumor Treatment Evaluation Study

The reactor facility at ORSU appears to be adequate for the planned *in-vitro* studies using AtT-20 and GH-3 cells. Dr. Stephen Binney, the ORSU lead reseacher has determined that 10 cm of lead in the reactor stringer port will effectively decrease the gamma from 1300 to 600 rads at 100 kW reactor power in a ten-minute experimental run. The estimated flux has been calculated to be 5 x 10^{10} neutrons per square centimeter per second or a fluence of 3 x 10^{13}. The gamma rad-to-thermal neutron fluence ratio has been estimated to be 2 x 10^{-11}, approximately four-fold better than the anticipated 10^{-10}. All measurements provide further support that the ORSU reactor will provide an excellent environment for the *in-vitro* and *in-vivo* experiments.

Preliminary binding studies carried out on AtT-20 cell membrane preps run over a corticotropin releasing hormone (CRH) affinity column suggest that a "purified" receptor preparation was obtained and that this prep should be an excellent immunogen for the production of monoclonal antibodies against the CRH receptor in BALB/C mice. CRH stimulation tests have been run on AtT-20 cells. The preliminary results of this first pilot experiment indicate that miniaturization of the *in-vitro* stimulation tests, in terms of the number of cells needed to obtain adequate ACTH release into the culture media, is achievable. This will be important, in terms of tissue conservation, in the stimulation studies carried out in human pituitary tumor cells.

Task 3: Physiological Response Evaluation and Interdiction

The contract with the University of Rochester is not yet finalized.

Project 3: Human Pharmacokinetics

The first successful MRI of the brain of a dog infused with natural BSH has been completed (reported under Project 1, Task 5) by INEL and UofU researchers.

A meeting was held between Project 3 researchers and UofU medical personnel to outline the objectives of this task. Meeting participants included neurosurgeons, animal service personnel, and Medical Imaging Research Laboratory personnel. Dr. M. Peter Heilbrun, chief of neurosurgery, suggested that the use of a glio model from the University of Maryland be investigated rather than spontaneous tumor dogs. This meeting will be held each month at UofU to facilitate interdepartmental communications at UofU.

Project 4: Drug Interaction and Toxicity

This contract is still in negotiation with ISU.

B. MELANOMA RESEARCH

Project 1: Boron Localization Screening

WSU researchers have investigated animal suppliers that carry genetically immunodeficient animals. According to the National Academy of Sciences and several calls to various animal suppliers, only two U.S. companies carry immunodeficient animals: Harlan Sprague Dawley (Indianapolis, IN) and Taconic Farms (Germantown, NY). The only immunodeficient animals available, besides mice, are rats. There are no immunodeficient animals (rabbits, guinea pigs, hamsters) commercially available, and availability of immunodeficient rats is poor.

Screening of Liposome BNCT Compounds: WSU researchers injected 48 BDF mice subcutaneously into the dorsal hip with 2 x 10^6 viable B16-BL6 murine melanoma cells in a volume of 0.2 mL of saline solution. Tumors were evident and were approximately 1.0 cm in diameter by August 26, 1991. The mice were then inoculated intravenously into the tail vein with 200 μL of the liposome compound ($Na_4B_{20}H_{17}OH$ in 9% lactose, 5 mM phosphate buffer) obtained from UCLA researchers. Control mice were inoculated with 200 μL of saline solution and tissues sampled (6-8 mice per time point) at 0 (control), 6, 12, 18, 24, and 36 hours post inoculation, frozen, and sent to INEL for boron analysis. Tissues to be sampled include tumor, liver, spleen, brain, kidney, skin, skeletal muscle, and blood.

Project 2: Biodistribution, Pharmacology, and Toxicity of Boron Delivery Agents

There was no activity to report this month.

Project 3: Large Animal Model Studies

Potential patients for large animal studies continue to be identified. There was no other activity to report this month.

Project 4: Melanoma Detection and Boron Quantification by Scintigraphy

Large animal work is on hold until preliminary results with radiolabeled boron compounds are available from the small animal studies.

Project 5: Boronated Low Density Lipoproteins and Amino Acid Development and Evaluation

Prompt gamma boron analyses have been obtained on a series of low-density lipoprotein (LDL) samples loaded with a variety of simple alkyl and aryl closo carboranes by the University of California at San Francisco (UCSF) researchers. In general, these are similar to values obtained previously by this method. The trend of these results suggests that: (1) simple carboranes (such as ortho, meta, methyl, and even phenyl) do not reconstitute well, and (2) longer chain saturated (hexyl) and unsaturated (alkyl and butenyl) derivatives can be successfully and efficiently reconstituted into LDLs. A significant lowering of the average protein content of reconstituted solutions was also observed, which, in most cases, paralleled reconstituted efficiencies. Even with allyl carborane (the best case), the average protein content of the reconstituted solution was only 50-60% of what is obtained using elaidyl carborane carboxylate as the boron source.

Direct comparison of prompt gamma and ICP-AES boron concentrations is not yet possible, and it appears that either the LDL matrix or the stable and very hydrophobic nature of the carboranes used causes unexpected problems in the ICP-AES analytical process. A more detailed report will be prepared for September 1991.

The stereospecific carboranyl alanine synthesis is moving ahead rapidly. UCSF researchers have found that $TiCl_4$ is an effective Lewis acid replacement for di-n-butylboron triflate. Excellent yields have been obtained with enantiomeric with excesses of 93:7 or better. It is planned to repeat, optimize, and scale-up this procedure. If successful, D or L carboranyl alanine in 60-70% overall yield could be produced.

Project 6: Boronated Liposome Development and Evaluation

Researchers at UCLA have encapsulated $Na_4B_{20}H_{17}OH \cdot 3H_2O$ into liposomes. This compound is one of the hydrolysis products of the octadecahydroicosoborate(2-) photoisomer (i-$B_{20}H_{18}^{2-}$). The liposomes were sent to researchers at WSU (reported under Project 1) for murine experiments using a melanoma tumor line. Boron analysis of the tissue samples from this experiment is in progress at INEL. A separate batch of liposomes containing $K_4B_{20}H_{17}OH \cdot 3H_2O$ is being prepared and will be sent to Vestar, Inc. for murine experiments utilizing the EMT6 tumor line. Results from this experiment will allow the comparison of the results from the murine experiment with data obtained previously with EMT6 tumors.

Development of the synthesis and chemistry of new boron species as candidates for liposomal delivery is continuing. The synthetic route to obtain the amine derivatives of $B_{20}H_{18}^{2-}$, $B_{20}H_{17}NH_3^{3-}$ has been developed. Current efforts are centered on purification of this species and the expansion of this synthetic route to obtain additional amine derivatives $B_{20}H_{17}NH_2R^{3-}$. Investigations of the chemistry of $B_{10}H_{13}CO_2H^{2-}$, and $B_{10}H_9NCO^{2-}$ are continuing. All three of these compounds have recently been characterized by single crystal x-ray diffraction.

C. ADMINISTRATION

Georgia Tech Research Reactor (GTRR): A Memo of Understanding was signed by the Vice President of Interdisciplinary Programs for Georgia Institute of Technology (GIT). The Memo provides the basis for GIT and INEL engaging in a joint endeavor to evaluate BNCT using the GTRR. The Memo is awaiting signature by EG&G officials.

European Collaboration on Boron Neutron Capture Therapy (ECBNCT)/Petten: The U.S. Department of Commerce, Export Control Division, has approved the release of the dose-planning software requested by Dr. Detlef Gabel, European Collaboration on Boron Neutron Capture Therapy. This software will be exchanged for the European BSH human pharmacokinetic data. DOE-HQ Legal Office is now reviewing the agreement.

Budget: Congressional subcommittee actions the last week of July 1991 left some confusion as to the fate of the $7.5 M authorized by Congress in FY-91. The Joint Conference Committee reprogrammed the funds for BNCT research, making the funding unavailable for PBF modifications, but did not specify INEL BNCT research. The plan of Senate supporters to hardwire the funds to INEL when the bill reached the Senate floor was not successful. At this time, the INEL BNCT research budget is unknown for FY-92. DOE-HQ notified INEL BNCT Program management on August 14, 1991 that the $7.5 M reprogrammed by the House and Joint Conference Committee for FY-92 BNCT research is Idaho money.

DOE-ER Peer Review: The DOE-ER peer review of the INEL BNCT Program was scheduled for September 11-12, 1991. During the week of August 5, 1991, DOE-ER requested that the Program Plans for the INEL BNCT Brain Tumor and Melanoma Research Programs be updated for the peer review. The review of the Program would be based on these plans and supporting references. On August 29, 1991, DOE-ER officially postponed the peer review pending "major program redirection."

Miscellaneous: Dr. Greg Storr (ANSTO assignee) has reported for work and is working on the GTRR filter design, benchmarking, and validation of the treatment planning system, and calculations for supporting experimental dosimetry.

Papers, Meetings, Etc.: Dr. David W. Nigg (INEL) will present an invited paper, coauthored by F. J. Wheeler, D. E. Wessol, and C. A. Atkinson (INEL) on "Radiation Physics Aspects of Boron Neutron Capture Therapy" at the upcoming American Nuclear Society topical meeting on New Horizons in Radiation Protection and Shielding, Pasco, WA, April 26-30, 1992.

Floyd Wheeler (INEL) was invited to be a guest speaker at the International Workshop and Plenary Meeting of the European Collaboration on Boron Neutron Capture Therapy, "Towards Clinical Trials of Glioma with BNCT," September 18-20, 1991 at Petten, The Netherlands. His subject is "Dose Calculations Based on Image Reconstructions." Dr. Ronald V. Dorn (INEL/MSTI) will also give an oral presentation at this meeting. Dr. Y. D. Harker and Cecilia Amaro (INEL) have also submitted a paper for presentation at this meeting, entitled "Neutron and Gamma Measurements at the High Flux Reactor HB11 Beam."

Floyd Wheeler (INEL) was invited to present a paper at the International Workshop on NCT Dosimetry, at Massachusetts Institute of Technology, Cambridge, MA in September 1991.

Dr. G. H. Glover, J. M. Pauly, (Stanford) and K. M. Bradshaw (INEL) have submitted a paper, "Imaging ^{11}B with Three-Dimensional Projection Reconstruction," to the *Journal of Magnetic Resonance in Imaging*.

Dr. D. Robert Lu and Corey Munro (ISU) submitted a paper, "Quantitative Analysis of Mercaptoundecahydrododecaborate by Fourier Transform Infrared Spectroscopy," to *Pharmaceutical Research* for publication.

Presentations: A BNCT seminar was given August 22, 1991, by Dr. Jacquelyn Yanch (MIT), "Accelerator-Based Neutron Sources for BNCT," and Ms. Jean Moran (MIT/INEL summer student), "A Benchmark Radiation Dose Distribution Analysis for BNCT."

D. PBF TECHNICAL SUPPORT AND OPERATIONS

Work packages for tasks that must be completed if PBF is prepared for BNCT or decontamination and decommissioning (D&D) are being updated by Power Reactor Programs Reactor Safety Analysis personnel with support from EG&G Idaho Engineering Department. The updating involves rescheduling and resource loading for work packages that were prepared early in calendar year 1991. These packages include: (1) safety analysis report review and edit, (2) loss of coolant accident (LOCA) pipe removal and annulus cleanup, (3) raw water system upgrade and backflow preventer installation, (4) building temperature monitoring system installation, and (5) reactor vessel nozzle weld mockup.

Inspection of the PBF canal fuel storage racks for structural integrity and cadmium content continues. Training of the reactor fuel handlers on the Detailed Operating Procedure (DOP) was completed by the EG&G Reactor Training Group and the engineer was responsible for the DOP. An 80-gram Pu/Be neutron source for the cadmium content measurement was transported from the Test Reactor Area to PBF. Moving this source required the generation and approval of a minimal transport plan. A door seal on the large truck door was replaced and a successful building leak test was performed in preparation for fuel movement in the facility. The inspection DOP was started and measurement of the cadmium content in the permanent fuel storage rack was completed. The permanent fuel storage rack will be visually inspected using an underwater television camera before fuel transfer between the permanent and temporary fuel storage racks begins. The fuel rack inspection is scheduled to be completed before the end of September 1991.

Summary cost estimates and abbreviated plans were developed to support a Congressional request to DOE for a four-year BNCT Program. These cost estimates were based on a plan to modify the GTRR and maintain PBF in a condition that would provide latitude for programmatic decisions to complete modifications to PBF based on data from GTRR. These cost estimates were transmitted to DOE-ID.

Preparation of cost estimates for correction of identified deficiencies from the DOE Tiger Team audit was completed. These items are being forwarded for incorporation and prioritization as part of the INEL Corrective Action Plan.

The scheduled preventive maintenance performed in August included: (1) auxiliary air compressor, (2) 5/15-ton overhead crane, (3) hot-waste storage tank transfer pump, (4) control room nitrogen system, (5) constant air monitors, (6) stack gas monitor, (7) chemical treatment pump, (8) plant air compressor, (9) reactor building supply fans, (10) fire doors and extinguishers, and (11) relamping.

Training conducted during August consisted of: (1) PBF hazardous communication for crafts, (2) operations safety meeting, (3) emergency brigade fire hose training, (4) bus driver training, (5) emergency control center communication drill, and (6) abnormal and facility walkthrough examination for shift supervisor.

APPENDIX A

LARGE ANIMAL MODEL STUDIES

SUMMARY OF PATIENT DATA

INEL BNCT CANINE TUMOR TREATMENT STUDY

ANIMAL	SEX/AGE	NAME OF DOG	DIAGNOSIS	BORON DOSE (mg ^{10}B/ kg bw)	DATE	START TIME[1]	DURATION MINUTES[2]	CALCULATED DOSE (cGy)	^{10}B ESTIMATED AVG (ppm)	SURV.	DAYS	DEATH DATE	DEATH CAUSE
35447-79	F/7	"Pugee" Krebs	Astrocytoma[6]	50	07/07/89	375	77.8	1923	18.5	No	348	06/20/90	Urinary Obstruction
35447-80	M/4	"Mugsy" Marshall	Astrocytoma[3]	50	08/07/89	369	78.0	1722	21.6	No	12	08/19/89	Anesthesia
35447-83	M/11	"Rusty" Collins	Meningioma[4]	50	08/25/89	430	68.5	1829	21.4	No	170	02/11/90	Focal Encephalomalacia
35447-87	M/*	"Benji" Williams	Meningioma[6]	50	09/28/89	420	80.3	1653	20.6	No	140	02/14/90	Euthanasia-(recurrent clinical signs)
35447-93	F/6	"Brandy" Grudzinski	Oligodendroglioma[6]	50	10/30/89	310	68.1	1912	24.9	No	300	08/27/90	Neurologic deterioration
35447-94	F/5	"Brandy" Hoff	Meningioma[4]	50	10/25/89	464	86.0	1887	14.3	Yes			
35447-95	M/6	"Godfrey" Beers	Meningioma[6]	50	10/24/89	388	63.3	1743	24.5	No	0.5	10/25/89	Neurologic deterioration
35447-100	F/7	"Juno" Bagley	Meningioma[6]	50	11/30/89	315	73.0	2185	28.9	No	43	01/12/90	Euthanasia
35447-108	F/4	"Trixie" Herklotz	Papilloma[3]	50	02/16/90	225	49.0	1900	51.9(?)	No[5]	(a)	06/??/90	Lost followup
35447-118	F/9	"Scuzzy" Jenkins	Astrocytoma[6]	50	10/19/90	170	75.0	2300	85.3	No	158	03/26/91	Unknown
35447-129	F/6	"Two Wide" Marshall	Choroid plexus papilloma[3]	50	10/18/90	210	116.0	2141	56.9	Yes			
35447-132	M/13	"Sarge" Smith	Meningioma[6]	50	10/19/90	198	164.0	2300	34.5	No	54	12/12/90	Stomach surgery complications (GDV)

[1] Time from start of boron injection to start of irradiation.
[2] Irradiation time in minutes.
[3] Diagnosis from CT and/or MRI scans.
[4] Biopsy confirmed.
[5] Did not improve neurologic status.
[6] Postmortem histopathology report

(a) Dog died sometime week of June 11, 1990, was buried without necropsy, owner did not return messages or communicate with WSU.
* "Benji" Williams age is unknown
GDV = gastric dilatation volvulus

INEL BNCT CANINE TUMOR TREATMENT STUDY

ANIMAL	SEX/AGE	NAME OF DOG	DIAGNOSIS	BORON DOSE (mg ^{10}B/ kg bw)	DATE	START TIME[1]	DURATION MINUTES[2]	CALCULATED DOSE (cGy)	^{10}B ESTIMATED AVG (ppm)	SURV.	DAYS	DEATH DATE	DEATH CAUSE
35447-134	F/8	"Peggy" Cunningham	Meningioma[6]	50	10/29/90	198	190.0	1729	20.6	No	33	12/01/90	Neurological complications
35447-139	M/11	"Hobart" Felder	Meningioma[6]	50	01/22/91	160	83.0	2300	57.5	No	13	02/04/91	Toxic shock[7]
35447-140	F/3	"Muffy" Lower	N/A	50	01/22/91	149	152.0	2300	40.3	Yes			
35447-142	F/6	"Sugar" Ellsworth	Pending	50	01/23/91	168	105.0	2300	44.5	No	181	07/23/91	Euthanasia: brain necrosis
35447-147	M/9	"Bomber" Buck	Malignant meningioma[6]	50	02/07/91	206	132.0	2300	37.1	No	102	05/21/91	Euthanasia: recurrent clinical signs
35447-151	M/6	"Dudley" Fiset	N/A	50	02/28/91	211	69.0	2300	67.6	Yes			
35447-152	M/10	"Zar" Walter	Meningioma[6]	50	03/19/91	204	78.4	2300	60.8	No	99	06/26/91	Euthanasia heart-based tumor (unrelated to meningioma)
35447-155	F/11	"Bessie" Blish	Meningioma[6]	100	08/09/91	202	24.0	2600	101.6	No	3	08/12/91[8]	

[1] Time from start of boron injection to start of irradiation.
[2] Irradiation time in minutes.
[3] Diagnosis from CT and/or MRI scans.
[4] Biopsy confirmed.
[5] Did not improve neurologic status.
[6] Postmortem histopathology report.
[7] Infection in rear leg.
[8] Unidentified at necropsy.

"Penny" Bird, #35447-136: Health deteriorated too quickly for radiation treatment; received boron injection; moved to pharmacokinetics study.

INEL BNCT CANINE PHARMACOKINETIC STUDY
SUMMARY OF PATIENT DATA
BSH INTRAVENOUS INJECTIONS STUDY

ANIMAL	NAME OF DOG	EUTHANASIA DATE	EUTHANASIA MIN[1]	CASE SUMMARY	PATHOLOGY DIAGNOSIS	DOSE (mg/kg)	BLOOD SERUM AND URINE ANALYSIS	TISSUE ANALYSIS	CT UNENH.	CT ENH	MRI UNENH.	MRI ENH
35447-1	"Muffy" Klugh	03/23/87	540	Yes	Pituitary adenoma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-2	"Stashi" Christensen	05/18/87	750	Yes	No tumor/positive boron control	57	Yes	Yes	N/P	N/P	No	No
35447-3	"King" Henry	05/18/87	Control	Yes	No tumor/negative boron control	0	Yes	N/P	N/P	No	No	No
35447-14	"Marsha" Despain	06/30/87	780	Yes	Invasive adenocarcinoma	62	Yes	Yes	Yes	Yes	Yes	Yes
35447-15A	"Amos" Vallangdigham	08/03/87	780	Yes	Invasive nasal carcinoma	59	Yes	Yes	Yes	Yes	Yes	Yes
35447-18	"Slim" Pozzobon	09/14/87	770	Yes	Invasive nasal adenocarcinoma	30	Yes	Yes	Yes	Yes	Yes	Yes
35447-20	"Mischief" Scott	11/02/87	90	Yes	Meningioma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-23	"Rocky" Christensen	11/13/87	780	Yes	Pituitary adenoma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-24	"Mariah" May	11/24/87	720	Yes	Subarachnoid cyst	55	Yes	Yes	Yes	Yes	Yes	Yes
36845-25	"Sandy" Frazier	01/26/88	780	Yes	Meningioma	53	Yes	Yes	Yes	Yes	Yes	Yes
35447-28	"Boots" Belisle	02/22/88	125	Yes	Regional demyelinative disease	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-30	"Sunny" Seeley	03/01/88	420	Yes	Pituitary adenocarcinoma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-32	"Pip" Hahn	02/26/88	410	Yes	Meningioma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-33	"Coco" Pechtel	03/23/88	420	Yes	Nasal adeno carcinoma	56	Yes	Yes	Yes	Yes	Yes	Yes
35447-37	"Tucker" Reeves	04/14/88	420	Yes	No tumor/positive boron control	10	Yes	Yes	N/P	N/P	No	No
35447-39	"Fritts" Coglan	05/02/88	100	Yes	Meningioma	10	Yes	Yes	Yes	Yes	Yes	Yes
35447-40	"Rocky" Underwood	05/03/88	420	Yes	Fungal granuloma	30	Yes	Yes	Yes	Yes	Yes	Yes
35447-43	"Blue" Archer	05/23/88	420	Yes	Diffuse cortical astrocytoma	52	Yes	Yes	N/P	N/P	Yes	Yes
35447-49	"Jenny" Nelson	06/29/88	420	Yes	Diffuse astrocytoma	33	Yes	Yes	Yes	Yes	Yes	Yes
35447-50	"Caesar" Chenoweth	07/13/88	420	Yes	Meningioma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-54	"Licorice" Meyers	08/03/88	410	Yes	No tumor/positive boron control	55	Yes	Yes	Yes	Yes	Yes	Yes

[1] 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

INEL BNCT CANINE PHARMACOKINETIC STUDY
SUMMARY OF PATIENT DATA
BSH INTRAVENOUS INJECTIONS STUDY

ANIMAL	NAME OF DOG	EUTHANASIA DATE	EUTHANASIA MIN[1]	CASE SUMMARY	PATHOLOGY DIAGNOSIS	DOSE (mg/kg)	BLOOD SERUM AND URINE ANALYSIS	TISSUE ANALYSIS	CT UNENH.	CT ENH	MRI UNENH.	MRI ENH
35447-55	"Kelley" Langsston	08/17/88	410	Yes	Diffuse astrocytoma	55	Yes	Yes	No	No	Yes	Yes
35447-57	"Rafferty" Reber	09/01/88	410	Yes	Meningioma (plasmapheresis)	50	Yes	Yes	No	Yes	Yes	Yes
35447-59	"Heidi" Boyer	09/12/88	180	Yes	Meningioma	55	Yes	Yes	No	Yes	Yes	Yes
35447-62	"Chester" Scott	10/09/88	180	Yes	Meningioma	55	Yes	Yes	No	Yes	Yes	Yes
35447-67	"Muffet" Hammel	11/01/88	180	Yes	Astrocytoma	55	Yes	Yes	No	Yes	N/P	N/P
35447-70	"Mac" Meyers	11/15/88	180	Yes	Fibrillary astrocytoma	55	Yes	Yes	No	Yes	Yes	Yes
35447-71	"Jake" Brede	01/04/89	180	Yes	Choroid plexus papilloma	55	Yes	Yes	Yes	Yes	N/P	N/P
35447-72	"Mandy" Ross	02/07/89	495	Yes	Choroid plexus papilloma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-76	"Scotty" Klemm	05/28/89	410	Yes	Protoplasmic astrocytoma	55	Yes	Yes	No	Yes	Yes	Yes
35447-86	"Brutus" Halverson	09/11/89	240	Yes	Pituitary adenocarcinoma	50	Yes	Yes	Yes	Yes	Yes	Yes
35447-88	"Scamper" Brewster	10/10/89	420	Yes	Pituitary adenocarcinoma	55	Yes	Yes	N/P	N/P	Yes	Yes
35447-97	"Kolsa" Joy	12/07/89	420	Yes	No tumor	55	Yes*	Yes	Yes	Yes	Yes	Yes
35447-101	"Ginger" Mott	12/12/89	180	Yes	Choroid plexus papilloma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-104	"Killer" Divine	01/19/90	180	Yes	Choroid plexus papilloma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-117	"Toby" Page	04/27/90	180	Yes	Meningioma	50	Yes	P	Yes	Yes	No	No
35447-116	"Taffy" Gruel[2,3]	05/05/90	300	Yes	Cerebellar fibrillary astrocytoma	55	Yes*	P	Yes	Yes	Yes	Yes
35447-1846	N/A	05/23/90[4]	N/A	No	Normal laboratory dog	100	Yes	N/A	No	No	No	No
35447-2173	N/A	05/24/90[4]	N/A	No	Normal laboratory dog	100	Yes	N/A	No	No	No	No
35447-2174	N/A	05/24/90[4]	N/A	No	Normal laboratory dog	100	Yes	N/A	No	No	No	No

[1] Euthanasia time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.
[2] Boron pharmacokinetic data obtained on these animals using MRS.
[3] Three-dimensional chemical shift imaging (CSI).
[4] Normal laboratory dogs - treated, not euthanized
(P) Partial results
N/A Not applicable
N/P Not Performed

INEL BNCT CANINE PHARMACOKINETIC STUDY
SUMMARY OF PATIENT DATA
BSH INTRAVENOUS INJECTIONS STUDY

ANIMAL	NAME OF DOG	EUTHANASIA DATE	MIN[1]	CASE SUMMARY	PATHOLOGY DIAGNOSIS	DOSE (mg/kg)	BLOOD SERUM AND URINE ANALYSIS	TISSUE ANALYSIS	CT UNENH.	CT ENH	MRI UNENH.	MRI ENH
35447-121	"Shorty" Morgan	07/02/90	180	Yes	Pituitary adenoma	55	Yes*	Yes	Yes	Yes	Yes	Yes
35447-126	"Beau" Smith	07/26/90	180	Yes	Pituitary adenocarcinoma	55	Yes*	Yes	Yes	Yes	Yes	Yes
35447-127	"Sam" Warner	07/31/90	180	Yes	Reticulosis	55	Yes*	Yes	Yes	Yes	Yes	Yes
35447-128	"Niki" Fox[2,3]	08/05/90	297	Yes	Choroid plexus papilloma	55	Yes*	Yes	Yes	Yes	Yes	Yes
35447-136	"Penny" Bird	12/05/90	170	Yes	Fibrillar/pilocytic astrocytoma	55	Yes*	Yes	Yes	Yes	No	No
35447-149	"Shandy" McKeever	02/05/91	180	Yes	Reticulosis	55	No	Pending	Yes	Yes	No	No
35447-153	"Dingo" Martin	03/19/91	170	Yes	Diffuse astrocytoma	110	No	Pending	Yes	Yes	No	No
35447-1846	N/A	03/25/91[5]	180	Yes	Normal laboratory dog	100	Yes	Yes	No	No	No	No
35447-2174	N/A	03/27/91[5]	180	Yes	Normal laboratory dog	100	Yes	Yes	No	No	No	No
35447-363	N/A	04/05/91	180	Yes	Normal laboratory dog	100	Yes	Pending	No	NO	No	No

[1] Euthanasia or irradiation time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.
[2] Boron pharmacokinetic data obtained on these animals using MRS.
[3] Three-dimensional chemical shift imaging (CSI).
[4] Normal laboratory dogs - treated, not euthanized
[5] Normal laboratory dogs - treated previously, now euthanized

(P) Partial results
N/A Not applicable
N/P Not Performed
* Serum only (no urine)

INEL BNCT CANINE PHARMACOKINETIC STUDY
SUMMARY OF PATIENT DATA
BSH INTRA-ARTERIAL INJECTIONS STUDY

ANIMAL	SEX	DATE	EUTHANASIA (MIN)[1]	BLOOD SERUM AND URINE ANALYSIS	TISSUE ANALYSIS
2181	M	10/19/89	420	Yes	Yes
2067	F	10/26/89	420	Yes	Yes
2148	F	11/16/89	420	Yes	Yes

[1] Euthanasia or irradiation time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.

INEL BNCT CANINE TUMOR TREATMENT STUDY
PHASE II - SURGERY/IRRADIATION

ANIMAL	SEX/AGE	NAME OF DOG	BIOPSY DIAGNOSIS	SURGERY DATE	IRRAD. DATE	BORON DOSE (mg ^{10}B/ kg/bw)	START TIME[1]	DURATION MINUTES[2]	CALCULATED DOSE (cGy)	^{10}B ESTIMATED AVG (ppm)	SURV.	DAYS	DEATH DATE/CAUSE
35447-154	F/12	"Mokie" Elkin	Meningioma	05/29/91	--	---	---	---	---	---	No	0.5	05/30/91 Necrotizing encephalitis secondary to surgery complications
35447-157	F/10	"Maggie" Peterson	Meningioma	08/06/91	--	---	---	---	---	---	No	1.0	08/07/91 No cause identified at necropsy
35447-158	F/5	"Nikki" Woods	Granulomatous inflammation	08/14/91	--	---	---	---	---	---	Yes	N/A	N/A

[1] Time from start of boron injection to start of irradiation.
[2] Irradiation time in minutes.

INEL BNCT CANINE PLASMAPHERESIS STUDY

GROUP	ANIMAL	SEX	PLASMA EXCHANGE DATE	FIRST MIN[2]	SECOND MIN[2]	THIRD MIN[2]	EUTHANASIA (MIN.)	BLOOD SERUM & URINE ANALYSIS	TISSUE ANALYSIS
1	2095[1]	M	06/08/88	360	---	---	430	Yes	Yes
1	2084[1]	M	06/09/88	360	---	---	446	Yes	Yes
1	2109[1]	F	06/10/88	360	---	--	410	Yes	Yes
1A	2114[1]	F	08/18/89	360	---	---	445	Yes	Yes
1A	2140[1]	F	08/10/89	365	---	---	455	Yes	Yes
1A	2117[1]	M	08/11/89	360	---	---	417	Yes	Yes
1B	2139[1]	F	07/31/89	362	---	---	750	Yes	Yes
1B	2169[1,3]	M	08/02/89	363	---	---	770	Yes	Yes
1B	2127[1]	F	08/01/89	383	---	---	800	Yes	Yes
2	2097	M	06/14/88	360	---	---	413	Yes	Yes
2	2074	M	06/15/88	360	---	---	410	Yes	Yes
2	2092	F	06/16/88	360	---	---	400	Yes	Yes
2A	2066	F	08/17/89	360	---	---	390	Yes	Yes
2A	2145[3]	F	08/14/89	422	---	---	440	Yes	Yes
2A	2155	M	08/15/89	360	---	---	395	Yes	Yes
2A	1902	F	09/07/90	360	---	---	401	No	No
3	2103	M	06/20/88	360	---	---	755	Yes	Yes
3	2081	M	06/22/88	360	---	---	755	Yes	Yes
3	2089	F	06/24/88	360	---	---	790	Yes	Yes

[1] Control Animal (reinfused same boronated plasma that had just been extracted).
[2] Time from start of boron injection.
[3] Dog went into respiratory arrest at 412 minutes, but was revived.

INEL BNCT CANINE PLASMAPHERESIS STUDY

GROUP	ANIMAL	SEX	PLASMA EXCHANGE DATE	PLASMA EXCHANGE FIRST MIN[2]	PLASMA EXCHANGE SECOND MIN[2]	PLASMA EXCHANGE THIRD MIN[2]	EUTHANASIA (MIN.)	BLOOD SERUM & URINE ANALYSIS	TISSUE ANALYSIS
3A	2076	F	08/04/89	365	---	---	760	Yes	Yes
3A	2112	M	08/03/89	374	---	---	775	Yes	Yes
	2149	M	09/27/89	---	---	---	420	Yes	Yes
	2131	F	09/28/89	---	---	---	420	Yes	Yes
	2165	F	09/27/89	---	---	---	420	Yes	Yes
	2143	M	09/28/89	---	---	---	420	Yes	Yes
	2179	M	09/29/89	---	---	---	420	Yes	Yes
	2182	F	09/29/89	---	---	---	420	Yes	Yes
	2148	M	11/16/89	---	---	---	420	Yes	Yes
	2181	M	10/19/89	---	---	---	420	Yes	Yes
	2067	F	10/26/89	---	---	---	420	Yes	Yes
4	2096	M	06/27/88	360	470	600	640	Yes	Yes
4	2104	M	06/28/88	360	480	600	660	Yes	Yes
4	2098	F	06/29/88	385	545	640	785	Yes	Yes
5	2091	M	08/18/88	120	---	---	163	Yes	Yes
5	2073	F	09/08/88	130	---	---	160	Yes	Yes
5	2090	M	09/09/88	129	---	---	180	Yes	Yes
5	2078[1]	F	09/15/88	120	---	---	180	Yes	Yes
6	2093	M	10/07/88	360	400	---	455	Yes	Yes
6	2086	F	10/13/88	360	401	---	480	Yes	Yes
6	2068	M	09/23/88	405	505	---	560	Yes	Yes
6	2082[1]	M	10/28/88	365	400	---	440	Yes	Yes

[1] Control Animal (reinfused same boronated plasma that had just been extracted).
[2] Time from start of boron injection.

INEL BNCT CANINE PLASMAPHERESIS STUDY

GROUP	ANIMAL	SEX	PLASMA EXCHANGE DATE	PLASMA EXCHANGE FIRST MIN[2]	PLASMA EXCHANGE SECOND MIN[2]	PLASMA EXCHANGE THIRD MIN[2]	EUTHANASIA (MIN.)	BLOOD SERUM & URINE ANALYSIS	TISSUE ANALYSIS
A	II79	F	07/20/90	120	---	---	180	No	No
A	EG79	M	07/23/90	120	---	---	180	Yes	No
A	ACK79	M	08/08/90	120	---	---	180	Yes	No
B	G-1	F	03/16/90	145	---	---	225	Yes	Yes
B	G-8	F	03/22/90	120	---	---	180	Yes	Yes
B	G-10	F	05/04/90	120	---	---	280	Yes	Yes
B	G-11	F	06/06/90	120	---	---	255	Yes	Yes
B	2146	F	09/01/90	155	---	---	205	Yes**	Yes
C	G-2	F	03/23/90	360	---	---	440	Yes	Yes
C	G-6	F	03/23/90	370	---	---	440	Yes	Yes
C	G-7	F	04/06/90	360	---	---	460	Yes	Yes

[1] Control Animal (reinfused same boronated plasma that had just been extracted).
[2] Time from start of boron injection.
* Dosage was 100 mg boron/kg body weight.
** Serum only (no urine)

INEL BNCT CANINE DOSE-TOLERANCE STUDY

ANIMAL	SEX	IRRADIATION DATE	IRRADIATION START TIME[3]	IRRADIATION DURATION (MINS)	IRRADIATION CALCULATED DOSE (cGy)	ppm ^{10}B EST AVG	BLOOD SERUM URINE ANAL.	SURVIVING	DAYS	EUTHANASIA/DEATH DATE	EUTHANASIA/DEATH CAUSE	TISSUE ANALYSIS
1592[1]	M	01/11/89	345	58.0	1273	31.1	Yes	No	0	01/11/89	Euthanasia	Yes
1587[1]	M	01/12/89	21	36.0	1275	57.8	Yes	No	0	01/12/89	Euthanasia	Yes
966	M	02/08/89	235	48.0	1453	47.6	Yes	No	365	02/08/90	Euthanasia	N/A
1588	M	02/09/89	220	49.0	1258	38.5	Yes	No	368	02/12/90	Euthanasia	N/A
995	M	02/09/89	238	42.0	1275	47.8	Yes	No	365	02/09/90	Euthanasia	N/A
1591	M	02/10/89	194	90.0	2629	45.5	Yes	No	368	02/13/90	Euthanasia	N/A
1564	M	02/28/89	204	87.0	2545	45.6	Yes	No	379	03/14/90	Euthanasia	N/A
997	M	03/02/89	190	74.0	2687	59.6	Yes	No	375	03/12/90	Euthanasia	N/A
983	M	03/02/89	160	149.0	3834	38.6	Yes	No	128	07/08/89	Seizures	N/A
1590	M	03/01/89	176	140.0	3800	41.4	Yes	No	155	08/05/89	Seizures	N/A
946	M	04/11/89	195	109.0	3821	57.1	Yes	No	137	08/26/89	Neurologic disease	N/A
985	M	04/13/89	170.0	168.0	6363	62.7	Yes	No	153	09/13/89	Neurologic disease	N/A
1700	M	04/12/89	182.0	166.5	6374	63.5	Yes	No	158	09/17/89	Neurologic disease	N/A
980[2]	M	04/11/89	155.0	120.0	Sham	4.0	Yes	No	372	04/18/90	Euthanasia	N/A
1589[2]	M	04/15/89	125.0	120.0	Sham	4.0	Yes	No	370	04/20/90	Euthanasia	N/A
2255	M	01/31/90	N/A	157.0	1000	0	No	No	369	02/04/91	Euthanasia	N/A
2256	M	01/30/90	N/A	236.0	1500	0	No	No	90	04/30/90	Euthanasia	Yes
2257	M	02/01/90	N/A	157.0	1000	0	No	No	369	02/05/91	Euthanasia	N/A
2258	M	01/31/90	N/A	236.0	1500	0	No	No	91	05/02/90	Euthanasia	Yes
2259	M	02/01/90	N/A	157.0	1000	0	No	No	365	02/01/91	Euthanasia	N/A
2260	M	02/02/90	N/A	236.0	1500	0	No	No	101	05/14/90	Euthanasia	Yes
2261[2]	M	02/05/90	N/A	N/A	N/A	N/A	No	No	N/A	08/08/90	Euthanasia	N/A
2262	M	02/01/90	N/A	157.0	1000	0	No	No	361	01/28/91	Euthanasia	N/A
2263	M	02/05/90	N/A	236.0	1500	0	No	No	98	05/14/90	Euthanasia	Yes
2264	M	02/02/90	N/A	236.0	1500	0	No	No	88	05/01/90	Euthanasia	Yes
2265	M	02/05/90	N/A	157.0	1000	0	No	No	360	01/31/91	Euthanasia	N/A
2266[2]	M	02/05/90	N/A	N/A	N/A	N/A	No	No	N/A	08/13/90	Euthanasia	N/A

[1] Dosimeter animals euthanized after irradiation.
[2] Control dogs given sham irradiations (0 cGy)
[3] Time from start of boron administration
N/A Not applicable

INEL BNCT CANINE DOSE-TOLERANCE STUDY
(continued)

ANIMAL	SEX	IRRADIATION DATE	IRRADIATION START TIME[3]	IRRADIATION DURATION (MINS)	IRRADIATION CALCULATED DOSE (cGy)	ppm ^{10}B EST AVG	BLOOD SERUM URINE ANAL.	SURVIVING	DAYS	EUTHANASIA/DEATH DATE	EUTHANASIA/DEATH CAUSE	TISSUE ANALYSIS
2318	M	08/08/91	N/A	196.0	1250	0	No	Yes				
2442	M	08/08/91	N/A	196.0	1250	0	No	Yes				
2914	M	08/09/91	N/A	196.0	1250	0	No	Yes				
2314	M	08/22/91	199.0	64.3	2700	65.2	Pending	Yes				
2746	M	08/21/91	170.0	51.0	2700	84.1	Pending	Yes				
2449	M	08/23/91	N/A	196.0	1250	0	No	Yes				
2785	M	08/23/91	184.0	43.6	2700	101.9	Pending	Yes				

[1] Dosimeter animals euthanized after irradiation.
[2] Control dogs given sham irradiations (0 cGy)
[3] Time from start of boron administration
N/A Not applicable

INEL BNCT BMRR CALCULATED DOSE CONTRIBUTIONS AT LOCATION OF THE PEAK BLOOD-VOLUME DOSE
(Dose rate components at peak dose location)

DATE	SUBJECT	Beam Size (cm)	$\dot{D}_b$	$\dot{D}_f$	$\dot{D}_g$	$\dot{D}_n$	$\dot{D}_r$
12/16/88	Dog head phantom						
01/10/89	Dog head phantom						
01/11/89	Dog 1592	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
01/12/89	Dog 1587	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/08/89	Dog 966	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/09/89	Dog 1588	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/09/89	Dog 995	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/10/89	Dog 1591	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/28/89	Dog 1564	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
03/01/89	Dog 1590	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
03/02/89	Dog 983	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
03/02/89	Dog 997	5 x 10	0.1680	0.1680	1.6700	0.2600	2.0920
04/11/89	Dog 946	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
04/12/89	Dog 1700	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
04/13/89	Dog 985	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
07/07/89	Dog 35447-079, "Pugee"	10 x 10	0.2750	0.3000	2.4200	0.4300	3.1500
08/07/89	Dog head phantom	10 x 10	0.3480	0.3580	3.1200	0.6070	4.0850
08/07/89	Dog 35447-080, "Mugsy"	10 x 10	0.2310	0.3000	1.9210	0.4030	2.6240
08/25/89	Dog 35447-083, "Rusty"	10 x 10	0.2660	0.3000	2.4800	0.4280	3.2080
09/28/89	Dog 35447-087, "Benji"	10 x 10	0.2160	0.3000	1.735	0.3770	2.4120
10/24/89	Dog 35447-095, "Godfrey"	10 x 10	0.2580	0.3000	2.1500	0.4505	2.9005
10/25/89	Dog 35447-094, "Brandy"	10 x 10	0.2920	0.3000	2.3300	0.5090	3.1390
10/31/89	Dog 35447-093, "Brandy"	10 x 10	0.2521	0.3000	2.3000	0.4396	3.0396
11/30/89	Dog 35447-100, "Juno"	10 x 10	0.2430	0.3000	2.2300	0.4250	2.9550
02/16/90	Dog 35447-108, "Trixie"	10 x 10	0.2630	0.3000	2.092	0.4580	2.8500

$\dot{D}_b$ = Dose rate (Cgy/(min·MW·ppm)) from the $^{10}B(n,\alpha)^7Li$ reaction.
$\dot{D}_f$ = Dose rate (Cgy/(min·MW)) from above-thermal neutron (primarily hydrogen recoil).
$\dot{D}_g$ = Gamma dose rate (cGy/min·MW).
$\dot{D}_n$ = Dose rate (cGy/min·MW) from the $^{14}N(n,p)^{14}C$ reaction, assuming 1.87 weight percent nitrogen in brain tissue (also a peak location).
$\dot{D}_r = \dot{D}_f + \dot{D}_g + \dot{D}_n$

INEL BNCT BMRR CALCULATED DOSE CONTRIBUTIONS AT LOCATION OF THE PEAK BLOOD-VOLUME DOSE (continued)
(Dose rate components at peak dose location)

DATE	SUBJECT	Beam Size (cm)	$\dot{D}_b$	$\dot{D}_f$	$\dot{D}_g$	$\dot{D}_n$	$\dot{D}_r$
10/19/90	Dog 35447-118 "Scuzzy"	10 x 10	0.331	0.398	2.450	0.555	3.734
10/18/90	Dog 35447-129 "Too Wide"	10 x 10	0.325	0.352	2.797	0.546	4.020
10/19/90	Dog 35447-132 "Sarge"	10 x 10	0.289	0.387	2.406	0.484	3.566
10/29/90	Dog 35447-134 "Peggy"	10 x 10	0.279	0.342	2.258	0.468	3.347
01/22/91	Dog 35447-139 "Hobart"	10 x 10	0.316	0.405	2.692	0.530	3.943
01/22/91	Dog 35447-140 "Muffy"	10 x 10	0.233	0.340	1.761	0.391	2.726
01/23/91	Dog 35447-142 "Sugar"	10 x 10	0.310	0.340	2.715	0.520	3.885
02/07/91	Dog 35447-147 "Bomber"	10 x 10	0.288	0.352	2.456	0.263	3.548
02/28/91	Dog 35447-151 "Dudley"	10 x 10	0.336	0.418	2.560	0.563	3.877
03/19/91	Dog 35447-152 "Zar"	10 x 10	0.311	0.362	2.802	0.522	3.997

$\dot{D}_b$ = Dose rate (Cgy/(min·MW·ppm)) from the $^{10}B(n,\alpha)^7Li$ reaction.
$\dot{D}_f$ = Dose rate (Cgy/(min·MW)) from above-thermal neutron (primarily hydrogen recoil).
$\dot{D}_g$ = Gamma dose rate (cGy/min·MW).
$\dot{D}_n$ = Dose rate (cGy/min·MW) from the $^{14}N(n,p)^{14}C$ reaction, assuming 1.87 weight percent nitrogen in brain tissue (also a peak location).
$\dot{D}_r = \dot{D}_f + \dot{D}_g + \dot{D}_n$

* Beginning with dog 35447-118, "Scuzzy," $\dot{D}_{other}$ has been included in $\dot{D}_r$. This dose rate has been included to account for all components not treated explicitly, most Cl, O, and C. It has been defined to be equivalent to $\dot{D}_B$ at 1ppm ^{10}B.

** Dose rates were calculated with head 1 mm from beamport. All previous dogs were calculated with head 1 cm from beamport.

INEL BNCT CANINE MELANOMA PHARMACOKINETIC STUDY
SUMMARY OF PATIENT DATA
D, L-BPA STUDY

ANIMAL	NAME OF DOG	DATE	BORON DOSE	FORM OF BPA**	ADMINISTRATION ROUTE*	COLLECTION LENGTH	SURGERY OR EUTHANASIA	DATE
39412-001	"Cindy" Coyne	01/11/89	50 mg/kg	D,L HC1	Orally	6 hrs	Euthanasia	01/11/89
39412-002	"Smokey" Griffith	01/18/89	50 mg/kg	D,L HC1	Orally	6 hrs	Euthanasia	01/18/89
39412-003	"Minnie" Martin	02/10/89	50 mg/kg	D,L HC1	Orally	6 hrs	Euthanasia	02/10/89
39412-004	"Tracker" Gill	04/25/89	183 mg/kg	D,L Nat	SQ,QID	36 hrs	Euthanasia	04/26/89
39412-005	"Percie" Nissley	06/07/89	200 mg/kg	D,L Nat	SQ,QID	48 hrs	Surgery	06/09/89
39412-006	"Heidi" Meshishnek	08/16/89	200 mg/kg	D,L Nat	SQ,QID	44 hrs	Surgery	08/18/89
39412-007	"Corky" Treadway	08/21/89	478 mg/kg	D,L Nat	SQ,QID	48 hrs	Surgery	08/23/89
		10/27/89	500 mg/kg	D,L Nat	Orally	6 hrs	Euthanasia	10/27/89
39412-008	"Lucy" Dowling	08/23/89	203 mg/kg	D,L Nat	SQ,QID	47 hrs	Surgery	08/24/89
39412-009	"Peanuts" Wetterayer	09/05/89	250 mg/kg	D,L Nat	SQ,QID	12 hrs	Euthanasia	09/06/89
39412-010	"Mindy" Sachtjen	09/14/89	750 mg/kg	D,L Nat	SQ,QID	48 hrs	Euthanasia	09/16/89
39412-011	"Benji" Gebhard	10/02/89	400 mg/kg	D,L Nat	SQ,QID	48 hrs	Surgery	10/04/89
39412-012	"Muff" Hoglund	10/11/89	491 mg/kg	D,L Nat	Oral,QID	48 hrs	Euthanasia	10/13/89
39412-013	"Corky" Newby	11/14/89	750 mg/kg	D,L Nat	Orally	6 hrs	Euthanasia	11/14/89
39412-015	"Missy" Freeman	03/29/90	250 mg/kg	D,L Nat	Orally	6.5 hrs	Surgery	03/29/90
39412-016	"Lucky" Nisonger	04/10/90	250 mg/kg	D,L Nat	Orally	5.5 hrs	Surgery	06/06/90
39412-017	"Winston" Sistek-Lane	04/26/90	250 mg/kg	D,L Nat	Orally	6.5 hrs	Surgery	04/26/90
39412-017	"Winston" Sistek-Lane	09/28/90	48 mg/kg	D,L in M	IV	7.0 hrs	Euthanasia	09/28/90

* SQ = subcutaneously
QID = four times per day
BID = two times per day
IV = intraveneously
M = molecusol
** 3-p-Boronophenylalanine

APPENDIX B

ACRONYMS

Acronyms

AAPM	American Association of Physicists in Medicine
ACS	American Chemical Society
ADM	Action Description Memorandum
ANS	American Nuclear Society
ASN	American Society of Neuroradiology
ATCC	American Type Culture Collection
ATR	Advanced Test Reactor
AWU	Associated Western Universities
B/C	Boron-to-carbon
BME	Basal minimum Eagle
BMRR	Brookhaven Medical Research Reactor
BNL	Brookhaven National Laboratory
BNCT	Boron Neutron Capture Therapy
BPA	Boronophenylalanine
BSA	Bovine serum albumin
BSH	Borocaptate Sodium ($Na_2B_{12}H_{11}SH$)
BSS(B)	$B_{24}H_{22}SS^{4-}$
BSSO(B)	$B_{24}H_{22}S_2O^{4-}$
CAT	Corrective Action Team
CCF	Change control form
CD	Contrast diaphragm
CHNS	Carbon-hydrogen-nitrogen-sulfur
COCA	Consent Order Compliance Agency
CR-39	Allyl diglycol carbonate
CRADA	Cooperative Research and Development Agreement
CRF	Corticotropin releasing factor
CRH	Corticotropin releasing hormone
CSF	Cerebrospinal Fluid
CSI	Chemical shift imaging
CT	Computed tomography
D&D	Decontamination and decommissioning
DEA	Diethanolamine
DMAP	Diemethylaminopyridine
DMEM	Dulbeccos minimum essential medium
DMS	Data Management System
DOE	Department of Energy
DOE-ER	Department of Energy-Energy Research
DOE-HERAC	Department of Energy-Health and Environmental Research Advisory Committee
DOE-HQ	Department of Energy-Headquarters
DOE-ID	Department of Energy-Idaho Operations Office
DOE-NE	Department of Energy-Nuclear Energy
DOE-OHER	Department of Energy-Office of Health and Environmental Research
DOP	Detailed operating procedure
DORT	Two-dimensional S_n computer code
DSPC	Distearoyl phosphatadyl choline
EA	Environmental Assessment
ECBNCT	European Collaboration on Boron Neutron Capture Therapy
ECC	Elaidyl carborane carboxylate
EDF	Engineering Design File
EE	Environmental Evaluation

EGS	Engineering Graphics Systems
EGTA	ethylene glycol-dis(β-aminoethyl ether) MN,N,N',N'-Tetraacetic acid
EIRMC	Eastern Idaho Regional Medical Center
EKG	Electrocardiogram
EPA	Environmental Protection Agency
EPRO	Experimental Power Reactor Operator
ERDP	Exploratory Research and Development Project
ES&H	Environmental Safety and Health
ESMS	Event Sequence and Monitoring System
FCF	Facility Change Form
FDA	Food and Drug Administration
FIA	Flow injection analysis
FMEA	Failure Mode and Effects Analysis
GA	General Atomics
GE	General Electric
GHRH	Growth hormone releasing hormone
GIT-NRC	Georgia Institute of Technology-Neeley Research Center
GTRR	Georgia Tech Research Reactor
HAT	Hypoxanthane aminopterine thymidine
HDW	High pressure demineralized water
HEPA	High-efficiency particulate air filter
HERAC	Health Environmental Research Advisory Committee
HFR	High flux reactor
HMPAO	Hexamethyl-Propylene-Amineoxime
HP	Hewlett-Packard
HPLC	High Performance Liquid Chromatography
HPLC-UV	High Performance Liquid Chromatography-UltraViolet
IACUC	Institutional Animal Care and Use Committee
ICP-AES	Inductively Coupled Plasma-Atomic Emission Spectroscopy
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
IM	Ion microscope
IND	Investigational New Drug exemption from FDA
INEL	Idaho National Engineering Laboratory
INPO	Institute of Nuclear Plant Operations
IP-RP-HPLC	Ion pair-reversed phase-high performance liquid chromatography
ISU	Idaho State University
IV	Intravenous
KURRI	Kyoto University Reactor Research Institute
LDL	Low density lipoprotein
LET	Linear energy transfer
LOCA	Loss-of-coolant accident
LOFT/OECD	Loss-of-Fluid Test/Organization of Economic Cooperation and Development
MCNP	Three-dimensional Monte Carlo computer code
MIT	Massachusetts Institute of Technology
MR	Magnetic resonance
MRI	Magnetic resonance imaging
MRS	Magnetic resonance spectroscopy
MSTI	Mountain States Tumor Institute
MSU	Montana State University
NAS	National Academy of Sciences
NCAR	National Center for Atmospheric Research
NCI	National Cancer Institute
NCS	Network computing system
NDE	New Device Exemption (FDA)

NEPA	National Environmental Policy Act
NESHAPS	National Emission Standards for Hazardous Air Pollutants
NIM	National Institute of Medicine
NIST	National Institute of Science and Technology
NMR	Nuclear magnetic resonance
NWI	Northwest imaging
OCT	A low-temperature adhesive
OHSU	Oregon Health Sciences University
ORAU	Oak Ridge Associated Universities
ORNL	Oak Ridge National Laboratory
ORSU	Oregon State University
OSF	Open Software Foundation
OSHA	Occupational Safety Health Administration
OSU	Ohio State University
PBF	Power Burst Facility
PDARS	Patient Data Acquisition and Retrieval System
PET	Position Emission Tomography
PMT	Photo multiplier tube
PNL	Pacific Northwest Laboratory
POM	Plant operating manual
PRP	Power Reactor Programs
PTC	Permit to Construct
QC/QA	Quality control/quality assurance
RAP	Requirements Awareness Program
RBE	Relative Biological Effectiveness
RCRR	Reed College Research Reactor
RESL	Radiological and Environmental Sciences Laboratory
RF	Radiofrequency
RFP	Request for Proposal
RIS	Resonance ionization spectroscopy
RP-HPLC	Reversed phase-high performance liquid chromatography
RTT-MC	Monte Carlo Transport Module
SAR	Safety Analysis Report
SDD	System Design Description
SIMS	Secondary Ion Mass Spectrometry
SIRIS	Sputter-Initiated Resonance Ionization Spectroscopy
TLD	Thermoluminescent dosimeter
TRA	Test Reactor Area
TTAF	Test Train Assembly Area Facility
UC/Berkeley	University of California Berkeley
UC/Davis	University of California Davis
UCLA	University of California Los Angeles
UCSF	University of California San Francisco
UOR	Unusual occurrence report
UofR	University of Rochester
UofU	University of Utah
USDA	United States Department of Agriculture
WAS	Work Authorization Statement
WSU	Washington State University

END

DATE FILMED

01/06/92