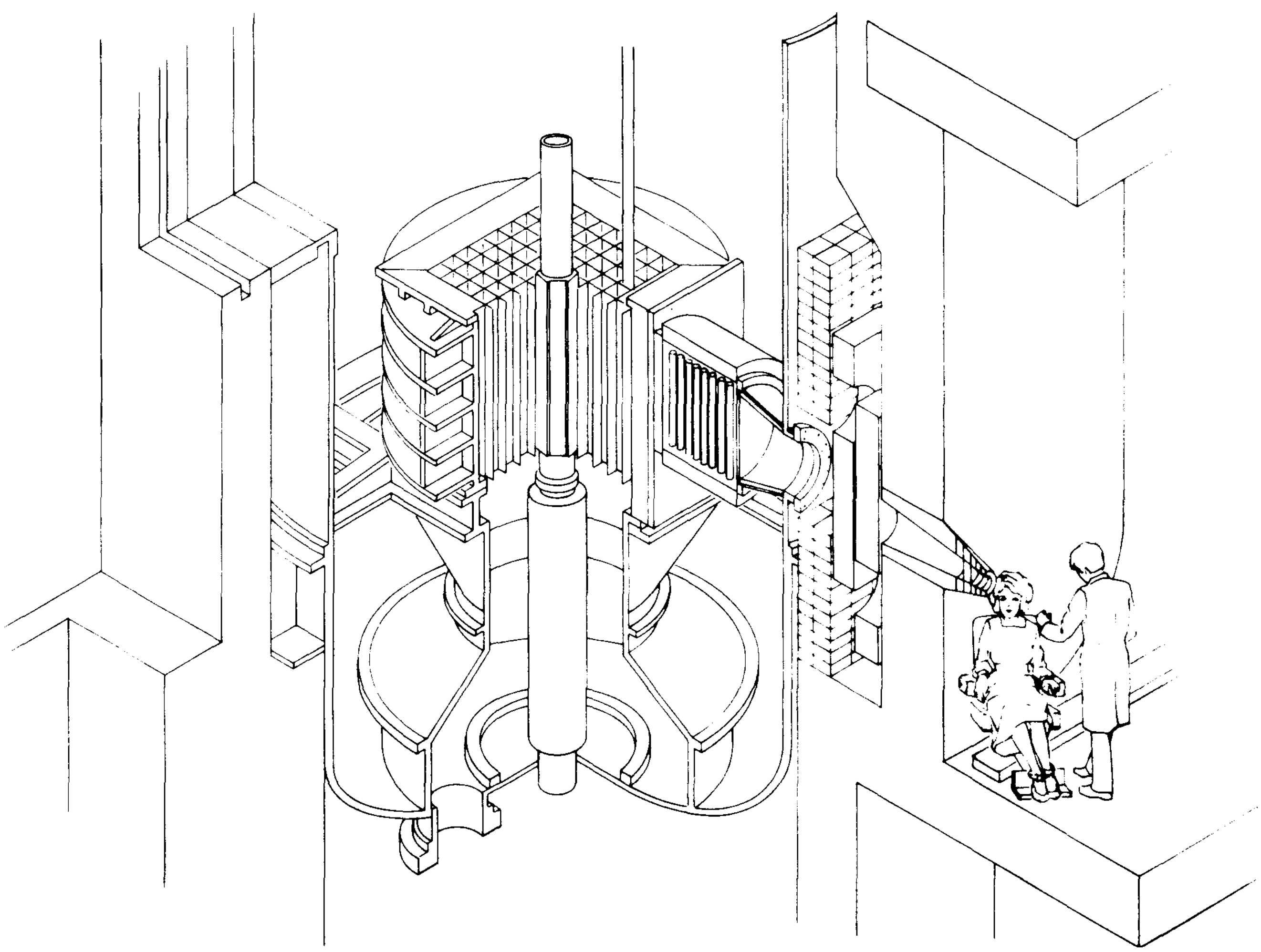
EGG-BNCT-7926
October, 1988

PBF/BNCT Program for Cancer Treatment

Volume 2, No. 10



Bulletin

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EGG-BNCT--7926-Vol.2-No.10

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PRINCIPAL INVESTIGATOR'S REPORT

Highlights of the BNCT Research Programs during October include the progress within these areas:

Project 1: Supporting Technology Development

Task 1: Gross Boron Analysis in Tissue Blood and Urine - Completion of digestion technique comparisons favor bomb digestion.

Task 2: Analytical Methodologies Development for BSH (Sodium Borocaptate) Purity Determination - Further development of the microbore HPLC technique.

Task 4: Boron Microscopic (Subcellular) Analytical Development - Further refinement of SIMS technique to allow conversion of SIM images of cultured cells into quantitative distributional maps. Plans also progressed for November meetings at Cornell and University of Rochester to hear proposals for further cooperative efforts between these institutions.

Task 5: Noninvasive Boron Quantification Determination - Completion of initial testing of RF subsystem modifications, development of MRI boron image analysis software, and initial investigations of boron imaging by coupled-proton excitation.

Task 6: Dosimetry - Ongoing preparation of hardware in support of dosimetry for BNL-canine irradiations. (BNL support also included establishment of working schedule for BMRR filter installation.)

Task 7: Analytical Radiation Transport and Interaction Modeling for BNCT - Further refinement in modeling techniques while awaiting shipment of the Apollo 10000.

Project 2: Large Animal Model Studies - Another dog with an enhancing brain mass was intensively studied this month. In addition, possible collaboration with the PET program at University of Washington was discussed.

Activities in the PBF technical support and operations areas are detailed. Administrative items round out this month's report.

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Principal Investigator
INEL PBF/BNCT Program

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PBF/BNCT PROGRAM MONTHLY BULLETIN

RESEARCH AND MEDICAL PROGRAMS

PROJECT 1 - SUPPORTING TECHNOLOGY DEVELOPMENT

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

Routine WSU canine research sample analyses by inductively-coupled plasma, atomic emission spectroscopy (ICP-AES) continues. Approximately 400 samples were processed in October.

Additional statistical analysis of the results from the digestion comparison study was performed using an analysis of variance technique. The results of this analysis showed that the bomb and the test tube digestion techniques, using a mixture of perchloric acid and hydrogen peroxide, produced analytical results that were not statistically different at the 95% confidence level. This was true for all of the tissue matrices tested. It was also determined that the analytical results obtained using the test tube digestion procedure (with a mixture of nitric acid and hydrogen peroxide) were not statistically different from those obtained with the digestion procedures mentioned above for three of the matrices (cerebral white, cerebral grey, and tongue) at the 95% confidence level. It was determined that the results obtained with this method for liver matrix were statistically different at the 95% confidence level and that the results obtained for the cerebral grey tissue barely met the criteria for the 95% confidence level. Two conclusions can be drawn from these results: (1) it appears that the bomb and test tube digestion procedures, using a mixture of perchloric acid and hydrogen peroxide, are comparable, and (2) that bomb and test tube digestion procedures, using a mixture of nitric acid and hydrogen peroxide, are comparable in some cases, but not all.

Given these two conclusions, the sample preparation and analysis pathways were examined to determine which of the two comparable digestion procedures was the most efficient in terms of labor cost. The result of this evaluation indicated no significant cost difference. The costs are comparable because the test tube procedure produced incomplete dissolution of the sample and required filtration. The ICP technique is succeptible to particulate material and the filtration required is quite rigourous. This filtration is very time-consuming and negates the shorter digestion time allowed by the test tube procedure. It is possible that the filtration times could be reduced if a device was designed and built which would allow multiple filtrations to be conducted at the same time.

Another important aspect of the comparison was that the test tube procedure required constant monitoring during the digestion phase. This contrasts with the bomb digestion procedure, in which samples are loaded into the digestion bombs, the bombs are placed in an oven, and the lab technician is free to do other work until the digestion is complete.

Additional considerations taken into account when comparing these digestion procedures included nonlabor cost and safety. The cost of the filters used in the test tube proceudre is approximately $1.25 each, even if purchased in quantity. Assuming preparation of 400 tissue samples/month, the cost/year for filters would be on the order of $6,000. In addition, the cost of the disposable test tubes is about $500/year; bringing the total cost to approximately $6,500/year. Additional costs would consist of acids, standards, etc. This annual cost, for one year ($6,500), is sufficient to purchase additional digestion bombs and a larger oven allows preparation of approximately 600 samples/month. The enhanced bomb preparation capability allows preparation of 200 samples/month more than the test tube procedure - at the same monthly cost. The use of perchloric acid also requires special facilities that are necessary for safe handling. For the evaluation tests, an existing INEL facility was used for handling perchloric acid. This facility is not available to the BNCT program on a routine basis. A cost estimate of between $15,000 and $20,000 was obtained for the procurement and installation of a standard perchloric acid hood, blowers, stainless steel duct work, etc., required for handling perchloric acid. Continued use of the bomb digestion procedure (at least for the present time) represents a more efficient, cost-effective, and safer procedure than the perchloric acid digestion procedure.

TASK 2: Analytical Methodologies Development for BSH Purity Determination

The mass spectrometer was out of service during the month because of equipment failure. The service visit scheduled, by the vendor, for the week of October 3 was delayed to the week of October 10. The service engineer visited the INEL facility, but was not able to correct all existing problems. An additional visit by a more experienced engineer is scheduled for the week of October 31. The service visits are being complicated by the fact that the mass spectrometer was manufactured in Great Britain and, subsequently, most of the best engineers are English. This requires security clearances for each service visit. While waiting for the mass spectrometer repairs to be completed, and in order to complete the matrix evaluation, work has been continuing on the development of the microbore HPLC technique. Experimentation has shown that the 10-cm microbore columns are unable to resolve the BSH compound from one of the synthetic reaction intermediates which is likely to be present as an impurity. Upon a review of the data, it was determined that a 15-cm column would not likely provide adequate resolution and a 25-cm column has been selected as the standard. Linear calibration curves have been obtained for the reaction intermediate of interest and the SS dimer species. These curves were obtained using instrumental conditions described previously and single component solutions. Experiments were conducted to determine if linear calibration curves could be obtained for solutions containing BSH, reaction intermediate, and SS compound. To date, the curves generated for this mixture have been slightly nonlinear and additional experiments are underway to determine if modified experimental conditions (specifically, ion pairing agent concentration) will result in linear curves. If this can be accomplished, it would represent a potential time savings. If it cannot, it is envisioned that a qualitative analysis of the BNCT compound would be performed and impurities identified either by retention time or mass spectrum. The appropriate single component standard curve could then be generated for use in quantitative analysis.

TASK 3: Analytical Methodologies Development for Active Form Identification

This task is presently unfunded.

TASK 4: Boron Microscopic (Subcellular) Analytical Development

Ion Imaging of Cell Cultures: Quantification - The bulk of the Cornell University effort for October has gone into refining the methodology for converting ion microscope (IM) images of cultured cells into quantitative distributional maps. Areas of progress are: (1) development of an upgraded digital imaging system, and (2) development of quantitative imaging standards.

A "still imaging sensor" utilizing solid state, charge-coupled device (CCD) technology has been evaluated for ion imaging and incorporated into the digital imaging system. Rather than the video format output used by most low-light sensors, this unit records "still" images on a digital CCD array for a user-specified duration and then dumps the digital image directly to the image processing system. This acquisition format allows full exploitation of the inherent linearity of response, high dynamic range, high quantum efficiency, and low noise characteristics of scientific-grade CCDs. Although certain applications still require the real-time output offered by the conventional video format, the CCD format is ideally suited for quantitative elemental imaging of cultured cells. The software development and performance evaluation for the CCD sensor were essentially completed in October. This sensor has greatly enhanced the ability to detect and quantitatively record low intensity ion images, particularly boron signals from $Na_2B_{12}H_{11}SH$-treated cells.

Quantitative Imaging Standards - Quantitative standards for relating ion signals to elemental concentrations have been developed. ICP-AES analyses of these standards at INEL are being used to characterize elemental levels. IM ion intentisities will be calibrated by correlation of ICP-AES and IM results.

TASK 5: Noninvasive Boron Quantification Determination

During the week of October 17-21, 1988, Ken Bradshaw (INEL) conducted hardware changes on the SIGNA, 1.5 Tesla unit at the General Electric, Waukesha, WI, MR facility. A copy of the trip report (KMB-30-88) is included as Attachment 2.

Modifications of the radio frequency (RF) subsystems for the GE SIGNA, 1.5 Tesla, magnetic resonance imaging (MRI) system have been completed and tested on a fully-functional system at the GE MRI facility in Wisconsin. The SIGNA system with the RF modifications was demonstrated to have better signal-to-noise and resolution capability, when gradients are applied, than the smaller and higher field (2 Tesla) GE CSI-II imager. ^{11}B imaging experiments were conducted using a 500-ml phantom containing a 200-ppm natural isotopic ratio BSH compound solution, placed in a 4-inch diameter, inductively-coupled RF coil. There was not enough MRI system bay time allotted by GE to do similar experimentation with the ^{10}B compound. Based on the bench testing done on the RF subsystem and similar experimentation done on the CSI-II imager, results obtained on the SIGNA system and CSI-II should be comparable. The hardware used to modify the MRI system in Wisconsin has been shipped to INEL and will be available by the end of October for installing the "boron imaging package" at Eastern Idaho Regional Medical Center (EIRMC).

In support of the hardware development for the GE SIGNA MRI system, Dr. Richards (UofW) has developed software for the MAC-II computer which will allow MRI users to analyze MRI images off-line. It is now possible to view four MRI images at the same time on the screen, do the necessary windowing and leveling with the computer mouse, and calculate T1 and T2 on regions of interest defined by the use of the mouse. This software will also be used in Task 7.

Dr. Richards is also investigating the possibility of doing proton imaging using protons coupled to the boron nuclei by examination of the water-suppressed, proton spectrum produced by the BSH compound (^{11}B). The water-suppressed, proton spectrum from a concentrated sample of the boron compound was measured and is shown in Figure 1. The proton spectrum showed proton resonances at 2.8, 0.42, and -1.04 ppm (frequency ppm) with water seen at 4.7 ppm. In the figure, zero ppm is the exciting frequency. (Tissue protons resonate in the region of 0.8 ppm to 7 ppm.) The T2 of the 0.42-ppm peak was found to be 35 msec. When albumin (7 mg/ml) was added to the solution, the proton spectrum revealed no peaks at 0.42 and -1.04 ppm, but a large peak at 1.9 ppm. It is not yet known if the peak (1.9 ppm) was due to the protons attached to the boron or the protons in the albumin. In either case, the BSH chemical structure changed when the protein was added, suggesting that the BSH compound does not maintain its original B-H structure when attached to protein.

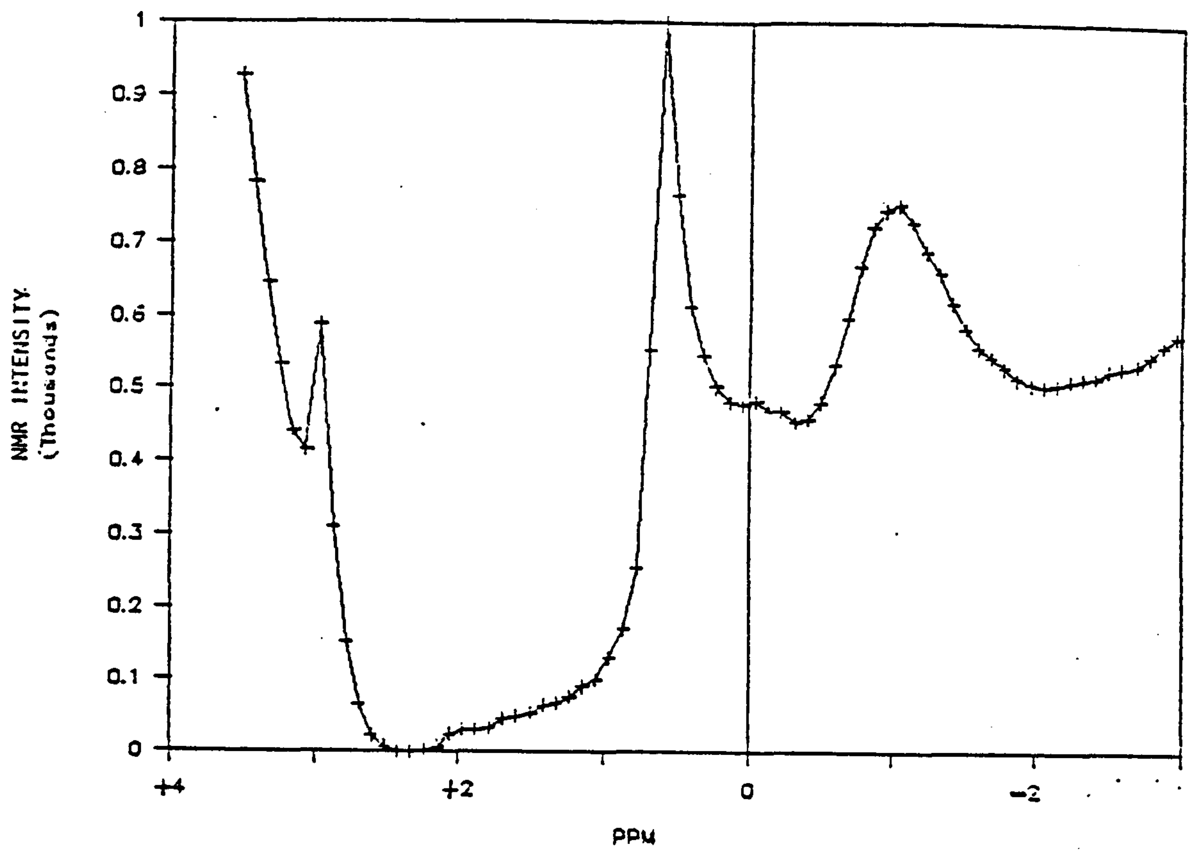

Figure 1. Water-suppressed proton spectrum of ^{11}B.

To further understand proton coupling with boron, and eventually determine what chemcial changes occur in the boron compound when in tissue, heteronuclear experimentation was done on a high-resolution spectrometry system (Bruker 4.7 Tesla) in the the Chemistry Department at the University of Washington. A high-resolution, ^{11}B spectrum of the boron compound was acquired with and without proton decoupling. The spectrum without decoupling (Figure 2) revealed six peaks caused by unequivalent borons being split by adjacent boron and proton nuclei. Peak #3 of Figure 2 is actually two peaks that cannot be resolved. When the spectrum was acquired with proton decoupling (Figure 3), there were four peaks. In comparing Figures 2 and 3, it can be seen that (when the protons decoupled) peaks 2 and 3 combine to form peak 8, peaks 3 and 4 form peak 9, and peaks 5 and 6 form peak 10. From this information, the boron cage borons were assigned to the two large resonances

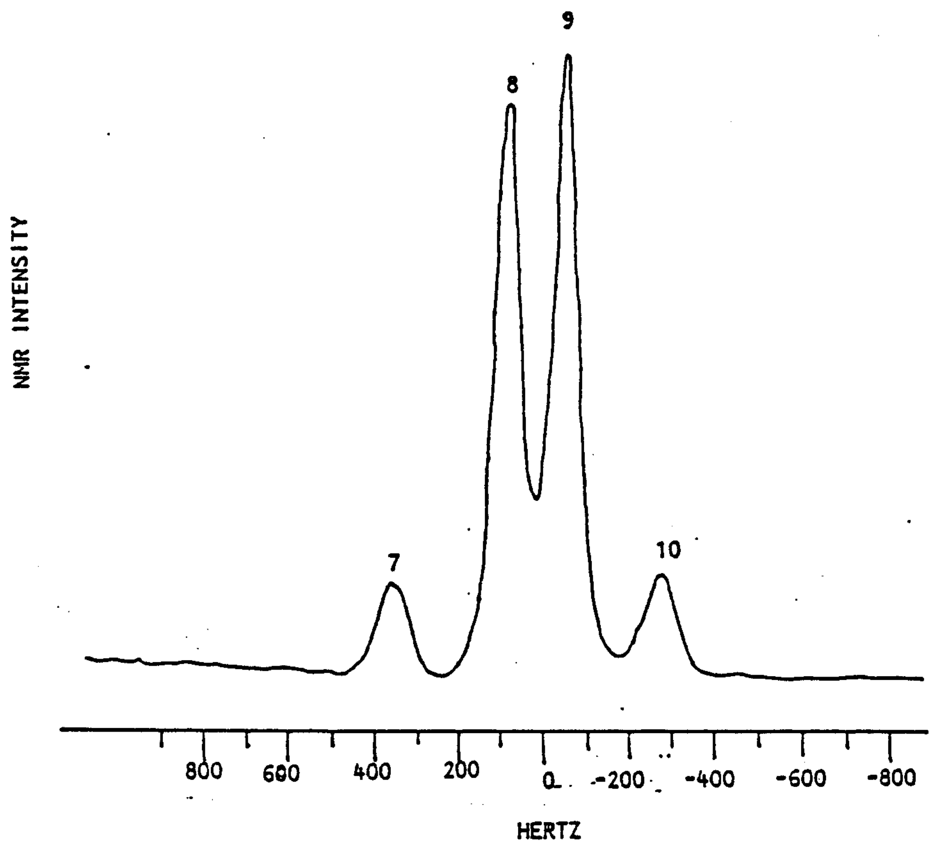

Figure 2. ^{11}B spectrum, proton coupled.

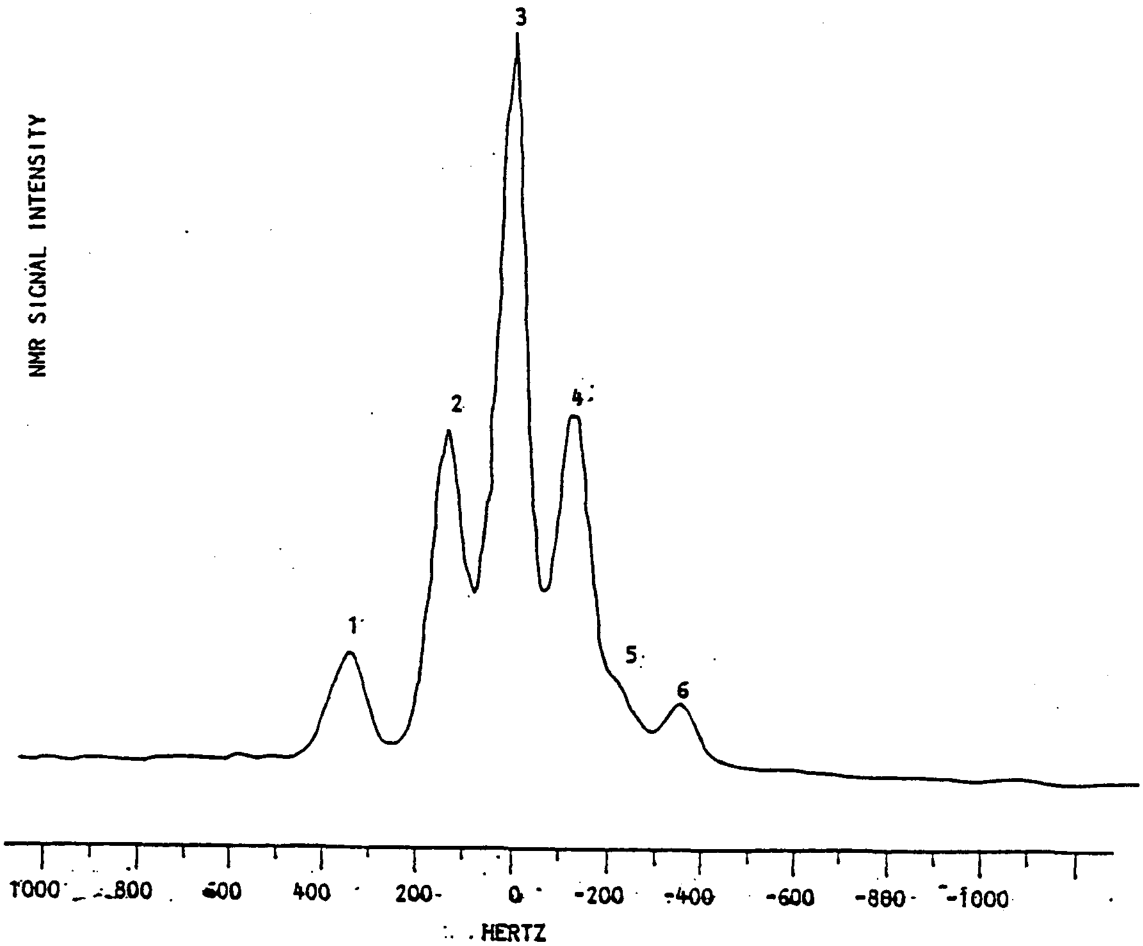

Figure 3. ^{11}B spectrum, proton decoupled.

in the middle (peaks 8 and 9), the S-H boron was assigned to peak 7 (since it did not change during decoupling), and the B-H boron was assigned to peak 10. The J coupling constant for boron-proton was also determined from these spectra to be 130 Hz.

Using this information, a spin-echo difference experiment was performed while observing protons. The result showed a large peak at 0.2 ppm; however, when the experiment was attempted with a piece of liver from a dog injected with the BSH compound (courtesy of Dr. Gavin at WSU), the experiment failed to demonstrate a proton peak connected to a boron. There are other heteronuclear experiments which may not be so dependent on resolving the boron-proton coupling that will be tried in order to answer some of the unresolved questions.

To determine if proton-boron coupling can be used to image boron within a tumor, it is critical the chemical changes that occur when the boron compound enters a tumor are identified. The proton peaks associated with the boron have to be positively identified so they can be separated from the other proton peaks resulting from nonboron-proton bonds in tissue. Since results from proton-boron experimentation on the GE CSI-II system using tissue samples provided by Dr. Gavin were found to be inconclusive, further work will be done on a high-resolution NMR spectroscopy system using the previously described techniques.

TASK 6: Dosimetry

The foil measurments taken at BMRR in June 1988 have been analyzed using the FERRET code to obtain the spectrum in the resonance region. The data from the fast neutron monitors are being incorporated and the results are expected the first week in November. 500 TLD-400 dosimeters have been received from Harshaw/Filtrol and are at the INEL/DOE Radiological Environmental Services Laboratory (RESL) for evaluation and selection. Lithium-hydroxide monohydrate, containing 600 grams of 94% ^{6}Li, is being ordered from ORNL to be cast into polyethylene for use in defining the irradiation areas for the phantom and dog irradiations. The desired locations for implanted wire and TLD dosimeters within the phantom, and for the first two dogs to be irradiated at BMRR, have been provided to INEL by Dr. Gavin (WSU).

TASK 7: Analytical Radiation Transport and Interaction Modeling for BNCT

Shipment of the Apollo 10000 has been delayed for two weeks because of equipment failure during qualification and checkout. Documentation, software, and miscellaneous pieces of equipment have arrived at INEL and administrative documentation is currently being reviewed. Contract negotiations with the University of Utah are proceeding. A tentative agreement has been reached and is in review by the University of Utal legal staff and INEL contracts personnel.

BNCT accounts and accesses for the Magnetic Fusion Energy (MFE) computers have been established. The MFE computers use the Cray Time-Sharing System (CTSS) of operation and will require familiarization.

Initial concepts for the source generator that describes the neutron energy spectrum and angular distribution leaving the neutron filter have been formulated and will be coded and tested in the upcoming weeks. The best estimate for the beam spectrum and angular distributions now comes from the unadjusted DOT-RZ calculational model. These data may be adjusted when better models become available and when comparisons are made with detailed dosimetry. These angular fluxes will be processed into a form usable by Monte Carlo and stored in restricted files which can be easily used during irradiation planning. The planner will not need to consider angular fluxes and will be able to easily rotate the beam to the desired orientation and combine results for multiple beam directions.

INEL has generated profilometer data defining the lucite canine phantom geometry and a study has been initiated to determine the best material to be used for a beam delimiter for the canine phantom studies. For now, the phantom has been modeled only approximately using regular geometry input. RAFFLE Monte Carlo neutron calculations are being performed to assess neutron shielding material effectiveness. A thick neutron shield is unacceptable because this would unacceptably reduce the neutron flux by the R^2 effect. Too thin a shield is unacceptable since the collateral dose would be too high. Lithiated polyethylene using lithium-enriched in ^{6}Li has been selected for the initial case.

PROJECT 2 - LARGE ANIMAL MODEL STUDIES

The preliminary data collection and scan acquisition is continuing on the normal laboratory dogs that will be a part of the BNCT radiation tolerance dose studies conducted at BMRR. Computed tomographic (CT) and magnetic resonance (MR) scans are completed for the majority of the dogs. The first set of dogs in the dose tolerance study are scheduled for irradiation at BNL in early January 1989.

Dr. Gavin met with imaging researchers in the Positron Emission Tomography (PET) Cancer Program Project at the University of Washington in Seattle, WA on October 24 to discuss collaboration with their research involving PET of brain tumors. Selected dogs which have brain tumors, irradiated in the BNCT project, will also undergo PET scanning as a collaborative effort with this research group. In addition, a subset of healthy dogs in the radiation dose tolerance study will have PET scans prior to radiation and at selected time intervals following radiation. The PET scanning protocol will include the use of ^{18}F-glucose compound and a ^{15}O compound to quantitate metabolism and profusion of normal brain, irradiated brain, and tumor tissue in those dogs with brain tumors.

With the exception of samples from one dog, all samples from the laboratory dogs in the plasmapheresis experiment have been submitted to INEL for ICP analysis. Liver and spleen samples were obtained from the plasmapheresis dogs, fast-frozen, and sent to Cornell for boron ion microscopy.

Several dogs underwent diagnostic workup for central nervous system (CNS) disease this month; one dog was found to have an enhancing mass of the caudal fossa. This dog underwent boron infusion and, in addtion to regular sample collection, fast-frozen liver and spleen samples were obtained for subcellular boron imaging with ion microscopy techniques at Cornell University. Tumor tissue, liver, and spleen samples from this dog were also shipped to Dr. Richards at University of Washington for spectroscopic examination.

The latest information on large animal model experiments is summarized on Pages 11 and 12.

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/A	N/A	N/A	N/A
35447-3	"King" Henry	5/18/87	Control	Yes	No tumor/negative boron control	Control	Yes	N/A	N/A	N/A	N/A
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	(P)	Yes	Yes	Yes	Yes
36845-25	"Sandy" Frazier	1/26/88	770	Yes	Meningioma	Yes	No	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	(P)	N/A	N/A	N/A	N/A
35447-39	"Fritts" Coglan	5/2/88	110	Yes	Meningioma	Yes	No	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	(P)	No	N/A	N/A	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

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

		EUTHANASIA		CASE		BLOOD SERUM AND	TISSUE	CT		MRI	
ANIMAL	NAME OF DOG	DATE	MIN*	SUMMARY	PATHOLOGY DIAGNOSIS	URINE ANALYSIS	ANALYSIS	UNENH.	ENH	UNENH.	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	No	No	Yes	Yes	Yes	Yes
35447-55	"Kelley" Langsston	8/17/88	410	Yes	No	No	No	N/A	N/A	Yes	Yes
35447-57	"Rafferty" Reber	9/1/88	(?)	Yes	No	No	No	No	Yes	Yes	Yes
35447-59	"Heidi" Boyer	9/12/88	180	Yes	No	No	No	No	Yes	Yes	Yes
35447-62	"Chester" Scott	10/9/88	180	Yes	No	No	No	No	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

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BNL Support

A working schedule for the BMRR filter installation and initial testing is given in Table 1. The aluminum oxide filter will be installed in stages to permit measurement of the neutron spectrum, neutron current, and gamma dose rate with aluminum oxide tile in the outboard filter end and the presently installed aluminum and D_2O mixture in the intermediate zone.

Table 1. BMRR Neutron Filter Installation and Testing Schedule

Oct. 27 - Nov. 1	Ship aluminum oxide, neutron filter sections from INEL to BNL.
Nov. 7 - 10	Make bismuth filter section and install Bismuth, cadmium, and the tapered aluminum oxide outboard filter section. Return presently existing material to the center filter section.
Nov. 10 - 18	BNL will make neutron spectrum, neutron current, and gamma dose rate measurements on this intermediate filter configuration as requested by Dr. Ralph Fairchild (BNL).
Nov. 21 - 23	Remove neutron filter material from the center filter section and replace with aluminum oxide filter sections, completing the BMRR filter installation.
Nov. 28 - Dec. 9	Complete neutron spectrum, neutron current, and gamma dose rate measurements. Mount the canine-head phantom and measure the thermal neutron flux and gamma dose rate as a function of position.
Jan. 9	Preparations complete for initial irradiation of canines at BMRR.

Most of the Al_2O_3 ceramic tile, scheduled to be shipped from Coors' Ceramics of Golden, CO during the week ending October 7, 1988, was rejected at the Coors' plant during final inspection. This rejection caused most of the lot to be scrapped and new green tile cut and fired. A new shipment date was negotiated with Coors' and the final shipment was made from the Coors' plant on October 21. This was five weeks later than the initially negotiated delivery date.

The aluminum housings for the central and outer sections of the filter were completed and the boxes loaded with Al_2O_3 ceramic tile. The outer section was shipped to BMRR October 27; the remaining central section is scheduled to be shipped November 1. The Neutron Filter Lift Fixture was load tested during the week ending October 28 and will be shipped to BMRR with the central section.

A documentation package has been assembled for the BMRR neutron filter design activity and will be sent to BMRR for review. Delivery of the neutron filters, lift fixture, and documentation package will meet the committed delivery date of November 15.

Summary documentation (EDF PBF-BNCT-105) has been distributed defining the analytical physics methods and analyses used for unfolding the BMRR neutron spectrum measurements. The calculations for the tungsten foils, are being redone using the more recent cross sections for tungsten in the evaluated nuclear data file (ENDF). Dr. John Ryskamp (INEL) has processed these newer materials with the ENDRAFL code so these calculations can be updated.

INEL has received a request from BNL to negotiate, with Babcock and Wilcox, a number of changes to the original proposal for the construction of fuel elements for BMRR. INEL is presently reviewing this request.

Programmatic/Administrative

During the week of October 10, contractor evaluation site visits were made to two companies that responded to the INEL request for a long-term boron compound supply. The third responding company will be visited the first week in November. These visits are conducted as part of the contractor selection process for the competitively bid, BSH supply contract.

Additional documents have been added to the BNCT library since Vol. 2, No. 4 of the Bulletin, dated April 1988, was issued. Library index pages 21-27 are included as Attachment 1 to this document. If you do not have a complete listing of the Library Index, please contact Mrs. Ackermann in the Program Office - (208) 526-9264.

Meetings, Conferences, and Proceedings

Dr. Kraft (WSU) attended the annual meeting of the American College of Veterinary Radiologists (ACVR) in Washington, D.C., October 20-25, 1988, and gave an oral presentation on "Magnetic Resonance Imaging of Canine Brain Lesions".

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
BNCT	12	$Na_2B_{12}H_{11}SH$	500 mg
	15	$Na_2B_{12}H_{11}SH$	.140 gms
	14	$Na_2B_{12}H_{11}SH$ (BNCT 14 returned by W.A.)	~ 2 gms
	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
	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
BNCT	26	$Na_4B_{12}H_{11}SOSB_{12}H_{11}$	400 mg
	23	$Na_4B_{12}H_{11}SOSB_{12}H_{11}$	1 gm
BNCT	16	$CH_3(CH_2)_2N(CH_3)CS$	5 gm
	18	$LiB_{12}H_{11}XH_2C$	1 gm

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MAJOR UPCOMING EVENTS(1)

Nov 1-4, 1988	Fourth Asia and Oceania Congress of Nuclear Medicine (Asia and Oceania Congress of Nuclear Medicine), Taipei, Taiwan
Nov 4-6, 1988	Current Clinical Role of Nuclear Medicine: Comparison with Other Modalities (sponsored by Society of Nuclear Medicine, Southeastern Chapter's 29th Annual Meeting), Charleston, SC
Nov 4-6, 1988	Fourth Northeast Regional Scientific Meeting (New England and Greater New York Chapters, Society of Nuclear Medicine), Boston, MA
Nov 4-6, 1988	International Conference on Clinicial Applications and Issues of Magnetic Resonance Imaging (sponsored by Diagnostic Imaging), Washington, D.C.
Nov 17-18, 1988	Third International Workshop on Monoclonal Antibodies and Breast Cancer (John Muir Cancer and Aging Research Institute), San Francisco, CA
Nov 27-Dec 2, 1988	Radiological Society of North America, Chicago, IL
Dec 13-14, 1988	Third Australia-Japan Workshop on Neutron Capture Therapy for Malignant Melanoma, Sydney Australia
Feb 25-Mar 1, 1989	Society for Magnetic Resonance Imaging, Los Angeles, CA
March 18-23, 1989	37th Annual Scientific Meeting Radiation Research Society/Ninth Annual Meeting North American Hyperthermia Group, Seattle, WA
March 18-24, 1989	American Society of Neuroradiology, Orlando, FL
March 30-31, 1989	International Workshop on Neutron Beam Design and Development for Neutron Capture Therapy, Mass. Institute of Technology.
April 15-19, 1989	71st Annual Meeting of the American Radium Society, Virgin Islands.

(1) Please contact Arlene Ackermann, BNCT Research Programs Office, for further information on upcoming meetings.

May 7-10, 1989	7th International Symposium: Radionuclides in Nephro-Urology (sponsored by International Society of Nephrology and American Society of Hypertension), Williamsburg, VA
May 19-24, 1989	American Society of Neuroradiology, Orlando, FL
Jun 13-16, 1989	Society of Nuclear Medicine, St. Louis, MO
Jul 23-27, 1989	Joint Meeting of the American Association of Physicists in Medicine (AAPM) with the Radiological Society of North America, Memphis, TN
October, 1989	Western Society of Neuroradiology, (place to be determined)
Aug 5-9, 1990	Joint Meeting of the American Association of Physicists in Medicine (AAPM) with the Radiological Society of North America, St. Louis, MO
Aug 27-31, 1990	V World Congress, World Federal of Nuclear Medicine and Biology, Montreal, Canada

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Attachment 2

EG&G Idaho

"Providing research and development services to the government"

INTEROFFICE CORRESPONDENCE

Date: October 24, 1988

To: D. L. Miller

From: K. M. Bradshaw

Subject: REPORT OF TRIP TO GE MEDICAL SYSTEMS OCT. 17-21 - KMB-30-88

During the week of October 17-21, 1988, all of the RF hardware changes which were required to allow the GE 1.5 Tesla whole body MRI system (Signa) to operate at the two boron isotope frequencies (20.49 MHz for ^{11}B and 6.86 MHz for ^{10}B) were brought together and integrated into a functional system at the GE MR facility. Of particular interest, the RF amplifier purchased from Kalmus Engineering was used in place of the normal MR RF amplifier and performed within specification.

Imaging feasibility experiments were performed at 20.49 MHz (^{11}B) on a 500 ml phantom containing a 200 ppm BSH compound within a 4-in. inductively coupled RF solenoid coil. Various pulse sequences were used in order to assess capability that is presently found within Signa's existing repertoire of spectroscopy pulse sequences.

At present, the only procedure Signa has of displaying localized spectroscopy results is chemical shift imaging (CSI). A CSI sequence called SPECFIDCSIP.PSD was used and found to give some localizing information. This sequence does not start acquiring data until the Free Induction Decay (FID) of ^{11}B has already decayed substantially. The sequence was designed around nuclei which had longer T2's. We will have to either modify this sequence or derive our own if we are to image boron in tissue. Even though the sequence used was not optimum, I was able to obtain a display of a 16 x 16 pixel chemical shift representation of a 3-cm slice through the 500 ml phantom.

After it was shown that Signa could be used to do boron spectroscopy without adversely affecting the system, the modified equipment was shipped to Idaho where it will be installed at EIRMC. It also should be noted that to install the modified equipment and begin boron spectroscopy or to remove the equipment and restore proton imaging to an existing Signa, takes about 15 minutes to half an hour.

It appears that to do any work using boron imaging techniques will require placing Signa in the spectroscopy mode, which is accessed via the Signa research mode. Most commercial imaging sites, i.e., EIRMC and Northwest Imaging, are in the Signa clinical mode preventing access to the spectroscopy mode. Usually, to get spectroscopy at a site requires the purchase of a spectroscopy package and a research agreement. This price may vary from $35,000 to $120,000, the lower price only being software and some support. Although something may be worked out for siting boron imaging capability at EIRMC for a limited time at no cost, a more extensive use of spectroscopy will probably require the purchase of at least the software package.

Discussions were also held during this trip with GE representatives responsible for arranging research agreements and doing the cost estimating for any equipment made at GE for our use. In the beginning there was a commitment on our part to pay for any equipment that was needed to allow Signa to function at the lower boron isotope frequencies. At the time of this report, I have not received an answer to our inquires regarding this commitment. We still need to be prepared at some future time to respond to such a request (probably on the order of $10,000).

In regard to a research agreement, support for this project on behalf of GE has continued only upon the personal commitment of Felix Wehrli who now works for the University of Pennsylvania. GE said they would continue to honor the original commitment of letting me come to their facility to do work, but I sensed that it would be a low priority when it came to additional support. I was told that a formal research agreement which we sought in the beginning would be necessary only if the Signa system was applied to boron imaging with humans.

cc: D. M. Adams
J. G. Crocker
M. L. Griebenow
D. L. Rittenhouse
Central Files
File B4.8, B8
K. M. Bradshaw File