

**BROOKHAVEN NATIONAL LABORATORY**

**BIOLOGY DEPARTMENT**

# **BNL-4 RUN**

## **FINAL REPORT**

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## EXECUTIVE SUMMARY

During the spring of 1998, a series of radiobiological and physics experiments were performed using the BNL's Alternating Gradient Synchrotron to accelerate iron and gold ion beams (Experiment 919, BNL-4). These experiments were part of NASA's Space Radiation Health Program (SRHP) heavy ion radiobiology research program at BNL.

A total of 22 proposals were approved to participate in the BNL-4 run, 16 of which were returnees from 1997's BNL-3. Six groups were new participants. From the total number 22 were full proposals and 1 was a piggyback experiment. Twenty one institutions from United States, and 1 from Australia were represented, totaling 65 users. A total of 1183+ biological samples were irradiated at the AGS A-3 beam line, employing 84 hours of beam time. In addition, 35 hours were used for physics experiments, and a total of 23 hours were necessary for beam characterization, dosimetry, and calibration.

During BNL-4, AGS provided iron beams with two energies: 1 GeV/nucleon (1.06 GeV/nucleon\*, LET: 148 keV/ $\mu\text{m}$ ), and 0.6 GeV/nucleon (0.565 GeV/nucleon\*, LET: 177 keV/ $\mu\text{m}$ ) for biology and physics experiments. The dose/rates used were as low as 90 cGy/min and as high as 9 Gy/min for 1 GeV/nucleon, and from 45 cGy/min up to 10 Gy/min for 0.6 GeV/nucleon iron beams. The spill rate employed was 30 spills/min with a duration of 500 msec/spill. The spill fluence was (particles/spill)  $1.4 \times 10^8$  (max) and  $6.5 \times 10^6$  (min) for 0.6 GeV/nucleon, and  $1.67 \times 10^8$  (max) and  $1.67 \times 10^7$  (min) for 1 GeV/nucleon. The intensities (particles/ $\text{cm}^2/\text{sec}$  on target) used during the run were  $5.88 \times 10^5$  (max) and  $2.65 \times 10^4$  (min) for 0.6 GeV/nucleon, and  $6.33 \times 10^5$  (max) and  $6.33 \times 10^4$  (min) for 1 GeV/nucleon. A 7.5-cm diameter beam spot was employed for the exposures.

As a pilot run, AGS delivered gold beams with a nominal energy of 10.78 GeV/nucleon (LET: 1445 keV/ $\mu\text{m}$ ) for a limited series of biological and physics experiments. The dose/rate used was 0.15 Gy/min, the spill rate employed was 20 spills/min, with a duration of 1 sec/spill. The spill fluence was (particles/spill)  $1.4 \times 10^5$ . The intensity (particles/ $\text{cm}^2/\text{sec}$  on target) used during the run was 1080. A 7.5-cm diameter beam spot was employed for the exposures. A total of 24 hours were used to expose biological samples and plastic detectors at the AGS D-1 beam line, employing 8 hours for biology, 0.5 hour for physics, and 15.5 h for dosimetry and beam characterization.

Several improvements were implemented in the logistic support and dosimetry system. Two new incubators were installed in the tissue culture room at staging area. In support of the dosimetry system, a new x-ray film developer was installed in the proximity of the staging area, allowing for a quick turn-around to develop exposed x-ray films for beam uniformity diagnostics. In addition, an extra workstation with a flat-bed scanner and a computer was set up in the control room for the densitometric analysis of the developed films. Finally, a phosphor imager system was installed on the Beam line to allow for a real time assessment of the iron beam uniformity.

Radiobiological experiments employed cells, tissues, and intact specimens, which required a complex coordination and planning of their respective logistic support. Biological studies used human, mouse,

rat, hamster and canine cell lines (25), human-hamster hybrid cell lines, chick neural tissue (retina) and intact specimens (rodents). The full program was completed in 8 days (180 hours) under the AGS's operation schedule directives and with the allocated beam time dedicated for the NASA radiobiology program.

\* Actual beam energy on target

## BNL-4 PARTICIPANTS

Exp.	Participants	Affiliation	Title
B-1	J. Miller L. Heilbronn C. Zeitlin R.P. Sigh M. Nyman W. Holley W. Schimmerling	Lawrence Berkeley National Laboratory, CA " " " " " NASA, HDQ, Washington DC	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Ph.D., Co-Worker Ph.D., Co-Worker Ph.D., Co-Worker Ph.D., Co-Worker Ph.D., Co-Worker
B-2	D. Chen * T. Hei	Los Alamos National Laboratory, NM Columbia University, NY	Ph.D., Principal Investigator Ph.D., Co-W
B-3	T.C. Yang * H. Wu K. George V. Willingham	NASA, Johnson Space Flight Center, TX Kelsey-Seybold Co., TX KRUG, TX KRUG, TX	Ph.D., Principal Investigator Co-Worker Co-Worker Co-Worker
B-7	B. Rabin J. Joseph B. Shukitt-Hale J. McEwen	University of Maryland Baltimore County, MD " " "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Investigator Tech. Support
B-9	B. Sutherland P. Bennett J. Sutherland J. Trunk P. Snyder M. Leander N. Metting	Brookhaven National Laboratory, NY " " " " " Pacific Northwest National Laboratory, WA	Ph.D., Principal Investigator MS., Biology Associate. Ph.D., Co-Worker Co-Worker Student, Co-Worker Student, Co-Worker Ph.D., Co-Worker
B-10	R. Winegar L. Lutze-Mann P. Chang	SRI International, CA U. of New South Wales, Sidney, Australia SRI International, CA	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Ph.D., Co-Worker
B-12	T. Hei C. Piao R. Miller	Columbia University, NY " "	Ph.D., Principal Investigator Co-Worker Co-Worker
B-13	E. B-Kubiczek G. Harrison R. Ove	University of Maryland, MD " "	Ph.D., Principal Investigator Ph.D., Co-Worker Ph.D., Co-Worker
B-14	N. Metting B. Sutherland	Pacific Northwest National Laboratory, WA Brookhaven National Laboratory, NY	Ph.D., Principal Investigator Ph.D., Co-Investigator
B-15	C. Waldren * M. Lenarczyk T. Hei	Colorado State University, CO " Columbia University, NY	Ph.D., Principal Investigator Co-Investigator Ph.D., Co-Investigator
B-18	P. Cooper B. Rydberg E. Kwoh	Lawrence Berkeley National Laboratory, CA " "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Co-Investigator
B-19	A. Kronenberg C. Wiese S. Gauny	Lawrence Berkeley National Laboratory, CA " "	Ph.D., Principal Investigator Post-Doctoral Student Senior Research Associate
B-20	A. Kronenberg A. Grosovsky C. Wiese S. Gauny	Lawrence Berkeley National Laboratory, CA University of California Riverside, CA Lawrence Berkeley National Laboratory, CA "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Post-Doctoral Student Senior Research Associate
B-23	A. Brooks S. Bao K. Rithidech	Washington State University, WA " SUNY Stony Brook, NY	Ph.D., Principal Investigator Co-Worker Ph.D., Co-Worker
B-24	T. Borak B. Gersey	Colorado State University, CO	Ph.D., Principal Investigator Student, Co-Worker

<b>Exp.</b>	<b>Participants</b>	<b>Institution</b>	<b>Title</b>
B-25	H. Evans J. Schwartz T. Evans	Case Western Reserve University, OH " "	Ph.D., Principal Investigator Co-Investigator Assistant
B-26	W. Morgan C. Limoli	University of California, CA "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator
B-30	P. Kale	Alabama Agricultural and Mechanical U., AL	Ph.D., Principal Investigator
B-31	Barcellos-Hoff S. Ravani S. Costes	Lawrence Berkeley National Laboratory, CA " "	Ph.D., Principal Investigator Assistant Graduate Assistant
B-32	J. Dicello S. Howard J. Williams J. Strandberg D. Huso Y. Zhang	NSBRI, John Hopkins University, MD " " " " "	Ph.D., Principal Investigator MD, Ph.D., Co-Worker Sc.D. Co-Worker Ph.D. Co-Worker DVM, Ph.D., Co-Worker M.D. Co-Worker
B-33	R. Sinden L. Braby J. Ford	NSBRI, John Hopkins University, MD " "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Research Associate
B-34	J. Bedford T. Hei	Colorado State University Columbia University, NY	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator
B-35 (* )	T. Jorgensen	Georgetown University Medical C., DC	Ph.D., Principal Investigator

(\* ) Piggyback experiment with B. Sutherland (B-9)

## **PARTICIPANTS STATISTICS**

<b>PARTICIPANTS</b>	<b>BNL-4</b>
<b>Ph.D., Principal Investigators</b>	<b>21</b>
<b>Ph.D., Co-Principal Investigators</b>	<b>7</b>
<b>Co-Investigator, Investigator</b>	<b>4</b>
<b>Co-Workers</b>	<b>9</b>
<b>Ph.D.</b>	<b>9</b>
<b>MD, Ph.D.</b>	<b>1</b>
<b>DVM, Ph.D.</b>	<b>1</b>
<b>M.D.</b>	<b>1</b>
<b>Sc.D.</b>	<b>1</b>
<b>Students</b>	<b>3</b>
<b>Post-Doctoral Students</b>	<b>1</b>
<b>Research Associates</b>	<b>2</b>
<b>Research Assistants</b>	<b>1</b>
<b>Assistants</b>	<b>3</b>
<b>Technicians</b>	<b>1</b>
<b>Total:</b>	<b>65</b>

## IRON RUN DATES

Run dates	Scheduled		Actual	
	Date	Time	Date	Time
Run start	5/2	0800	5/4	0800
Run end	5/10	2400	5/11	2130
Tuned into cave	5/3	1600	5/3	1300
<b>Beam delivered for Biology</b>				
Fe 1 GeV/n	5/4	1600	5/4	0800
End run	5/10	2100	5/11	2130
<b>Fe 0.6 GeV/n</b>				
End run	5/9	1730	5/10	1215

## BEAM TIME DESCRIPTION (hours)

Total Clock Time	(from 5/4 0800 to 5/11 2130)		158.5
Total Beam-on Time			142
Total Beam-off time			16.5
<b>Beam Time for Biology</b>			
1 GeV/n	75		
0.6 GeV/n	9		
Sub-total		84	
<b>Beam Time for Physics</b>			
1 GeV/n	26		
0.6 GeV/n	9		
Sub-total		35	
<b>Beam time for dosimetry, calibration etc.</b>			
1 GeV/n	16		
0.6 GeV/n	7		
Sub-total		23	
<b>Totals</b>		<b>142</b>	

## GOLD RUN DATES

	Scheduled		Actual	
<b>Run dates</b>	<b>4/27-29</b>		<b>4/29 - 4/30</b>	
	<b>Date</b>	<b>Time</b>	<b>Date</b>	<b>Time</b>
<b>Tuned into cave (B1)</b>	<b>4/27</b>	<b>1600</b>	<b>4/29</b>	<b>1600</b>
<b>Beam delivered for Biology</b>				
<b>Au 11 GeV/n</b>	<b>4/28</b>	<b>1600</b>	<b>4/29</b>	<b>1600</b>
<b>End run</b>	<b>4/29</b>	<b>2400</b>	<b>4/30</b>	<b>2400</b>

Beam Time Description (hours)		
<b>Total Clock Time</b>	<b>(from 4/29 1600 to 4/30 2400)</b>	<b>32</b>
<b>Total Beam Time (idem beam on)</b>		<b>24</b>
<b>Total Beam-off time</b>		<b>6</b>
<b>Beam Time for Biology</b>	<b>(4 hrs for Yang and 4 hrs for Morgan)</b>	<b>8</b>
<b>Beam Time for Physics</b>		<b>0.5</b>
<b>Beam time for dosimetry, calibration etc.</b>		<b>15.5</b>

## BNL-4 GOLD RUN PARTICIPANTS

Exp.	Participants	Affiliation	Title
B-1	J. Miller L. Heilbron	Lawrence Berkeley National Lab., CA "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator
B-3	T.C. Yang * K. George M. Vazquez	NASA, Johnson Space Flight Center, TX KRUG, TX Brookhaven National Laboratory, NY	Ph.D., Principal Investigator Co-Worker Ph.D. Co-Worker
B-26	W. Morgan C. Limoli M. Vazquez	University of California, CA " Brookhaven National Laboratory, NY	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Ph.D. Co-Worker

## BEAM CHARACTERISTICS

	<sup>56</sup> Fe <sup>26</sup> 600 MeV/n	<sup>56</sup> Fe <sup>26</sup> 1000 MeV/n	<sup>29</sup> Au <sup>179</sup> 10.8 GeV/n
<b>Fluence (particles/cm<sup>2</sup>/sec)</b>			
<b>Maximum on target</b>	5.88 x 10 <sup>5</sup>	6.33 x 10 <sup>5</sup>	1080
<b>Minimum on target</b>	2.65 x 10 <sup>4</sup>	6.33 x 10 <sup>4</sup>	
<b>Spill rate</b>	30 spills/min	30 spills/min	20 spills/min
<b>Spill length</b>	500 msec	500 msec	1 sec
<b>Particles/spill</b>			
<b>Maximum</b>	1.4 x 10 <sup>8</sup>	1.67 x 10 <sup>8</sup>	1.4 x 10 <sup>5</sup>
<b>Minimum</b>	6.5 x 10 <sup>6</sup>	1.67 x 10 <sup>7</sup>	
<b>Beam spot diameter</b>	7.5 cm	7.5 - 9 cm	7.5 cm
<b>Beam cut off length.</b>	<1%	<1%	TBD
<b>Actual Energy</b>			
<b>Extracted</b>	610+/-10 MeV/n	1087 MeV/n	10.78 GeV/n
<b>On Target</b>	565+/-10 MeV/n	1060 MeV/n	TBD
<b>Actual LET</b>	177 keV/μm	148 keV/μm	1445 keV/μm
<b>Dose/rate recorded.</b>			
<b>Maximum</b>	10 Gy/min	9.0 Gy/min	0.15 Gy/min
<b>Minimum</b>	0.45 Gy/min	0.9 Gy/min	TBD
<b>Minimum dose exposure</b>	0.05 Gy	0.05 Gy	0.1 Gy
<b>No of hours for beam characterization and dosimetry</b>	7	16	24

## BNL-4 EXPERIMENTERS AND RUN STATISTICS

Exp. ID	Principal Investigator	Energy	Beam Time Approved	Beam Time Used	Dose Range (cGy)	Dose/Rate (cGy/min)	Number of Samples
B1e	Miller	1 GeV 600 MeV	14 14	14 9	NA	NA	NA
B2	Chen	1 GeV	2	0.5	NA	NA	NA
B3	Yang	1 GeV	4	4	50 - 400	100	90
B7	Rabin	1 GeV 600 MeV	4 1.5	4 2.5	10 - 100	50	78
B9	Sutherland	1 GeV 600 MeV	3 1.5	5 2.5	NA	NA	NA
B10	Winegard	1 GeV	6	4	100	100	60
B12	Hei	1 GeV	6	2.5	10 - 300	100	80
B13	Kubiczek	1 GeV	5	5	50 - 350	100 - 200	70
B14	Metting	1 GeV	5	3.5	5 - 50	100	80
B15	Waldren	1 GeV	3	1.5	50 - 200	100	45
B18	Cooper	1 GeV 600 MeV	7	4 3.5	100 - 8000	100 - 700	NA
B19-20	Kronenberg	1 GeV	16	13	30 - >2000	<100 - 700	150
B23	Brooks	1 GeV	1.5	1	50 - 200	100	15
B24	Borak	1 GeV	12	12	NA	NA	NA
B25	Evans	1 GeV	2.5	2	0.5 - 2.5	100	24
B26	Morgan	1 GeV	2	3.5	10 - 1000	200	40
B30	Kale	600 MeV	0.5	0.5	80 - 160	<100	3
B31	Barcellos-Hoff	1 GeV	3	2.5	80	100	32
B32	Dicello	1 GeV	16	16.5	10 - 100	100	300
B33	Sinden	1 GeV	2	1.5	10 - 200	100	100
B34	Bedford	1 GeV	1.5	1	84 - 125	100	16
B35	Jorgensen*	1 GeV	NA	NA	NA	NA	NA
<b>Totals</b>			<b>133 hr</b>	<b>119 hr</b>	<b>5 to 8000cGy</b>	<b>50 to 900 cGy</b>	<b>1183+</b>

## BNL-4 PARTICIPANTS AND BIOLOGICAL SAMPLES

<b>Exp.</b>	<b>Title</b>	<b>Participants</b>	<b>Biological sample</b>
B-2	Radiation Induced Genomic Instability	D. Chen (PI)	Human cell line (reduced expression of Rad51 and hhRad52 genes)
B-3	Effect of Shielding on the Induction of Oncogenic and Cytogenetic Damages	T.C. Yang (PI)	Mouse Fibroblasts (C3H10T1/2) Human Fibroblasts Human Lymphocytes Human mammary epithelial cells Canine kidney cells (MDCK)
B-7	Effects of Exposure to Heavy Particles	B. Rabin (PI)	Rod. Sprague-Dawley
B-9	DNA Damage and Restoration in Mammalian Cells and Tissues	B. Sutherland (PI)	Human skin fibroblast and epithelial cells
B-10	Molecular Analysis of HZE Damage in Transgenic Mice	R. Winegar (PI)	Transgenic Mice: C57lacZ, CBA1acZ, p53 hemizygous lacZ, p53 nullizygous lacZ
B-12	Cytogenetic and Neoplastic Transforming Effects of heavy Ions in mammalian Cells	T. Hei (PI)	Human epithelial cells: bronchial cells BEP2D and breast cells MCF-1F
B-13	Molecular Damage by 1 GeV/amu Fe-ions	E. B-Kubiczek (PI)	Human cell lines: (MCF7, PC3, WT,ADR AND HCT15)
B-14	Effect of Heavy Ion Exposure on a Mechanism of Cell-Cycle Regulation	N. Metting (PI)	Human skin fibroblasts Human keratinocytes
B-15	HZE Radiation Genotoxicity in Mammalian Cells	C. Waldren (PI)	Human-hamster hybrid cell line (A <sub>L</sub> )
B-18	DNA Repair and early Development of Chromosomal Changes	P. Cooper (PI)	Human fibroblasts (GM38)
B-19	Mutagenesis Studies in Human Cells	A. Kronenberg (PI)	Human lymphoid cells (TK6) WTK-bclX <sub>L</sub>
B-20	High LET Radiation and Genomic Instability in Human Cells	A. Kronenberg (PI)	TK6 cells
B-23	In Vivo Induction and Repair of Genomic Instability	A. Brooks (PI)	Rat epithelial cells from lungs, trachea and bone marrow.
B-25	Induction of Genomic Instability in Human Lymphoblasts	H. Evans (PI)	Human lymphoblast (TK6 and WTK1)
B-26	Mechanisms of High LET Genomic Instability	W. Morgan (PI)	GM10115 Cell line
B-30	Iron Ion Mutagenesis	P. Kale (PI)	Drosophila
B-31	Epithelial Transformation & Carcinogenesis	Barcellos-Hof f	Mice
B-32	Tumor Formation in Rat Mammary Gland	J. Dicello	Sprague-Dawley Rats
B-33	Quantitation of Radiation Induced Deletion and Recombination Events with Repeated DNA Sequences	R. Sinden	Fibrosarcoma cell lines (F14C-23 and 122-2)
B-34	HZE Radiation Induced Chromosomal Instability	J. Bedford	Human fibroblast