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PROPOSAL

to

NATIONAL CANCER INSTITUTE

2-17-76

by

The University of New Mexico
Health Sciences Center

Cancer Research & Treatment Center
Albuquerque, N.M. 87131

T-032

CANCER RESEARCH AND TREATMENT CENTER PROGRAM
(TITLE OF PROPOSED PROJECT)

Principal Investigator

Co-Principal Investigator(s)

Name: M. M. Kligerman, M.D.

NONE

Title: Director

Soc. Sec. No. [REDACTED]

Dept.: Cancer Research and
Treatment Center

New or renewal proposal: renewal

Amount requested: \$1,388,480

Proposed starting date: 1 May 1976

If renewal, identification number of

previous grant: 5-P01-CA-16127-02

Proposed duration in months: 12

Submitted by: (in. Inves.)	Morton M. Kligerman	<i>M. Kligerman</i>	Director, CRTC	(505) 277-3631	23 Jan 76
	Name	Signature	Rank/Title	Phone	Date

Business Office	Warren Baur	<i>Warren Baur</i>	Assoc. Asst. Comptroller	277-6264	1/26/76
	Name	Signature		Phone	Date

Approved by:	Morton Kligerman	<i>M. Kligerman</i>	Director of Cancer Center	277-3631	23 Jan 76
	Name	Signature		Phone	Date

Approved by:	Robert B. Kugel	<i>Robert B. Kugel</i>	VP/Health Sciences	277-6464	21 Dec 75
	Name	Signature		Phone	Date

FILE BARCODE



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FOR

00133494.001

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P01

ON ALL PAGES
CA 16127-03

**APPLICATION
FOR CONTINUATION GRANT**

TOTAL PROJECT PERIOD

FROM: 05/01/74

THROUGH: 04/30/77

REQUESTED BUDGET PERIOD

FROM: 05/01/76

THROUGH: 04/30/77

TO BE VERIFIED BY APPLICANT. CHECK INFORMATION IN ITEMS 1 THROUGH 6. IF INCORRECT, FURNISH CORRECT INFORMATION IN ITEM 13.

1. TITLE

CANCER RESEARCH AND TREATMENT CTR PROGRAM

2A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Name and Address, Street, City, State, Zip Code)		4. APPLICANT ORGANIZATION (Name and Address, Street, City, State, Zip Code)	
KLIGERMAN, MORTON M UNIVERSITY OF NEW MEXICO CANCER RES AND TREATMENT CTR ALBUQUERQUE, N MEX 87131		UNIVERSITY OF NEW MEXICO CANCER RES & TREATMENT CENTER ALBUQUERQUE, N MEX 87131	
2B. DEGREE	2C. SOCIAL SECURITY NO.	5. PHS ACCOUNT NUMBER	
MD	[REDACTED]	1856000642A1	
2D. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT		6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF APPLICANT ORGANIZATION	
CANCER RES & TREATMENT CENTER		COMPTROLLER UNIVERSITY OF NEW MEXICO ALBUQUERQUE, N MEX 87131	
2E. MAJOR SUBDIVISION			
HEALTH SCIENCES CENTER			
3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR INSTITUTIONAL GRANT PURPOSES			
20 OTHER			

COMPLETE THE FOLLOWING (See Instructions)

7. RESEARCH INVOLVING HUMAN SUBJECTS (See Instructions)		8. INVENTION CERTIFICATION (See Instructions)	
<input type="checkbox"/> NO <input checked="" type="checkbox"/> YES APPROVED: <u>Sept. 2, 1975</u> DATE		<input checked="" type="checkbox"/> NO <input type="checkbox"/> YES - NOT PREVIOUSLY REPORTED <input type="checkbox"/> YES - PREVIOUSLY REPORTED	
9. PERFORMANCE SITE (S)		TELEPHONE INFORMATION	
Cancer Research and Treatment Center University of New Mexico Albuquerque, New Mexico 87131 Congressional District #1 Los Alamos Scientific Laboratory Los Alamos, New Mexico 87545 Congressional District #1		11A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (ITEM 2A) Morton M. Kligerman, M.D. 505 277-3631	
		11B. NAME OF BUSINESS OFFICIAL (ITEM 6) Warren Baur Associate Comptroller 505 277-6264	
		11C. NAME AND TITLE OF ADMINISTRATIVE OFFICIAL (ITEM 15B) Warren Baur Associate Comptroller 505 277-6264	
10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD		12B. COUNTY OF APPLICANT ORGANIZATION SHOWN IN ITEM 4	
\$1,388,480		Bernalillo County	
12A. CONGRESSIONAL DISTRICT OF APPLICANT ORGANIZATION SHOWN IN ITEM 4			
Congressional District #1			

13. USE THIS SPACE FOR CORRECTIONS TO ITEMS 1 THROUGH 6. INDICATE THE NUMBER(S) WHERE ANSWER(S) APPLY

CHANGE ITEM #5 to: 776225.

14. CERTIFICATION AND ACCEPTANCE. WE, THE UNDERSIGNED, CERTIFY THAT THE STATEMENTS HEREIN ARE TRUE AND COMPLETE TO THE BEST OF OUR KNOWLEDGE AND ACCEPT, AS TO ANY GRANT AWARDED, THE OBLIGATION TO COMPLY WITH PUBLIC HEALTH SERVICE TERMS AND CONDITIONS IN EFFECT AT THE TIME OF THE AWARD.

SIGNATURES (Signatures required on original copy only. Use ink. "Per" signatures not acceptable.)	15A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR	DATE
	15B. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION <i>Warren Baur</i>	DATE 1/30/76

PHS 2590-1 OPTIONAL
REV. 1-70

**RETURN COMPLETED APPLICATION TO PHS AS SOON AS POSSIBLE:
NO LATER THAN 1 MARCH 1976**

1091819

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5-P01-CA-16127-03

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A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD

PERSONNEL		TIME OR EFFORT % / MRS. (c)	ARY COSTED (d)	FRINGE BENEFITS (See instructions) (e)	TOTAL (f)
NAME (Last, First, Initial) (a)	TITLE OF POSITION (b)				
	PRINCIPAL INVESTIGATOR				
See Attached Budget Sheets					
Subtotals				\$	\$
TOTAL (Columns (d) and (e))					\$ 730,498
CONSTANT COSTS (See instructions)					\$ 4,000
See Attached Sheets					
EQUIPMENT					
See Attached Sheets					
					\$ 43,750
SUPPLIES					
See Attached Sheets					
					\$ 51,384
TRAVEL	DOMESTIC	See Attached Sheets			\$ 23,170
	FOREIGN				\$ - 0
PATIENT COSTS (See instructions)					\$ 200,000
See Attached Sheets					
ALTERATIONS AND RENOVATIONS					\$ - 0
OTHER EXPENSES (Itemize)					
See Attached Sheets					
					\$ 335,670
TOTAL DIRECT COST (Enter on Page 1, Item 10)					\$1,388,482

INDIRECT COST (See instructions)	53.18% SAW*	Date of DHEW Agreement: 24 April 1975	<input type="checkbox"/> Not Requested
	% 10C*		<input type="checkbox"/> Under negotiation with:

*If this is a special rate (e.g. off-site), explain.

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SECTION II—BUDGET (USUALLY 12 MONTHS)

May 1, 1976

April 30, 1977

OR TOTAL

A. ITEMIZE DIRECT COSTS REQUESTED FOR FISCAL BUDGET PERIOD

PERSONNEL		TIME OR EFFORT (HRS.) (c)	SALARY REQUESTED (d)	FRINGE BENEFITS (See Instructions) (e)	TOTAL (f)
NAME (Last, First, Initial) (a)	TITLE OF POSITION (b)				
Kligerman, M.	PRINCIPAL INVESTIGATOR	35			
Shaw, Dori	Admin. Coordinator	35			
New Hire	Dept. Secretary	35			
Wilson, Stephany	Assoc. Admin. for Res	40			
Talley, Fran	Admin. Secretary	50			
New Hire	Technical Writer	100			
Furman, John	Business Manager	40			
Grant, Alan	Accounting Supervisor	40			
De Palma, Jane	Clerk III	40			
Barela, Inez	Accounting Tech.	75			
Moore, Pat	Appointments Coord.	30			
Hilber, Allison	Dept. Secretary	50			
* (Off Site Personnel at Los Alamos)					
* (O/H at 33.41% of S/W)					
			Subtotal	\$ 85,343	\$ 13,655

Indicate cost of each item listed below

TOTAL (Columns (d) and (e))

\$ 98,998

CONSTANT COSTS (See Instructions)	General Consultants	\$2,400			\$ 4,000
	Scientific Advisory Committee	1,600			

EQUIPMENT

SUPPLIES General Office Supplies

Photographic Film

Mag Card I.B.M. Typewriter supplies

\$ 5,884

TRAVEL	DOMESTIC	Instate per diem	5,500	Mileage	\$1,500	\$ 8,500
		Out-of-state trips	1,500			
	FOREIGN					\$ - 0 -

PATIENT COSTS (See Instructions)

ALTERATIONS AND RENOVATIONS

OTHER EXPENSES (Itemize)

Medical Liability Insurance \$35,000

Communications

Research Reports Expense For Graphics,

Publication Work, Making, Copying

I.B.M. Mag Card Typewriter Rental

\$9,400

\$ 44,400

TOTAL DIRECT COST (Enter on Page 1, Item 10)

\$ 161.78

INDIRECT COST (See Instructions)

_____ % SAW*

_____ % TOC*

*If this is a special rate (e.g. off-site), explain.

Date of DHEW Agreement:

Not Requested

Under negotiation with:

BIOMATHEMATICS SECTION II—BUDGET (USUAL 12 MONTHS)

FROM May 1, 1976

THROUGH April 30, 1977

GRANT NUMBER CA 16127 - 03

2. ITEMIZE DIRECT COSTS REQUESTED FOR THIS BUDGET PERIOD

PERSONNEL		TIME OR EFFORT %/MOS. (c)	SALARY REQUESTED (d)	FRINGE BENEFITS (SEE INSTRUCTIONS) (e)	TOTAL (f)	
NAME (Last, First, Initial) (a)	TITLE OF POSITION (b)					
Kligerman, M.M., M.D.	PRINCIPAL INVESTIGATOR	N/A	-0-	-0-		
Barnard, R.L.	Chief, Biometry	50				
Selheimer, C.	Clinical Research Crd	100				
New Hire	Protocol Nurse	100				
Fullilove, J.	Programmer	50				
Stauffer,	Programmer	50				
Dike, L.	Systems Programmer	50				
New Hire	Statistician	50				
Espinosa, P.	Department Secretary	88				
New Hire	Staff Secretary	100				
New Hire	Data Entry Clerk	100				
Subtotals			\$ 92,414	\$ 14,786		
(Indicate cost of each item listed below)					TOTAL (Columns (d) and (e))	\$ 107,200
CONSTANT COSTS (See instructions)						\$ -0-
EQUIPMENT						
Magnetic Tape Drive \$5,000						
Two Computer Terminals 3,500						
						\$ 8,500
SUPPLIES						
Computer Expendables \$4,500						
Office Supplies 1,500						
						\$ 6,000
TRAVEL						
DOMESTIC Mileage & Perdiem for two trips						\$ 1,000
FOREIGN						\$ -0-
PATIENT COSTS (See instructions)						\$ -0-
ALTERATIONS AND RENOVATIONS						\$ -0-
OTHER EXPENSES (Items)						
Computer Hardware Maintenance 12,000						
Protocol Forms Reproduction 3,000						
Communications 2,000						
						\$ 17,000
TOTAL DIRECT COST (Enter on Page 1, Item 10)						\$ 139,700

INDIRECT COST (See instructions)

_____% SEW*
 _____% TOC*
 *If this is a special rate (e.g. off-site), explain.

Date of DHEW Agreement:

Not Requested
 Under negotiation with:

CLINICAL OPERATIONS
SECTION II - BUDGET (USUALLY 12 MONTHS)

May 1, 1976 April 30, 1977 CA 16177 - 07

PERSONNEL		TIME OR EFFORT (% FRS. (c))	SALARY REQUESTED (d)	FRINGE BENEFITS (See Instructions) (e)	TOTAL (f)
NAME (Last, First, Initial) (a)	TITLE OF POSITION (b)				
Kligerman, M.M., M.D.	PRINCIPAL INVESTIGATOR	N/A	-0-	-0-	
Sala, Jose	Medical Director	10			
New Hire	Chief Surg. Oncologist	50			
New Hire	Chief Med. Oncologist	50			
Hilgers, Robert	Chief Gyn. Oncologist	25			
New Hire	Asst. Gyn. Oncologist	25			
Bergreen, Peter	Urological Oncologist	10			
Herzon, Frederick	Otolaryngologist	10			
Strickland, Robert	Gastroenterologist	20			
New Hire	Psychiatrist	25			
Bleakly, Martha	Nurse V	30			
Seymour, Beverly	Nurse III	50			
New Hire	Social Worker	100			
Reichel, Sandra	Dept. Secretary	40			
New Hire	Staff Secretary - M.O.	50			
New Hire	Licensed Pratic. Nurse	100			
Hipps, Linda	Dept. Secretary	10			
			Salary's	\$142,975	\$22,876

(Indicate cost of each item listed below)

TOTAL (Columns (d) and (e))

\$165,851

EQUIPMENT	Operating Table (50%)			\$13,040
SUPPLIES	Office Supplies \$1,500			
	Clinical Supplies 1,500			\$3,000
OTHER EXPENSES (Itemize)	Communications			
	Reproduction			\$2,160
TOTAL DIRECT COST (Enter on Page 3, Item 10)				\$186,051

INDIRECT COST
(See Instructions)

_____ % S&W*
_____ % IDC*

*If this is a special rate (e.g. off-site), explain.

Date of OHEW Agreement: _____

Not Requested
 Under negotiation

SECTION II—BUDGET

A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD

PERSONNEL		TIME OR EFFORT %/HRS (c)	SALARY REQUESTED (d)	FRINGE BENEFITS (SEE INSTRUCTIONS) (e)	TOTAL (f)	
NAME (Last, First, Initial) (a)	TITLE OF POSITION (b)					
Kligerman, M.M., M.D.	PRINCIPAL INVESTIGATOR	N/A	-0-	-0-		
Subtotal			\$	\$		
(Indicate cost of each item listed below)					TOTAL (Columns (d) and (e))	\$
CONSULTANT COSTS (See instructions)						\$
EQUIPMENT						\$
SUPPLIES						\$
TRAVEL	DOMESTIC					\$
	FOREIGN					\$
PATIENT COSTS (See instructions)						\$
ALTERATIONS AND RENOVATIONS						\$
OTHER EXPENSES (Itemize)						\$
Subcontract to Los Alamos Scientific Laboratory (See Attached)						\$ 252,111
TOTAL DIRECT COST (Enter on Page 1, Item 10)						\$ 252,111

INDIRECT COST (See instructions)	_____ % SAW*	Date of DHEW Agreement: _____	<input type="checkbox"/> Not Requested
	_____ % TOC*		<input type="checkbox"/> Under negotiation with: _____
*If this is a special rate (e.g. off-site), explain.			

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B. Supplemental information regarding items in the proposed budget for the next period or

require explanation or justification. (See instructions.)

Other Expenses - Los Alamos Scientific Laboratories Subcontract

I. Personnel

<u>Name</u>	<u>Title of Position</u>	<u>Time Or Effort %/Hrs.</u>
Kligerman, M.M., M.D.	Principal Investigator	
Lundy, A.	Engineering Physicist	25
Kittel, R.	Computer Programmer	50
Berardo, P. Ph.D.	Physicist	100
Schillaci, M. Ph.D.	Physicist	50
Hutson, R. Ph.D.	Physicist	13
Rivera, O.	Electronics Tech.	50
Bush, E.	Mechanical Engineer	15

Subtotal \$83,045

II. Supplies

Electronic Parts	\$24,000
Chemicals	2,000
Hardware & Fittings	4,000
Computer Expendables	13,000
Metal & Plastic Stores	8,000
Polaroid Film	2,000
Small Hand Tools	2,000
Office Supplies	2,245

Subtotal \$57,245

III. Other Expenses

Shop Services	\$10,000
Central Computing Services	8,000
Electronics & Instrumentation Services	8,000
Lab Services	4,000
Drafting	2,000
Maintenance: Magnets	7,000
Power Supplies	9,000
Control Systems & Computer	10,000
Target	10,000

Subtotal \$68,000

Total Direct

\$208,290

Indirect 52.77% S/W

43,823

Grand Total \$252,113

SECTION II—BUDGET (USUALLY 12 MONTHS)

May 1, 1976 (April 30, 1977) CA 10127 - 03

PERSONNEL		TIME OR EFFORT (% MRS)	SALARY REQUESTED	FRINGE BENEFITS (See Instructions)	TOTAL
NAME (Last, First, Initial)	TITLE OF POSITION	(c)	(d)	(e)	(f)
Kligerman, M.M., M.D.	PRINCIPAL INVESTIGATOR	N/A	-0-	-0-	
Sala, Jose	Prof. of Radiology	20			
Powell, Terry	Asst. Prof. Radiology	50			
Sachs, Marvin	Chief Radiation Tech.	50			
Hipps, Linda	Dept. Secretary	20			
Wilson, Maureen	Staff Secretary	40			
Subtotal			\$ 45,068	\$ 7,211	
TOTAL (Columns (d) and (e))					\$ 52,279
CONSTANT COSTS (See Instructions)					
EQUIPMENT					
SUPPLIES					
Patient Positioning and Fixation Supplies				1,370	
Blocking Materials				1,280	
Office Supplies				550	
Clinical Supplies (gowns, sterile mtl., examining aids)				2,300	
					\$ 5,500
TRAVEL					
DOMESTIC					\$ -0-
FOREIGN					\$ -0-
PATIENT COSTS (See Instructions)					
ALTERATIONS AND RENOVATIONS					
OTHER EXPENSES (Items)					
Photography Processing \$1,000					
Communications				} 4,000	
Reproduction					
Equipment Maintenance					
					\$ 5,000
TOTAL DIRECT COST (Enter on Page 3, Item 10)					\$ 62,779

INDIRECT COST (See Instructions) _____ % S&W _____ % 10C*
 *If this is a special rate (e.g. off-site), explain.

Date of DHEW Agreement: _____

Not Pre-estimated
 Under negotiation with _____

1091829

SECTION II—BUDGET (USUALLY 12 MONTHS)

May 1, 1976

April 30, 1977

PERSONNEL		BUDGET PERIOD			TOTAL (f)
NAME (Last, First, Initial) (a)	TITLE OF POSITION (b)	TIME OR EFFORT %/MRS. (c)	SALARY REQUESTED (d)	FRINGE BENEFITS (See instructions) (e)	
Kligerman, M.M., M.D.	PRINCIPAL INVESTIGATOR	N/A	-0-	-0-	
Kelsey, Charles	Professor Radiology	25			
Criswell, Lena	Dent. Secretary	50			
Stevens, Marcus	Radiological Eng.	50			
New Hire	Ph. D. Physicist	100			
New Hire	Technician	100			
Subtotal			\$ 68,495	\$ 10,959	
TOTAL (Columns (d) and (e))					\$ 79,454
CONSTANT COSTS (See instructions)					\$ -0-
EQUIPMENT					
Treatment Verification Equipment		6,000			
Electron Treatment Equipment		2,000			
Immobilization and Reposition Equipment		2,000			
					\$ 10,000
SUPPLIES					
Electronic Components and Supplies		4,500			
Mechanical Components and Supplies		4,500			
Office Supplies		1,000			
					\$ 10,000
TRAVEL					
DOMESTIC					\$ -0-
FOREIGN					\$ -0-
PATIENT COSTS (See instructions)					\$ -0-
ALTERATIONS AND RENOVATIONS					\$ -0-
OTHER EXPENSES (Itemize)					\$ -0-
TOTAL DIRECT COST (Enter on Page 1, Item 10)					\$ 99,45

INDIRECT COST (See instructions)	_____ % S&W*	Date of DHEW Agreement: _____	<input type="checkbox"/> Not Requested
	_____ % TOC*		<input type="checkbox"/> Under negotiation with:
*If this is a special rate (e.g. off-site), explain: _____			

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PATIENT CARE COSTS - YEAR 3 PROTOCOL FUNDS

I. In-Patient

Pion \$170/day X 8 days X 60 pt's	= \$81,600
Radiation Therapy \$170/day X 8 days X 20 pt's	= \$ 27,200
Chemotherapy \$125/day X 8 days X 20 pt's	= <u>\$20,000</u>
Subtotal	\$128,800

II. Out-Patient

Travel to Albuquerque 110 trips X \$300 each	\$33,000
Travel to Los Alamos 48 trips X \$50 each	<u>2,400</u>
Subtotal	\$35,400

III. Per Diem and Housing

Skin 18 pt's X 26 days X \$20	\$ 9,360
Head & Neck 24 pt's X 42 days X \$20	<u>20,160</u>
Subtotal	\$29,520

IV. Diagnostic Tests *

Laboratory	\$ 2,500
X-Ray	1,750
Incidental	<u>2,030</u>
Subtotal	\$ 6,280
Grand Total	\$200,000

*Charges incurred at participating hospitals

DO NOT TYPE IN THIS : CE-BINDING MARGIN

B. Supplemental information regarding ITEMS in the proposed Budget for the next period which require explanation or justification. (See instructions)

Almost all items in this budget were explained in the original application, and reflect an extension of activity already approved by the NCI into Year 3 of the grant. A larger proportion of the funds are designated for personnel costs, since the University of New Mexico Personnel Department is projecting a 12 percent salary increase for the coming fiscal year, as opposed to the 5 to 10 percent originally projected.

Equipment funds are designated for the purposes approved by the NCI, although Radiation Therapy equipment funds are designated in the Biomedical Physics budget for the coming year, because these items will be operated and maintained by that group. A portion of the Radiation Therapy equipment funds are designated for use at the LAMPF Biomedical Facility, where we need additional clinical equipment to handle our anticipated patient load. Since the pion program is experimental, we are not permitted to charge patients for their care there. Thus, there is no patient revenue from which to purchase clinical equipment for the Biomedical Facility at LAMPF. A portion of the equipment funds designated for Diagnostic Radiology have been re-assigned to Clinical Operations, where we need partial support for equipping our operating room. The outpatient surgical suite has not been opened because of lack of equipment funds. Since we need to perform various endoscopic procedures, radioactive applications and implants, and biopsies for patients participating in the RTOG, SWOG, and pion protocols, we feel it is appropriate to request partial support for surgical equipment under this grant.

Travel assigned to the Administration budget is that required for senior staff participation in scientific meetings, meetings with NCI officials, and similar travel. Funds assigned to Biomathematics are for trips to Buffalo, New York, for coordination with the Radiation Therapy Oncology Group statistical support unit on data collection requirements and form design for the pion protocols. Other funds are for transportation of our radiotherapy and clinical support staff to and from Los Alamos for participation in the pion clinical trials and for travel by Tumor Registry staff to collect epidemiological data.

The other expense category includes \$35,000 for medical liability insurance for the Center and employees not covered by individual insurance under the UNM School of Medicine blanket policy. This is the estimated cost of 50 percent of our policy premium for the coming year. The other expense category also includes \$252,113 for the Los Alamos Scientific Laboratory subcontract, which is the amount originally recommended by the NCI Review Council plus the amount projected for LASL indirect costs.

SECTION III

SECTION III—FISCAL DATA CURRENT BUDGET PERIOD (USUALLY 12 MONTHS)	FROM	THROUGH	GRANT NUMBER
	1 May 1975	30 April 1976	5-POI-16127-02

The following pertains to your CURRENT PHS budget. Do not include cost sharing funds. This information in conjunction with that provided on Page 2 will be used in determining the amount of support for the NEXT BUDGET PERIOD.

A. BUDGET CATEGORIES		CURRENT BUDGET (As approved by awarding unit) (1)	ACTUAL EXPENDITURES THRU 12/30/75 (Report Date) (2)	ESTIMATED ADDITIONAL EXPENDITURES AND DEBITATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD (3)	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3) (4)	ESTIMATED UNENCUMBERED BALANCE (Subtract Col. 4 from Col. 1) (5)
Personnel (Salaries)		379,767	250,534	123,284	373,818	5,949
Fringe Benefits		60,799	29,637	30,174	59,811	988
Consultant Costs		6,748	6,024	8,356	14,380	(7,632)
Equipment		309,675	50,470	259,205	309,675	0
Supplies		32,421	31,597	824	32,421	0
TRAVEL	Domestic	12,000	9,221	2,779	12,000	0
	Foreign	0	0	0	0	0
Patient Costs		50,000	913	49,087	50,000	0
Alterations and Renovations		75,000	75,000	0	75,000	0
Other		249,228	95,578	152,955	248,533	695
Total Direct Costs		1,175,638	548,974	626,664	1,175,638	0
Indirect Costs (if included in award)		200,078	120,775	79,303	200,078	0
TOTALS →		\$1,375,716	\$669,749	\$705,967	\$1,375,716	\$0

Use space below to:

B. List all items of equipment purchased or expected to be purchased during this budget period which have a unit cost of \$1000 or more.

C. Explain any significant balance or deficit shown in any category of Column 5.

D. List all other research support for Principal Investigator by source, project title, and annual amount.

E. See Page 4 a.

C. See Page 4 c

D. PreClinical Studies of Pion Radiotherapy
Grant NCI 5 - POI - CA 14052 - 03
Funding For Year 3 \$758,919.00
Renewal Application is currently under review

Los Alamos Scientific Laboratory: Professional Services
Contract to Dr. M. Kligerman as Asst. Director for Radiation Therapy at LASL.
Annual funding at \$25,000.00.

B. Equipment**1. Equipment purchased during grant year (Value over \$1,000)****a. Biomathematics**

16K Parity Memory	\$2,501
-------------------	---------

b. Core Morphology

Diamond Knife and 4 Microtome Knives	\$1,650
--------------------------------------	---------

c. Diagnostic Radiology/Nuclear Medicine

Lymphangiography Equipment (50% of total cost of \$55,800)	\$27,900
--	----------

Mammography Unit (approximately 36% of total cost of \$39,915)	<u>12,410</u>
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Subtotal	\$40,130
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d. Biomedical Physics

Electronic Components and Equipment	\$1,500
-------------------------------------	---------

Machine Shop Equipment	1,600
------------------------	-------

Hard-Copy Scope Output	<u>4,500</u>
------------------------	--------------

Subtotal	\$7,600
----------	---------

Total Equipment Purchased	\$52,061
---------------------------	----------

2. Equipment to be purchased (Value over \$1,000)**a. Biomathematics**

Dial-up Communications Ports for Multi-Plexor Channel	\$2,250
---	---------

Communications Modems for Local Terminals	2,300
---	-------

Communications Modems for Two Dial-up Ports	
---	--

KG-11A Communication Arithmetic Unit Expansion Cabinet	2,949
--	-------

Communications Modem	
----------------------	--

Subtotal	\$7,499
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b. Core Morphology

Autotechnicon Ultra Model 3A with Mobile Base Cabinet	\$5,500
A.O. Microscope XH Series	<u>1,800</u>
Subtotal	\$7,300

c. BioMedical Physics

Scaler Timer	\$1,100
Interface for Scanning Densitometer	<u>1,000</u>
Subtotal	\$2,100

d. Radiation Therapy (for Clinical Research at Los Alamos
carry-over from Year 1)

Treatment Couches (2)	\$123,255
Simulator	92,210
End Window X-ray Tube and Generator	<u>15,000</u>
Subtotal	\$230,465

Total Equipment to be Purchased \$247,364

C. Explanation of Overages and Deficits in Current Budget Period.

General. All overages and deficits have been adjusted through requests to the prior approval board. Some of these requests have not had sufficient time to be approved and therefore do not reflect in the "Current Budget Period" report.

1. The surplus in salary will be transferred to the consultant category. This was necessary to cover the expenses of Mrs. Kay Marr, acting Business Manager, Dr. Charles Kelsey's work prior to his employment, and Dr. Jose Sala's work also prior to his employment.
2. The fringe benefits surplus is a direct result of the salary overage and will be eliminated when salaries are reduced.
3. The consultant category is presently at a deficit because of the reasons mentioned above. This will be reduced to zero by transferring monies from "Other" and "Salaries".

SECTION IV

APPLICANT: REPEAT GRANT NO. (AS SHOWN ON PAGE 1) →	CI: NUMBER	
SECTION IV—SUMMARY PROGRESS REPORT	5-P01-CA-16127-02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial) Kligerman, Morton M., M.D.	PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION UNM Cancer Research and Treatment Center	FROM 1 May 1975	THROUGH 1 January 1976
TITLE (Repeat title shown in Item 1 on first page) Cancer Research and Treatment Center Program		

1. List publications: (a) published and not previously reported; (b) in press. Provide five reprints if not previously submitted.
2. List all additions and deletions in professional personnel and any changes in effort.
3. Progress Report. (See Instructions)

1. PUBLICATIONS

- a. Amols, H.I.; Dicello, J.F.; and Lane, T.F. "Microdosimetry of Negative Pions," Proceedings of the Symposium on Microdosimetry (Abstract), Los Alamos Scientific Laboratory Report (LA-UR-75-537), 1975.
- b. Amols, H.; Dicello, J.; Lane, T.; Pfeufer, G.; Helland, J.; and Knowles, H. "Microdosimetry of Negative Pions at LAMPF," Los Alamos Scientific Laboratory Report (LA-UR-75-32), 1975.
- c. Antoine, J.E. "Diagnostic Oncologic Imaging," Current Problems in Radiology, Vol. 4, No. 6, November-December, 1974.
- d. Bearden, J.D.; Coltman, C.A.; Moon, T.E.; Costanzi, J.J.; Saiki, J.H.; Balcerzak, S.O.; Rivkin, S.E.; Morrison, F.S.; Lane, M.; and Spigel, S.C. "Combination Chemotherapy Using Cyclophosphamide, Vincristine, Methotrexate, 5-Fluorouracil, and Prednisone in Solid Tumors," submitted for publication to Cancer, 1975.
- e. Bodey, G.P.; Coltman, C.A.; Freireich, E.J.; Bonnet, J.D.; Gehan, E.A.; Haut, A.B.; Hewlett, J.S.; McCredie, K.B.; Saiki, J.H.; and Wilson, H.E. "Chemotherapy of Acute Leukemia in Adults: Comparison Between Arabinosyl Cytosine Alone and In Combination with Vincristine, Prednisone and Cyclophosphamide," Arch. Int. Med. 133: 1975.
- f. Dicello, J.F. "Dosimetry of Pion Beams," Proceedings, International Particle Radiation Therapy Workshop, Key Biscayne, Florida, October 1-3, 1975, in press.
- g. Doberneck, R., and Antoine, J.E. "Deglutition After Resection of Oral, Laryngeal and Pharyngeal Cancers," Surgery 75: 87-90, 1974.
- h. Gottlieb, J.A.; Baker, L.H.; Burgess, M.A.; Sinkovics, J.G.; Moon, T.; Bodey, G.O.; Rodriguez, V.; Rivkin, S.E.; Saiki, J.H.; and O'Bryan, R.M. "Sarcoma Chemotherapy," Cancer Chemotherapy Fundamental Concepts and Recent Advances, Proceedings of the 19th Annual Clinical Conference, University of Texas System Cancer Center. (Houston: M.D. Anderson Hospital and Tumor Institute, November 1974.)
- i. Herzon, F., and Antoine, J.E. "Mega Antrum," Annals of Otolaryngology, Rhinology, and Laryngology, in press, 1975.

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- j. Kligerman, Morton M. "Irradiation of the Primary Lesion of the Rectum and Rectosigmoid," Journal of the American Medical Association 231: 1381-1384, 1975.
- k. Kligerman, M.M. "Preoperative Radiation Therapy in Rectal Cancer," Cancer 36: 691-695, 1975. (Paper presented at the National Conference on Advances in Cancer Management, New York, 1974.)
- l. Kligerman, M.M.; Dicello, J.F.; Davis, H.T.; Thomas, R.A.; Sternhagen, C.J.; Gomez, L.; and Petersen, D.F. "Initial Comparative Response of Experimental Tumors to Peak Pions and X-rays," Radiology 116: 181-182, 1975.
- m. Kligerman, Morton M. "Meson Radiobiology and Therapy," Proceedings, Seventh International Conference on Cyclotrons and Their Applications. (Zurich, Switzerland, August 1975), in press.
- n. Kligerman, M.M. "Pion Radiation Therapy," Proceedings, International Particle Radiation Therapy Workshop, Key Biscayne, Florida (Chicago: American College of Radiology), in press, and Proceedings, LAMPF User's Group Meeting, November 10, 1975 (Los Alamos: Los Alamos Scientific Laboratory), in press.
- o. Kligerman, M.M.; Knapp, E.A.; and Petersen, D.F. "Biomedical Program Leading to Therapeutic Trials at Los Alamos," Cancer 36: 1675-1680, 1975.
- p. Kligerman, M.M., and Sternhagen, C.J. "Radiation Oncology," In Physiopathology of Cancer, ed., F. Homburger, 1975, in press. (Not included due to bulk.)
- q. Kligerman, M.M.; West, G; Dicello, J.F.; Sternhagen, C.J.; Barnes, J.E.; Loeffler, K.; Dobrowolski, F; Davis, H.T.; Bradbury, J.N.; Lane, T.F.; Petersen, D.F.; and Knapp, E.A. "Initial Comparative Response to Peak Pions and X-rays to Normal Skin and Underlying Tissue Surrounding Superficial Metastatic Nodules," American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine, in press. (Paper presented at the 57th Annual Meeting of the American Radium Society, San Juan, Puerto Rico, May 1975.)
- r. Knapp, E.A. "Physical Properties of Charged Particle Beams for Use in Radiotherapy," Proceedings, International Particle Radiation Workshop, in press. (Key Biscayne, Florida, October 1-3, 1975).
- s. Kopperman, M., and Antoine, J.E. "Primary Lymphangioma of the Calvarium," American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine 121: 118-120, 1974.

- t. Kornfeld, M.; Appenzeller, O.; Saiki, J.H.; and Troup, G.M. "Sea-Blue Histiocytes and Sural Nerve in Neurovisceral Storage Disorder with Vertical Ophthalmoplegia," Journal of Neurological Sciences 25: 291-302, 1975.
- u. Paciotti, M.A.; Bradbury, J.N.; Helland, J.A.; Hutson, R.L.; Knapp, E.A.; and Rivera, O.M. "Tuning of the First Section of the Biomedical Channel at LAMPF," Proceedings, Particle Accelerator Conference, March 12-14, 1975.
- v. Robbins, S.E., and Crawford, D.M. "Nursing and the Pion Project," American Journal of Nursing, submitted for publication.
- w. Saiki, J.H. "White Blood Cell Abnormalities," In Problem-Oriented Medical Diagnosis, ed., H. Harold Friedman and cons. ed., Solomon Papper. (Chicago: Little, Brown, & Company, Inc., 1975.)
- x. Sternhagen, C.J.; Powell, T.D., Key, C.R.; and Buechley, R. "Uranium Miners' Lung Cancer Incidence in New Mexico Region," Health Physics, in press. (Abstract).
- y. Todd, P.; Shonk, C.R.; West, G.; Kligerman, M.M.; and Dicello, J. "Spatial Distribution of Effects of Negative Pions on Cultured Human Cells," Radiology 116: 179-180, 1975.
- z. "Cancer Research with Negative Pions," #GAY-279, documentary film produced by Los Alamos Scientific Laboratory. (Copy on file with Dr. Francis J. Mahoney, National Cancer Institute.)

2. PERSONNEL CHANGES**a. Additions to Staff**

Berardo, P., Ph.D.	Physicist, (LASL employee)
Bleakly, M., R.N.	Head Nurse (Acting)
Bordin, G.M., M.D.	Assistant Professor, Department of Pathology, UNM School of Medicine
Crawford, D.M., R.N.	Nurse
Damron, J.R., M.D.	Diagnostic Radiologists, CRTC, and Assistant Professor, Department of Radiology, UNM School of Medicine
Furman, J.	Business Manager
Jojola, S.	Business Manager
Kelsey, C.R., Ph.D.	Chief, Biomedical Physics, CRTC, and Professor and Chief, Biomedical Physics Division, Department of Radiology, UNM School of Medicine
Lane, R.G., Ph.D.	Radiological Physicist, CRTC, and Assistant Professor, Department of Radiology, UNM School of Medicine
Powell, T.D., M.D.	Radiation Therapist, CRTC, and Assistant Professor, Department of Radiology, UNM School of Medicine
Sala, J.M., M.D.	Medical Director and Chief, Radiation Oncology Section, CRTC, and Professor, Department of Radiology, UNM School of Medicine
Selheimer, C., R.N.	Protocol Nurse
Smith, A.F., Ph.D.	Radiological Physicist, CRTC, and Assistant Professor, Department of Radiology, UNM School of Medicine
Young, Alma, M.D.	Assistant Professor, Department of Ob- stetrics and Gynecology, UNM School of Medicine
Yuhas, J.M., Ph.D.	Associate Director for Biology, CRTC, and Associate Professor and Chief, Radiobiology Division, Department of Radiology, UNM School of Medicine
Yurconic, M.	Chief Research Laboratory Technologist

b. Resignations/Terminations

Barnes, J.E., Ph.D.	Radiological Physicist
Jojola, S.	Business Manager
Lee, W.	Business Manager
Kelly, H.M.	Administrator
Robbins, S.E., R.N.	Nurse, Clinical Operations Administrator
Waddington, E., R.N.	Nurse

3. SUMMARY PROGRESS REPORT

a. Objectives

The objectives of this project are three-fold:

- (1) To establish at the University of New Mexico Cancer Research and Treatment Center the necessary core clinical, diagnostic, and laboratory facilities for support of human trials of negative pi mesons, using the proton linear accelerator at the Los Alamos Scientific Laboratory, and other clinical investigations and laboratory research programs.
- (2) To conduct human radiobiology studies, pilot trials, and eventually Phase III protocols for human trials of Pion radiation therapy at the LASL Clinton P. Anderson Meson Physics Facility, and
- (3) To participate in clinical investigations of the Radiation Therapy Oncology Group, Southwest Oncology Group, and other national cooperative organizations, as appropriate, and to initiate clinical investigations and laboratory research programs directed at improved cancer management for citizens of New Mexico and throughout the nation.

This report details progress toward those goals during the period 1 May 1975 to approximately 1 January 1976, and presents goals for Grant Year 3.

b. Current Studies

(1) Core Operations

(a) Administration. The principal development administratively has been the appointment of three new heads of units: an Associate Director for Biology, a Medical Director, and a Chief of Radiation Oncology, and a Chief of Biomedical Physics. In addition, the administrative function has been strengthened by a reorganization and the appointment of a new Business Manager. Also, the fiscal and management relations with LASL have been clarified and are operating smoothly.

(b) Biomathematics. The Biomathematics Division, redesignated the Biometry Division, has continued refinement of the protocol support function, computerized treatment planning, and financial systems development and implementation. Each CRTC case is reviewed at the time of the first patient visit for protocol accession, and procedures have been implemented for randomization, data collection, statistical analysis, and liaison with physicians and patients. Computerized treatment planning is operational, although some refinements are under way. Financial systems implemented include a billing system and a general ledger system.

A computerized patient record system is under development.

Statistical analysis of the animal and human radiobiology studies conducted at LAMPF has continued, including assistance in development of quantitative histological examination techniques for analysis of tissue samples. Data collection

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requirements for the pion protocols are being defined, in collaboration with Dr. Marvin Zelen of the Radiation Therapy Oncology Group (RTOG) statistical headquarters in Buffalo, New York.

(c) Core Morphology. Surgical pathology materials for some 220 patients have been examined and an additional 700 cases were seen in consultation with other pathologists from the city, state, or other states. Diagnostic electron microscopy was used to better define and more precisely classify neoplasms, the morphology of which was ambiguous at the level of light microscopy. Approximately one-fifth of these cases were at the CRTC, while the remainder were consultations for pathologists outside the Center.

In support of clinical investigations, the Core Morphology staff reviewed pathology materials for patients participating in the pion human radiobiology studies and the patients accessed on RTOG, Southwest Oncology Group (SWOG), and other protocols. A basic study plan was developed and implemented to apply quantitative histological examination techniques to tissues obtained at autopsy from patients participating in the tests of the comparative effects of pions and x-rays on metastatic nodules to the skin and the surrounding and underlying normal tissues.

(d) Basic Research. Although not funded by this grant, a basic research program is a goal of the CRTC and laboratory space for basic research was constructed on the third floor of the CRTC. Dr. John M. Yuhas has been appointed Associate Director for Biology. At the outset, the biology research program will concentrate on the preclinical studies of pion radiotherapy, leading to full-scale clinical trials, and on the use of radioprotective and radiosensitizing drugs in radiotherapy, on the nature of the induction of lung cancer, and on the factors which determine the spread of cancer throughout the body. The first project is being supported by Grant No. 5-P01-CA-14052-03, and grants-in-aid have been obtained or applications submitted for the second two. The fourth project will be proposed for funding in a separate research application in the near future. Pilot studies in the latter three areas are currently being supported by institutional funds.

Approximately \$65,000 in research equipment has been purchased for installation in the biology laboratories, and an additional \$100,000 has been devoted to development of the third-floor mouse holding area. Plans are under way for development of a larger animal facility in the basement of the CRTC for housing multiple species.

Negotiations are under way with potential research staff members who can undertake studies of immunological defenses against cancer, the nature of cancer formation, and defects in normal control mechanisms which lead to the appearance of cancer. Basic scientists will work closely with clinicians in the CRTC in attempting to provide the best possible cancer management for patients.

A battery of tests systems has been developed that will allow accurate quantitation of the effects of pions in a number of normal tissues, and baseline studies of the effects of control x-irradiation on critical normal structures are yielding new short-term assays which will provide earlier answers to radiobiological problems prior to clinical application of pions.

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(e) Clinical Operations. The CRTC opened its outpatient clinical facilities in January 1975. Patients who need hospitalization are admitted to the Bernalillo County Medical Center, adjacent to the CRTC, or to other Albuquerque hospitals. An eight-bed research unit is under construction at BCNC, partially supported by an allocation of \$75,000 for alterations and renovations under this grant.

A total of 13,087 patient visits have been recorded at the CRTC for the period January 2, 1975 to December 31, 1975. The number of monthly visits has increased from 271 in January to 1273 in December of 1975, with a high of 1749 recorded in October. New radiotherapy cases seen at the Center in Calendar Year 1975 totaled 405.

In addition to the on-going multidisciplinary joint clinics operation, specialty clinics at the CRTC include gynecological clinics, colposcopy clinic, and genito-urinary clinic. Equipment has been ordered for the outpatient surgical suite, and the unit will become operational soon.

Approximately 46 percent of CRTC patients are Bernalillo County residents, while 49 percent are State residents of counties other than Bernalillo and 5 percent are residents of other States. The latter percentage is expected to escalate when the CRTC again begins accessing cases for the pion program.

The CRTC Outreach Program, under which multidisciplinary physician teams visit other communities to participate in joint tumor conferences with local physicians, expanded to two additional cities, Las Cruces and Santa Fe, this year. The program now encompasses five communities (including Los Alamos, Gallup, and Roswell, in addition to the two above), and plans are to further expand the program when the CRTC contract with the NCI Division of Cancer Control and Rehabilitation for support of a Statewide Cancer Control Program is negotiated.

(2) Clinical Investigations

(a) Operation of the Biomedical Channel. The biomedical pion channel at LANP entered a planned shutdown phase for repairs and adjustments on December 21, 1974. The shutdown was planned to last six months, but has extended much longer than originally anticipated. The accelerator is operating well at this time, but the additional shielding required to protect personnel in the experimental theaters from radiation resulting from higher beam intensities is not yet in place. It is expected that the channel will be reactivated in early February. The beam was restricted to an intensity of 10 microamps last year to avoid accumulation of high levels of induced radiation in the accelerator tunnel which would prevent completion of the planned repairs and adjustments. The accelerator is expected to be reactivated at an intensity of 10 microamps so that comparison measurements can be made. The intensity will then be escalated to 100 microamps within two months, and over the course of the year to 50 percent of the design intensity of 1 milliamp.

During the shutdown period, preparation for patient treatment has continued so that large volumes can be irradiated when the beam is reactivated. This has included completion of the high-intensity target station, installation of a helium atmosphere container for dose distribution enhancement, installation of final slit assemblies, completion of computer programming required for automatic set-up of dose criteria, a study of channel performance from experimentally generated

magnetic tapes taken with the multiwire proportional counter system, development of an accurate beam model for treatment planning purposes, development of beams suitable for large volume static dose distributions, installation of a dynamic range shifter for swept beam irradiations, and completion of a computerized dosimetry system.

Unless beam is needed immediately for a particular biology problem, the beam time upon channel reactivation will be devoted entirely to physics for the first two months, so that baseline measurements and reliability can be established.

(b) Radiation Therapy Clinical Investigations. In the past 12 months, the Clinac 18 has been operating with minimum down-time, and a total of 405 new radiotherapy cases have been accessed by the CRTC. RTOG accessions have been sufficient to earn full membership in that cooperative study group. The cobalt unit at Lovelace-Bataan Medical Center is being acquired by the CRTC.

Data from the first human radiobiology tests at LAMPF were analyzed to determine radiobiological effectiveness of the pion beam as compared with 140 kv x-rays, in terms of response of normal tissues surrounding and underlying tumor nodules metastasized to the skin. An optical density measurement technique, applied to photographs of the irradiated areas, yielded an RBE for skin erythema of 1.43 at an optical density of 0.23. An attempt was made to assess intermediate-term reaction on tissue specimens taken at autopsy, using the quantitative histologic method of Chalkley counts. No significant differences were apparent among untreated skin, x-ray-treated skin, or pion-treated skin at five months after treatment.

(c) Cancer Chemotherapy Clinical Investigations. Participation by the UNM CRTC and UNM-Affiliated Hospitals in the Southwest Oncology Group (SWOG) is supported by NCI Grant No. R01-CA-12213-05 (J. H. Saiki, M. D., Principal Investigator), and by this grant. The Medical Oncology Section of the CRTC is seeing an average of 23 new patients per month, or approximately 276 new patients per year. Under the Leukemia-Lymphoma Program established five years ago at UNM, community physicians participate with the UNM group in the management of their patients on SWOG protocols. Currently, more than 90 percent of children with acute leukemia throughout the State, 50 percent of adults with acute leukemia, and 60 percent of patients with malignant lymphoma are treated under this program. During the first eight months of Calendar Year 1975, the UNM SWOG accessions totaled 90 patients and was expected to reach 135 by the end of the year, as compared with 104 for Calendar Year 1974. Approximately half of these cases were acute leukemias and lymphomas, with the remainder distributed among various solid tumors.

To provide a more comprehensive and multidisciplinary approach in the SWOG protocols, the CRTC has the active participation of chemotherapists, radiotherapists, and a gynecological oncologist, representing the CRTC, the UNM School of Medicine, UNM-Affiliated Hospitals, and various community hospitals. In addition to committee responsibilities within SWOG, UNM members developed protocols for the administration of 5-Azacytidine in acute leukemia, galactratol in multiple myeloma, and hexamethylmelamine in multiple myeloma, and defined the role of radiotherapy in the management of central nervous system metastasis from malignant melanoma. A repository for evaluation of tissue in all Phase III sarcoma studies was also established by UNM and the M. D. Anderson Hospital and Tumor Institute to allow

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uniformity of diagnosis, and to more closely evaluate and correlate the relationship between response, type of chemotherapy, and histologic type.

(d) Diagnostic Radiology and Nuclear Medicine. During the current grant year, diagnostic imaging equipment was installed in the Diagnostic Oncologic Imaging Section of the CRTC, adjacent to the Radiology Department of BCMC. The following equipment items are now in service: lymphangiography, mammography, polytomography, ultrasonography, magnascanner 1000, dynacamera 4/12, and thermography. An EMI scanner is available at BCMC for CRTC patients requiring brain studies. This unit and the ultrasound unit have been helpful in assessing tumor regression, as well as in tumor localization. It is expected that the ultrasonography unit will be linked with the treatment planning computer to provide advanced treatment planning capability for the pion clinical trials.

Analysis of data from two research projects dealing with lymph node localization is continuing and research papers are in preparation. These studies are providing information important to tumor localization for the pion clinical trials.

(e) Biomedical Physics. Dr. Charles R. Kelsey was appointed Chief of Biomedical Physics in August 1975, and two new biomedical physicists, Dr. Alfred R. Smith and Dr. Richard N. Lane, were appointed to the staff in September 1975. Physics support for conventional clinical radiotherapy has been under way with the Clinac 18 linear accelerator since it became operational in January 1975. Requirements for moving the Lovelace-Bataan cobalt unit to the CRTC have been established by the physics group, and a new base has been ordered. A videotape documentary will be produced when the cobalt unit is dismantled and moved to the CRTC for educational purposes. Computerized treatment planning has been implemented for patients being treated with the CRTC's Clinac 18 and orthovoltage unit, and the Lovelace-Bataan cobalt unit.

Specifications have been defined for the pion treatment couch and an identical couch to be placed in the simulator room at the LANPF Biomedical Facility. The couch design requires vertical and transverse motions, as well as the ability to rotate the patient about an axis parallel to the floor and perpendicular to the pion beam. The top section must be capable of transfer from the staging area for patient immobilization and set-up to the treatment room to allow rapid application of the pion beam.

Acquisition of the couch will allow definition of simulator requirements. Current plans are to link simulation with computerized optimization of treatment planning for patients selected for pion or conventional radiotherapy. The simulation system will require two image intensifier tubes and two x-ray tubes to obtain simultaneous anterior-posterior and cross-table lateral views of the anatomy. The system will be linked to the treatment planning computer, so that an image of the selected treatment plan can be superimposed on the fluoroscopic image of the patient's anatomy.

(3) Tumor Registry

Core support for epidemiology activities of the New Mexico Tumor Registry is provided under this grant, although major support for the Registry comes

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from a contract (No. N01-CP-33344) from the NCI Biometry Branch. The Registry is a participant in the Surveillance, Epidemiology, and End Results (SEER) Program, and serves more than 60 hospitals and clinics, providing a population-based cancer registry for the New Mexico and Navajo Reservation.

There are marked variations in cancer patterns among the region's major ethnic groups. Population definitions have been guided by comparisons between New Mexico and other states, especially recent mapping by county. New Mexico appears to have low lung cancer rates for males but not for females. For stomach cancer, both sexes show high rates, particularly in counties with a larger proportion of Spanish persons. A computer program, based on the previously developed Spanish-surname program, has been implemented to subdivide both the "Anglo" and "Spanish" groups. State population redefinitions by these subdivisions are in progress, as are county level population estimates for 1975.

A subcontract is currently in progress with the Los Alamos Scientific Laboratory to participate in a six-month planning effort aimed at designing and conducting a follow-up study of all plutonium workers in the United States. Research proposals have been submitted for studies of cancer incidence in New Mexico Indian and Spanish population groups of low genetic diversity and of the marked deficit of lung cancer in Spanish-American males (whose smoking habits, although not well documented, do not appear different from their Anglo neighbors who approach U. S. lung cancer rates).

c. Research Objectives for Year 3

Research objectives for each program component are contained in Attachment A (Detailed Progress Report). General objectives for Year 3 are:

- (1) To expand CRTC participation in national cooperative study groups; to initiate pion clinical tests with skin, head and neck, and other accessible sites at increased levels of beam intensity; and to further expand the potential study population available for the pion clinical trials.
- (2) To expand and refine the support systems necessary to widen implementation of the pion and other national research protocols (particularly bio-mathematics, core morphology, and diagnostic radiology support systems).
- (3) To improve conventional radiotherapy capabilities at the CRTC and continued development of complementary systems at LAMPF, in such areas as computerized treatment planning, localization (of tumors and body inhomogeneities), simulation and verification.
- (4) To expand the base of clinical activities at the Center through establishment of new specialty clinics, increased participation by UNM and private-practice physicians throughout the State, continued expansion of the CRTC Outreach Program, initiation of continuing education programs for private physicians, and improved clinical services.
- (5) To analyze mortality and morbidity data in further detail by ethnic group to take into account factors not yet addressed, such as altitude and occupational patterns.

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d. Significance

The significance of this program lies mainly in two areas:

(1) The CRTC is conducting at LASL the first therapeutic tests of negative pi mesons in the world, and are beginning to generate a body of knowledge that will be valuable not only in treatment of cancer patients (in the event pi mesons prove advantageous), but which in any case will be valuable to other installations in the world which are investigating or proposing to investigate the use of subatomic particles in cancer therapy. The CRTC is also contributing to the body of knowledge of the efficacy of conventional radiation through participation in national cooperative study groups.

(2) The establishment of the CRTC to plan, support, and implement the pion trials has also provided a medium for establishing a Center designed to serve as a model for delivery of cancer diagnosis, treatment, and follow-up services to the citizens of a sparsely settled state.

The medical and scientific interest around the country in the pion clinical trials, and the active participation of radiation therapists and scientists from various other institutions, have helped to infuse interest in cancer research programs of all types in New Mexico and are creating opportunities for other kinds of cancer research at the CRTC and LASL not necessarily related to radiation therapy. Similarly, this interest has carried over to the medical community and the citizens of our state. Their acceptance of the CRTC, as evidenced by our rapidly expanding caseload and invitations to expand our outreach program, is helping to ensure participation by New Mexico cancer patients in the pion clinical trials and other clinical research programs directed at improved cancer management.

e. Certification

The undersigned agrees to accept responsibility for the scientific and technical conduct of the project and for provision of required progress reports if a grant is awarded as a result of this application.

23 Jan 76
Date

M. Kligerman
Morton M. Kligerman, M. D.
Principal Investigator/Program
Director

• ATTACHMENT A
DETAILED PROGRESS REPORT

DETAILED PROGRESS REPORT1. OBJECTIVES

The objectives of this project are three-fold:

- a. To establish at the University of New Mexico Cancer Research and Treatment Center the necessary core clinical, diagnostic, and laboratory facilities for support of human trials of negative pi mesons, using the proton linear accelerator at the Los Alamos Scientific Laboratory, and other clinical investigations and laboratory research programs.
- b. To conduct human radiobiology studies, pilot trials, and Phase III clinical trials of pion radiation therapy at the LASL Clinton P. Anderson Meson Physics Facility.
- c. To participate in clinical investigations of the Radiation Therapy Oncology Group, Southwest Oncology Group, and other national cooperative organizations, as appropriate, and to initiate clinical investigations and laboratory research programs directed at improved cancer management for citizens of New Mexico and throughout the nation.

This report details progress toward those objectives during the period 1 May 1975 to approximately 1 January 1976, and presents goals in each of the core support and research areas for Grant Year 3.

2. CURRENT STUDIESa. Core Operations

(1) Administration. Dr. Jose M. Sala, formerly Chief of Radiation Therapy at the Ellis Fischel Hospital and more recently Chief of Radiation Oncology at the Cox Medical Center in Missouri, has joined the staff to become Chief of Radiation Therapy. He is also appointed Medical Director of the Cancer Center. Dr. John M. Yuhas of Oak Ridge National Laboratories has started as Associate Director for Biology, and Dr. Charles Kelsey has begun as Chief of Biomedical Physics.

Examination of the administrative structure of the Cancer Center including an internal audit, demonstrated several areas of weakness. The following changes have corrected the administrative side. The position of Administrator has been eliminated. His authorities have been dispersed among the several section and division chiefs, since it was discovered that the lay Administrator was incapable of dealing with the several highly specialized activities. Dr. J. M. Sala, as Medical Director, coordinates clinical activities; Dr. J. M. Yuhas, Associate Director for Biology, manages biological research at the Cancer Research and Treatment Center, as well as the pion preclinical studies carried out at the Health Research Laboratories of the Los Alamos Scientific Laboratory. Dr. Charles Key is Medical Director of the Tumor Registry. New space is currently being built in the basement of the Cancer Center, which enlarges the Tumor Registry work area. Ms. Stephany Wilson has been promoted to the position of Special Assistant to the Director and

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Associate Administrator for Research and Communications. Finally a new fiscal officer, Mr. John Furman, has been appointed. Under his direction and in cooperation with Mr. Robert Barnard, Chief of the Biometry Division, the business side of patient management is being placed in order, and budgetary control has been greatly strengthened.

At the suggestion of Dr. Richard Taschek, Associate Director for Research at LASL, quarterly meetings between the CRTC and LASL have been instituted. Attending these are Dr. Kligerman, Ms. Wilson, Mr. Furman, Dr. Kelsey, Dr. Yuhas, and Mr. Warren Baur, Associate Comptroller for Health Sciences, UNM, as well as Dr. Taschek, the two principal leaders for pion project affairs at Los Alamos, and appropriate LASL fiscal personnel. This has resulted in the elimination of procedural misunderstandings which developed from certain operational characteristics of ERDA. Currently, with these meetings and the basing of Ms. Wilson in Los Alamos, the interrelationship of CRTC-UNM and LASL has become a close and effective one.

(2) Biomathematics. The Biomathematics Division has been redesignated the Biometry Division, and Mr. Robert Barnard has been appointed Chief of that division. During this grant year, division efforts have been directed at protocol support, computerized treatment planning, and financial systems development and implementation. Development of a computerized patient record system for protocol cases has been initiated.

The protocol function, led by the Protocol Nurse, Ms. Carol Selheimer, assigned to the Biometry Division, has been defined and refined such that an efficient organized effort is established. Each new patient's record is reviewed for possible protocol accession at the time of the first patient visit, with the result that in the first year of clinic operation, Radiation Therapy Oncology Group (RTOG) accessions have been sufficient to earn full membership of the Center in that group. This will be described in greater detail under the Clinical Investigations portion of this report, but the responsibility for identifying potential protocol patients, assisting physicians in explaining research studies to patients, obtaining patient consent, and completing the necessary randomization procedure and study forms is assumed by the Protocol Nurse under physician guidance. This has reduced physician effort for such activity by 80 percent. The Biometry Division is also keeping detailed records on protocol patients and providing periodic statistical reports on case accession and outcome.

The data analysis requirements for the pion clinical trials are being defined and coordinated with Dr. Marvin Zelen of the RTOG statistical analysis group in Buffalo, New York. The biostatistician to be employed by the Biometry Division will work with Dr. Zelen's group.

The Chief of the Biometry Division is a member of the Biomedical Control Committee at the Los Alamos Scientific Laboratory Clinton P. Anderson Meson Physics Facility (LAMPF). This enables the CRTC Biometry group to have continuous input into the development and implementation of software and hardware for the pion biomedical channel at LAMPF.

Statistical analysis of the animal and human radiobiology studies conducted at LAMPF has continued in this grant year, including assistance to the Pathology Section in development and documentation of quantitative histological examination techniques for analyzing tissue samples from patients and animals after

irradiation with x-rays and pions.

Treatment planning programs written by Dr. John Cunningham of the Princess Margaret Hospital in Toronto, have been adapted for use on the CRTC PDP 11/40 computer and are operational. Additional programming is planned to improve the ease of use of these programs by the CRTC Biomedical Physics Section.

The Biometry Division has also designed and implemented a computerized billing system for the CRTC. Forty programs were written for this system and additional reporting programs can be added on demand. A general ledger system has also been written and is being implemented at this time. Twelve programs have been written for this system. The billing system includes an informational retrieval system for fast random access of records stored in computer files. This system will also be utilized in the computerized medical records system now under development and expected to be completed by the end of the current grant year. Initial implementation of the computerized medical records program will include 15 programs for maintenance and reporting. This billing and ledger system with its ready cost-accounting capability ensures appropriate allocation of charges to the several sources of funds which comprise the total CRTC budget.

(3) Core Morphology. The Core Morphology Laboratory was under construction during the first grant year and was ready for occupancy in February 1975. Equipment and supplies were ordered and installed and the necessary technical staff recruited. Dr. William C. Black was appointed Chief of the Pathology Section for the CRTC and retained his joint appointment as Associate Professor of Pathology with the UNM School of Medicine. During the current grant year, Dr. Gerald Bordin joined the School of Medicine Department of Pathology. A surgical pathologist with a primary interest in oncology, he works closely with Dr. Black, and has been appointed Chief of the Surgical Pathology Laboratory for the Bernalillo County Medical Center.

During the period January 1, 1975, to approximately November 1, 1975, surgical pathology materials pertaining to 220 patients seen in the CRTC were examined and a formal pathology report prepared. This activity was directed toward review of the original diagnosis for more precise classification of individual neoplasms including histological grade and for more precise clinical staging of neoplastic disease when possible. Approximately 700 surgical pathology cases were seen in consultation with other pathologists from the city, state, or other states. Diagnostic electron microscopy was used to better define and more precisely classify neoplasms, the morphology of which was ambiguous at the level of light microscopy. Approximately one-fifth of these cases involved patients being seen in consultation with pathologists from outside the Center.

In support of clinical investigations at the Center, the Core Morphology staff reviewed pathology materials for patients participating in the pion, RTOG, Southwest Oncology Group (SWOG), and other CRTC protocols (such as a hyperthermia pilot study now under way).

Tissues from four patients with metastatic carcinoma to the skin who participated in the pion human radiobiology studies were extensively studied via histological sections prepared from tissues obtained at autopsy. A basic study plan was developed for these patients and others who are expected to participate in this protocol when the pion beam is reactivated. The plan includes:

(a) Comparative effects of x-radiation and pions on tumor metastases in skin.

1) Tumor cell kill or damage consistent with lethal effect, qualitative aspects--cytological appearance of tumor cells (comparison of x-ray and pion-treated tissues).

2) Tumor cell kill or damage consistent with lethal effect, quantitative aspects.

a) Depth of tumor cell necrosis attributable to radiation.

b) Uniformity of radiation effect across the treatment field (parallel to skin surface).

c) Dose response in terms of tumor cell effect.

3) Host response in the area of the irradiated tumor.

a) Vascular

b) Inflammatory

c) Connective tissue stroma

(b) Comparative effects of x-rays and pions on normal skin (adjacent to but separate from metastatic nodules).

1) Epidermal thickness

2) Adnexae

a) Pilosebaceous apparatus

b) Sweat gland ducts and acini

3) Vascular structures

a) Arterioles

b) Venules

c) Capillaries (papillary dermis, upper reticular dermis, lower reticular dermis, and subcutaneum)

4) Connective tissue structure

a) Arrectores pilorum

b) Fibroblasts and collagen

c) Lipocytes

5) Leukocyte response, including melanin containing histiocytes.

5-P01-CA-16127-03

The results of these histological examinations are presented under the section of this progress report dealing with Clinical Investigations.

(4) Basic Research. Although not funded by this grant, a basic research program is a goal of the CRTC and laboratory space for basic research was constructed on the third floor of the CRTC. In August of 1975, Dr. John M. Yuhas was appointed Associate Director for Biology and joined the Center on January 1, 1976. Funding for his activities is being provided through Grant No. 5-P01-CA-14052-03, State appropriations to the CRTC, and other UNM funds. Between August 1975 and January 1, 1976, Dr. Yuhas spent one week per month consulting at the Center in preparation for the initiation of a full-scale research program in January. At the outset, the biology research program will concentrate on the preclinical studies of pion radiotherapy, leading to full-scale clinical trials, and on the use of radioprotective and radiosensitizing drugs in radiotherapy, on the nature of the induction of lung cancer, and on the factors which determine the spread of cancer throughout the body. Grants-in-aid for the first three projects have already been obtained or applications submitted, and the fourth project will be proposed for funding in a separate research application in the near future.

Mr. Michael Yurconic has joined the Center as Chief Technologist for the Biology Laboratories and is in charge of coordinating laboratory support for Dr. Yuhas' research and that of other investigators. Approximately \$65,000 in research equipment has been purchased for installation in the Biology Laboratories. This initial outlay will allow Dr. Yuhas' group to meet our present commitments for research and will provide a working facility for attracting other scientists. The third-floor animal facilities are being equipped for housing mice, and plans are under way for development of a larger animal facility in the basement of the CRTC for housing multiple species.

Negotiations are under way with potential research staff members. Two who are currently under serious consideration have been concerned with immunological defenses against cancer, the nature of cancer formation, and the defects in normal control mechanisms which lead to its appearance. Under the biology program being planned, the basic scientists will work closely with clinicians in attempting to provide the best possible cancer management for patients.

Progress during the past year has been most evident in the Preclinical Studies of Pion Radiotherapy. Dr. Leo Gomez of the Health Division at the Los Alamos Scientific Laboratory is assigned full-time to the preclinical studies project and has developed all of the shielding and exposure geometries for the pion experiments which will begin in the spring of 1976. Further, through individual effort and through consultation with a number of other laboratories, he has developed a battery of test systems that will allow accurate quantitation of the effects of pions in a number of normal tissues, i.e., the type of information required for optimal clinical testing of pions.

Drs. W. C. Black, R. E. Anderson, S. Jordan, C. R. Key, and M. Kornfeld of the CRTC Pathology Section and UNM School of Medicine Department of Pathology, have developed within the past year a variety of assays for radiation injury to normal tissues, which have previously gone unstudied, although they are critical tissues in radiotherapy. In addition, Dr. C. J. Sternhagen has continued development of another assay, radiation injury to the heart, which is another critical structure.

Dr. Gary W. West, who is completing his residency in radiotherapy at the Center, has initiated a research project on the interaction of radioprotective drugs and radiosensitizing drugs, in collaboration with Dr. Yuhas and Dr. D. F. Petersen, Alternate Division Leader, Health Division, LASL. The analyses of these interactions in vitro should provide valuable information regarding the clinical applicability of either or both drugs. A second project in the same area, initiated by Drs. Yuhas, Kligerman, and Petersen and Mr. Yurconic, has concerned the possibility of using both drugs in the same tumor-bearing host. Progress to date suggests that both drugs are well tolerated in combination, and that the combination increases the effectiveness of radiotherapy far better than could either drug alone.

(5) Clinical Operations. The CRTC opened its clinical facilities in January 1975. The CRTC is adjacent to the Bernalillo County Medical Center, the primary UNM teaching hospital, and is connected by corridor with BCMC on the patient clinic level. Patients receive care at the CRTC on an outpatient basis. A four-bed area is available where patients can stay up to 24 hours for recovery after outpatient surgery or extended chemotherapy procedures. Patients who require hospitalization are admitted to BCMC or other Albuquerque hospitals. An eight-bed research unit is under construction at BCMC, partially supported by an allocation of \$75,000 for alterations and renovations under this grant.

A total of 13,087 patient visits have been recorded at the CRTC for the period January 2, 1975 to December 31, 1975. The number of monthly visits has increased from 271 in January to 1273 in December of 1975, with a high of 1749 recorded in October. New radiotherapy cases seen at the Center in Calendar Year 1975 totaled 405.

Activities of the Medical Oncology unit are detailed later in this report under Cancer Chemotherapy Clinical Investigations. With the arrival in April 1975 of Robert Hilgers, M. D., a gynecological oncologist, the gynecology caseload at the Center has escalated dramatically. A weekly colposcopy clinic headed by Dr. Alma Young, began in January 1975, and tri-weekly gynecology clinics began in March. A genito-urinary clinic began in April. Equipment has been ordered for the outpatient surgical suite, and the unit will become operational when installation is complete.

Currently, cases are being referred to the Center from throughout the region. Approximately 46 percent of CRTC patients are Bernalillo County residents, while 49 percent are State residents of counties other than Bernalillo and 5 percent are residents in other States. The latter percentage is expected to escalate when the CRTC again begins accessing cases for the pion program.

The CRTC Outreach Program was expanded to include Las Cruces and Santa Fe, bringing to five the number of communities participating in this program. The others are Los Alamos, Gallup, and Roswell. Under this program, the CRTC sends multidisciplinary teams of UNM and community physicians to participate in joint tumor conferences with the local doctors. The teams visit on a monthly or bi-monthly schedule at the invitation of the local doctors. Further expansion of this program is planned when the CRTC completes negotiation of a contract with the NCI Division of Cancer Control and Rehabilitation for implementation of a statewide Cancer Control Program.

The nursing staff has been active in continuing education programs for nurses throughout the State, under the auspices of the CRIC and the American Cancer Society.

The recruitment of another medical oncologist and a surgical oncologist for the Center continued during the current grant year, with several potential candidates identified. It is expected that a medical oncologist will be appointed within a few months, although the appointment of a surgeon will require more time.

b. Clinical Investigations

(1) Operation of the Biomedical Channel. The biomedical pion channel entered a planned shutdown phase for repairs and adjustments on December 21, 1974. The shutdown had been planned to last for six months, but has extended much longer than originally anticipated. The accelerator is operating well at this time, but the additional shielding required to protect personnel in the experimental theaters from radiation resulting from higher beam intensities is not yet in place. It is not expected that protons will reach the biomedical channel until early February, after the shielding required for high intensity operations is in place and the high intensity beam line equipment which can be maintained with remote-control maintenance equipment has been installed. The beam was restricted to an intensity of 10 microamps last year to avoid accumulation of high levels of induced radiation in the accelerator tunnel which would prevent completion of the planned repairs and adjustments. The accelerator is expected to be reactivated at an intensity of 10 microamps so that comparison measurements can be made. However, the intensity will then be escalated to 100 microamps within two months, and over the course of the year to 50 percent of the design intensity of 1 milliamp, or approximately 500 microamps. Further increases in current will take place slowly thereafter until the maximum is reached.

During this shutdown period, preparation for patient treatment with the negative pion beam has continued at a high level of activity so that reasonable volumes can be irradiated when the beam is reactivated. Tests of skin and tissues of the head and neck will be initiated before the current grant year ends. Activities during this shutdown related to the clinical trials include:

(a) Completion of the high intensity target station with capability for 1 milliampere proton beam operation.

(b) Installation of a helium atmosphere container along the linac channel to enhance the achievable dose distributions.

(c) Installation of the final slit assemblies to provide flexible operation of the channel at a variety of dose configurations, all under computer set-up procedures.

(d) Completion of the computer programming to allow automatic set-up of dose criteria with simple operator commands from the control console.

(e) An in-depth study of the channel performance from experimentally generated magnetic tapes taken with the multiwire proportional counter system. Discrepancies between theoretically measured and experimentally determined performance have been reduced to tolerable levels with every expectation that new beam

tunes will be easily achieved when the channel is reactivated.

(f) Development of an accurate beam model for treatment planning purposes which allows rapid generation of dose distributions from input beam distributions. This model is essential for accurate assessment of inhomogeneities and bolus construction problems and this work is by far the most realistic attempt in particle radiotherapy to date.

(g) Development of several beam tunes suitable for large volume static dose distributions.

(h) Installation of the dynamic range shifter for swept beam irradiations.

(i) Completion of the computerized dosimetry system necessary to catalog the three-dimensional dose distributions available in the new large volume beams planned.

When the biomedical channel comes on line, the beam time will be devoted entirely to physics for the first two months, so that baseline measurements and reliability can be established, particularly those related to computerized codes for the production of specified beam configurations.

(2) Radiation Therapy Clinical Investigations. In the past year, two radiotherapists have been added. Jose M. Sala, M. D., Professor of Radiology and Chief of Radiation Oncology, has been appointed Medical Director of the Cancer Research and Treatment Center. Terry D. Powell, M. D., Assistant Professor of Radiology, has joined the faculty. This makes four radiation therapists at the Cancer Research and Treatment Center, one of whom is the Program Director. The reason for the increase in staff over and above the Program Director and Dr. Charles J. Sternhagen has been the rapid increase in cases and the anticipation of re-institution of human radiobiology pion tests in the late winter of 1975-76 or early spring.

Dr. Kelsey and Dr. Yuhas will be the active physicist and radiobiologist on the Committee for Human Trials of Pion Radiotherapy, UNM/LASL. Dr. Yuhas will also be one of the radiobiologists on the Human Radiobiology Committee for Pion Studies.

The Cancer Research and Treatment Center opened its doors on January 2, 1975, and a Clinac 18 was put into operation on January 15, 1975. Only a limited number of cases were accessed during the first month. However, the number increased steadily each month so that a total of 405 new cancer cases were treated by the Cancer Center radiotherapy staff in the first year of operation. This caseload acquisition is still climbing with no evidence of a plateau having been reached. It is conservative to say that the Center is now accessing cases at the rate of 500 patients a year.

This has brought the Clinac 18 to capacity operation for an eight-hour day. The technical staff are working for nine hours a day to accomplish this. Some 15 percent of our patients utilize the electron beam. This is a result of the combination of a renewed interest in optimizing treatment planning, as well as the presence of Dr. Alfred Smith in the Physics Section, because of his long experience

with the electron beam therapy when he was associated with Dr. Norah Tapley at M. D. Anderson Hospital.

The performance of the Clinac 18 has been outstanding. Down-time is averaging about one hour a week. It should be pointed out that 35 to 45 minutes of this down-time is the result of the manner in which the plastic covers of the accelerator are fixed to the frame. It takes only 10 to 20 minutes a week to make the corrective adjustments to the electronics. This has been brought to the attention of the Varian Corporation and re-design of the covers in accordance with our recommendations for more rapid access to the electronics is underway. Because of the success of the radiotherapy unit at the Cancer Center and our relationship with the Lovelace-Bataan Medical Center, it was decided in the fall of 1975 that the Cancer Center would purchase the Theratron 80 cobalt machine at the Lovelace Clinic and have it installed in the Cancer Center. This transfer should occur on or about February 1, 1976. From that time forward, all radiotherapy treatments required by Lovelace-Bataan Medical Center patients will be carried out at the Cancer Center. The radiation oncologists of the Cancer Research and Treatment Center will be at the Lovelace-Bataan Medical Center daily for consultation and decision-making on patients who might be candidates for radiation therapy. At the present time, all definitive cases treated at Lovelace are simulated at the CRTC.

The Cancer Center has been a provisional member of the RTOG. The accession of patients in the Calendar Year 1974 was difficult. In an analysis of the reason for such failure, when great interest was professed by the medical staff, it was found that too much time was required to: (1) determine if the case fitted into one of the RTOG protocols; (2) discuss with the patient and family the intent of the protocol; (3) go over the consent form in such a manner that the principle of "informed consent" was met; and (4) fill out the forms which did not require physician input. In February 1975, Ms. Carol Selheimer, a registered nurse with an interest in data management and clinical investigation, was employed as a "Protocol Nurse" to see if such an individual could solve these logistic problems. We have been uncommonly successful accessing 31 patients out of 405 available to us in the period of one year, a 7.6 percent success rate. Because of this, we have been informed by the RTOG Headquarters staff that we will be admitted to full membership at the January 15, 1976, meeting in San Diego. It appears that one protocol nurse for each 300 new cancer cases a year is required. An associate to Ms. Selheimer will be appointed soon, so that pion protocol patients will receive the same type of consideration.

The first human radiobiology tests were designed to compare the effects of pions and 140 kv x-rays on normal skin surrounding metastatic nodules. Preliminary tests on three patients were conducted to establish safe doses. Then a single patient with multiple metastatic melanoma nodules was selected and 18 of his nodules randomized to treatment with pions or x-rays at 55, 66, and 75 percent of a curative dose level of 5,200 x-ray rads in 19 days. Treatment was given in 15 fractions in 19 days, with the peak pion doses at one-half the level of the x-ray doses. The dose rate for the x-rays was 500 rads per minute, and for peak pions, 5-7 rads per minute. All areas were treated with a 3 cm cone, except one x-ray nodule in the middle dose range treated with a 5 cm cone. The beam profile across the 3-cm x-ray collimator was essentially flat over a central diameter of 2.3 cm, while that for pions was Gaussian with full width of half maximum of about 3 cm.

Color photographs were taken twice weekly with constant exposure, light-

ing, film, and filter. The maximum optical density of the skin reactions of the photographs was recorded using a McBeth densitometer Model 504, with a Kodak green filter #58. The Eastman Kodak Research Laboratory staff provided consultation. The densitometry measurements and observations by the radiation therapists indicated that maximum erythema occurred at six to seven weeks, with greater reaction to x-rays than to pions. Dose response curves were constructed by plotting the average values of the maximum skin effect at each dose level. The x-ray curve was linearly interpolated so that it could be compared with the pion curve at the optical density of 0.23, yielding an RBE for skin erythema of 1.43. A question was raised at a recent international particle therapy meeting about the degree of interpolation required to compare the x-ray curve with that for pions at the optical density of 0.23. On advice of Dr. Jack Fowler, the amount of interpolation required was calculated and found to be only 77 rads, or only 7.4 percent of the scale from the lowest to the highest x-ray dose. With the results available from this initial study, a broader spread of doses will be used in the repeat study so that this objection will be obviated.

The principal investigator points out one cause for concern. Since a larger area of skin was irradiated at the 90%+ isodose level with x-rays than with pions, this could account for the increased intensity of skin reaction with x-rays. A compensating filter for the 3 cm cone has been designed by Dr. Kelsey to match the 140 kv x-ray beam profile to the compensated and uncompensated pion beam profile. The compensated and uncompensated cones will be used to determine if significantly different reactions are obtained. Also, the human skin experiments to be repeated early next year will be done with a sharper pion beam.

After the patient's death, 25 weeks after irradiation, an attempt was made to assess intermediate-term reaction on specimens taken at autopsy, using the quantitative histologic method of Chalkley counts. Measurements were made on untreated skin, x-ray treated skin, and peak pion treated skin. With 600 fields counted, the measurements showed no significant differences among any of these groups in the mean number of the following types of cells or structures: collagen; capillaries/venules; arteries/arterioles; dermal appendages; or artifacts/tissue space. Thus, at five months after treatment, there were no untoward effects from pions or x-rays. A larger number of Chalkley counts will be made when the study is repeated, especially with higher dose rates.

(3) Cancer Chemotherapy Clinical Investigations. Participation by the UNM CRTC and UNM-Affiliated Hospitals in the Southwest Oncology Group (SWOG) is supported by NCI Grant No. R01-CA-12213-05 (J. H. Saiki, M. D., Principal Investigator), and by NCI Grant No. 5-P01-CA-16127-02. In January 1975, the Medical Oncology Division of the Department of Medicine, UNM School of Medicine, was moved to the Cancer Research and Treatment Center, where this activity is now centered. The Medical Oncology Section of the CRTC is seeing an average of 23 new patients per month, or approximately 276 new patients per year.

Under the Leukemia-Lymphoma Program established five years ago at UNM, community physicians participate with the UNM group in management of their patients on SWOG protocols. Currently, more than 90 percent of children with acute leukemia throughout the State of New Mexico are being treated under this program. More than 50 percent of all adult patients with acute leukemia throughout the State are also being treated under the program, as are approximately 60 percent of patients with malignant lymphoma. This has had a major impact on the awareness of practicing

physicians throughout the State of the most recent advances in cancer chemotherapy.

During the first eight months of Calendar Year 1975, the UNM SWOG accessions totaled 90 patients, with this number expected to reach 135 by the end of the year, as compared with 104 for Calendar Year 1974. Approximately half of these cases were acute leukemias and lymphomas, with the remainder distributed among myeloma and various solid tumors.

To provide a more comprehensive and multidisciplinary approach in the SWOG protocols, the CRTC has the participation of chemotherapists, radiotherapists, and a gynecological oncologist, representing the CRTC, the UNM School of Medicine, UNM-Affiliated Hospitals, and various community hospitals. Full members of SWOG are currently Drs. J. H. Saiki, Morton M. Kligerman and C. J. Sternhagen, CRTC; and Bruce Wimer and Donald C. Pinkerton, Lovelace-Bataan Medical Center. Associate members are Drs. Henry Saiers, Veterans Administration Hospital, and Doyle Simmons, St. Joseph Hospital. Proposed associate members are Drs. W. C. Black and Robert Hilgers of the CRTC. Drs. Saiki and Black are members of the SWOG Sarcoma Committee; Dr. Hilgers has been proposed for membership on the Gynecologic Oncology Committee; Dr. Pinkerton is a member of a Pediatric Division; and Drs. Kligerman, Sternhagen, and Simmons are members of the Radiotherapy Committee.

Dr. Saiki is serving as Study Chairman of SWOG Protocol 7209, 5-Azacytidine in Acute Leukemia, which is directed mainly at myeloblastic and monocytic leukemias. This protocol is to be closed soon. A total of 84 patients have been entered, and the complete remission rate of evaluable patients remains at approximately 30 percent. As a follow-up, a proposal has been submitted to the NCI Clinical Investigations Branch for a study for the evaluation of two schedules of administration of 5-Azacytidine in acute leukemia.

Dr. Black, along with Dr. William Russell of the M. D. Anderson Hospital and Tumor Institute, has established a repository for evaluation of tissue in all Phase III sarcoma studies. This repository will allow a uniformity of diagnosis, enabling the SWOG members to more closely evaluate and correlate the relationship between response, type of chemotherapy, and histologic type.

As Co-Chairman of SWOG Protocol No. 7424, Malignant Melanoma, Dr. Sternhagen developed the radiotherapy technique for this national protocol. Dr. Saiki and Dr. Saiers have collaborated to prepare SWOG Protocol No. 7520, Galactatol in Multiple Myeloma. A pilot study for use of hexamethylmelamine in multiple myeloma has been proposed by Dr. Keith Lanier and Dr. Saiki for possible future proposal as a group-wide study.

The Medical Oncology Section participated in the training or continuing education of 144 medical students, 15 interns, 25 residents, 200 practicing physicians 50 nurses, and 30 medical technologists during the past year. Four fellows were assigned to the Section during 1975, supported by the Veterans Administration Hospital Lovelace-Bataan Medical Center, Bernalillo County Medical Center, and an NIH Fellowship.

(4) Diagnostic Radiology and Nuclear Medicine. During the current grant year, diagnostic imaging equipment was installed in the Diagnostic Oncologic Imaging Section of the CRTC, which is adjacent to the Radiology Department of the Bernalillo County Medical Center. The following services are now available:

Dr. Antoine ("Subcutaneous Depth of Supraclavicular Lymph Nodes Opacified on Lymphangiography" and "Surgical Correlation with Radiographic Diagnosis of Para-Aortic and Pelvic Lymph Nodes as Seen on Lymphangiography") continued during the current grant year, and research papers are in preparation. These studies are providing information important to tumor localization for the pion clinical trials.

In the past year a Biomedical Physics Section has been established with the appointment of Dr. Charles A. Kelsey of the University of Wisconsin as Chief of the Biomedical Physics Section at the CRTC and Professor, Department of Radiology, UNM School of Medicine. Dr. Kelsey has had a continuing interest in neutron generators. A second appointee is Dr. Alfred Smith, who performed the inter-comparison of clinical neutron radiation programs when he was working with the Cancer Group at TAMVEC/M. D. Anderson Hospital. A third physicist is Dr. Richard G. Lane, whose major responsibility had been hospital radiation physics at the University of Wisconsin. All these men will be directly involved in the pion program at LASL, and in preparation of better techniques of treatment and patient immobilization for conventional radiation to be used as comparison radiation with the pion protocols.

Physics support for conventional clinical radiotherapy has been under way with the Clinac 18 linear accelerator since it became operational in January 1975. Clinical operations and dosimetry for the Clinac 18 are in effect for both electrons and photons, including the use of lead filters. The CRTC physics group has also supported clinical radiotherapy by CRTC radiotherapists at the Lovelace-Bataan Medical Center. Requirements for moving the Lovelace-Bataan cobalt unit to the CRTC have been established by the physics group, and a new base has been ordered. A videotape documentary will be produced when the cobalt unit is dismantled and moved to the CRTC, for use in training of biomedical physicists and radiotherapy residents. Computerized treatment planning has been implemented for patients being treated with the CRTC's Clinac 18 and orthovoltage unit, and the Lovelace-Bataan cobalt unit.

Working relationships have been established between the UNM Biomedical Physics Section and the LASL Medium Energy Physics Division staff assigned to the biomedical pion project. Responsibility for clinical physics is vested with the UNM group, while the LASL group is primarily concerned with delivery of the required beam to the treatment room.

Specifications have been defined for the pion treatment couch and an identical couch to be placed in the simulator room at the LAMPF Biomedical Facility. The couch design requires vertical and transverse motions, as well as the ability to rotate the patient about an axis parallel to the floor and perpendicular to the pion beam. The top section must be capable of transfer from the simulator room to the treatment room to allow rapid set-up under the pion beam.

Acquisition of the couch will allow the CRTC physics group to progress with definition of requirements for a simulator at the Biomedical Facility and with development of a realistic simulation program. Currently, plans are being made to link simulation with computerized optimization of treatment planning for patients selected for pion or conventional radiotherapy. After a patient's tumor and relevant inhomogeneities within the normal tissue structures have been localized, computerized treatment planning will be performed. When the radiotherapist has selected the optimum treatment plan, the simulator will be used to ensure that the selected treatment correlates with anatomical landmarks of the patient. Simulation will require two image intensifier tubes and two x-ray tubes to obtain simultaneous

anterior-posterior and cross-table lateral views of the anatomy. The television screens which present the image intensifier information will also be connected to the treatment planning computer, where the approved treatment plan is stored. When the physician indicates the location of critical anatomical landmarks and the location of the tumor, the computer will superimpose the treatment plan and the pion dose distribution over the fluoroscopic images. Thus, the physician will be able to determine whether an adequate margin has been allowed between the high-dose peak region and, for example, the spinal cord or other sensitive normal tissues. At the same time, he can check to ascertain whether the tumor volume will be adequately covered by the planned treatment volume.

c. Tumor Registry

Grant No. CA-16127 provides support for epidemiology activities by the New Mexico Tumor Registry, a division of the CRTC. Principal support for the Registry, a participant in the Surveillance Epidemiology and End Results (SEER) Program, is provided by a contract (N01-CP-33344) with the NCI Biometry Branch. The Registry serves more than 60 hospitals and provides a population-based cancer registry for New Mexico and the entire Navajo reservation, thus producing valid cancer incidence data for New Mexico's Anglo, Spanish-American, Indian, and Black populations.

There are marked variations in cancer patterns among the region's major ethnic groups, with cancers of stomach, gallbladder, and cervix most common in Spanish and Indians rather than in Anglos. Cancers of skin, breast, lung, colon, rectum, and endometrium are more common in the Anglo population. Population definitions have been guided by comparisons between New Mexico and other states, especially by Mason and McKay's recent 20-year cancer mortality summary and mapping, by county, for the United States. In these publications, and in our own work, New Mexico appears with very low lung cancer for males, but not females. For stomach cancer, both sexes show high rates. The counties with a large proportion of Spanish persons are even more extreme. Skin cancer, more prevalent among Anglos, is not usually fatal. A computer program, based on the previously developed Spanish surname program, has been developed to subdivide both the "Anglo" and "Spanish" groups. State population redefinitions by these subdivisions are in process, as are county level population estimates for 1975.

A subcontract is currently in progress with the Los Alamos Scientific Laboratory to participate in a six-month planning effort aimed at designing and conducting a follow-up study of all plutonium workers in the United States.

Two proposals for specific epidemiologic studies were submitted in September 1975 for funding as Cancer Research Emphasis Grants (CREG), and these are still in the review process.

The first of these, "Cancer Incidence in New Mexico Indians and Spanish," proposes to examine, in detail, the cancer experience of unique communities and subpopulations that are known to have low or very low genetic diversity. Analysis of high and low cancer rates among these homogeneous populations, even though the populations may be small, have a relatively high likelihood of providing new clues to cancer etiology. Existing records of the New Mexico Tumor Registry will be the basic source of information.

The second proposal, "Lung Cancer in New Mexico Ethnic Groups," proposes an initial case-control study to shed light on the marked deficit of lung cancer in Spanish-American males. Spanish smoking habits (not well documented) do not appear different from their Anglo neighbors (who approach U. S. lung cancer rates). Also, histology-specific lung cancer incidence rates for each sex and ethnic group will contrast with Kreyberg's "exogenous" and "endogenous" lung cancer types.

Specific activities during the current grant year have included:

(1) Preparation of population figures for the Navajo reservation portion of Arizona so that numerator data from Arizona Indians can be included in rate calculations.

(2) Refinement of New Mexico population data by ethnic group and age to county level.

(3) Subdivision of the "Anglo" population to identify subgroups for purposes of studying skin and other cancers.

(4) Further comparison of New Mexico's cancer incidence and mortality rates and trends with those of other areas in the United States and other countries of the world.

(5) Collaboration with the University of New Mexico's Environmental Pathology Working Group to establish an ongoing system for better correlating measurable environmental factors with a variety of human diseases, including cancer.

(6) Continued support of the New Mexico Tumor Registry's data collection, processing, and reporting activities.

(7) Documentation in support of planning and evaluation of a Comprehensive Cancer Control Program for New Mexico.

(8) Tabulation of cancer mortality in New Mexico by site, sex, and ethnic group for each year from 1969 through 1974. These tabulations have been sent to the Biometry Branch, NCI.

3. RESEARCH OBJECTIVES FOR YEAR 3

a. Core Operations

(1) Administration. The principal goal will be the development of computer systems to provide weekly reports to each section and division leader concerning fiscal status of his unit. Control of expenditures by budget category with almost instantaneous recall, will be such that the possibility of inadvertent or improper expenditures will be eliminated. The exercise of the internal audit, mentioned above, was so useful that this will become a standard procedure on a yearly basis.

Rules for the use of consultants are being implemented, with the requirement that consultants be "requisitioned" by voucher. This will give the central administration of the Cancer Center an opportunity to review each request before any commitment is made.

The decentralization of professional administrative activity should contribute to a more free and vigorous attitude on the part of section and division leaders.

(2) Biomathematics. During the coming year, the Biometry Division, in conjunction with other CRTC units, will be developing additional programs for radiation treatment planning, statistical analysis, patient scheduling, medical records, and administrative applications. The protocol patient coordination effort will be expanded to include SWOG accessions, and attempts to increase RTOG accessions will continue. The data collection and analysis for the pion human radiobiology studies, pilot studies, and Phase III protocols will be systematized and expanded.

(3) Core Morphology. Pathology review for CRTC patients is expected to increase significantly when the outpatient surgical suite is opened at the CRTC and biopsies are performed there. In addition, in-depth analysis of tissue specimens obtained from patients participating in the pion studies will be conducted according to the research plans established in this grant year. The histological examination of animal tissues irradiated by pions and x-rays is also expected to increase significantly as the x-ray control studies progress from pilot studies to more definite experiments and as pion experiments with animals are initiated.

(4) Basic Research. Plans for the coming year are to complete the first phase of the preclinical pion biology studies, which would allow initiation of full-scale clinical studies. A pion beam of sufficient intensity is expected to be available in the spring of 1976, and the longest term experiments with animals should be completed within one year. The majority will be finished long before that time. Funding for the radioprotective/radiosensitizing drug studies should be available by June of 1976, if this project is approved by the NCI, and for the lung carcinogenesis project at about the same time, if that project is approved by the U. S. Energy Research and Development Administration, and at least preliminary data should be available by the end of the year.

Development of the basement animal facilities should be under way, which would then allow use of the third-floor animal facility as an ultra-clean facility, for which it was designed.

Recruitment of research staff will continue, with a particular view toward recruitment of a cell kineticist and an investigator in chemical carcinogenesis, in addition to the research scientists identified in the progress report.

(5) Clinical Operations. The CRTC caseload has increased steadily since the clinic opened in January and has not yet appeared to reach a plateau. Thus, the new cancer cases accessed by the Center in the coming year should exceed 500. Because the CRTC staff includes the State's only gynecological oncologist, the caseload in this area has increased dramatically and the need for a second gynecological oncologist is already apparent. The search for a second medical oncologist will continue, as will the recruitment effort for a surgical oncologist.

Joint tumor conferences are currently being held weekly at the CRTC, and physicians are participating in other joint tumor boards in Albuquerque. It is anticipated that tumor boards at the CRTC will soon be held three days a week, and shortly thereafter on a daily basis, so each new case can be evaluated in a multi-

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disciplinary conference after diagnostic work-up. This was one of the original precepts of the Center's operational philosophy, and will be effected as soon as possible, now that a full-time Medical Director is on board. Medical staff policies and guidelines are also under development so that community physicians can begin to participate in the Center's clinical programs in the same way they participate in community hospital programs. The continuing education program, geared to the individual needs of physicians throughout the State, is expected to begin in the coming year.

b. Clinical Investigations

(1) Operation of the Biomedical Channel. While the final goal of irradiating large irregularly shaped tumors with a swept beam system may not be achieved for some time, it appears feasible to generate well documented static beams (as is done in other particle radiotherapy) within a few weeks of beam availability at LAMPF. The program to develop these clinically useful beams will involve a series of experiments relating to the flexible swept beam configuration, demonstrating proper reproducibility and dose homogeneity, and a program of applying, in a clinical situation, well documented static beams to certain selected tumor types. The successfully developed pion beam model must now be included in a sophisticated three-dimensional treatment planning program, first to verify dose distributions within the body for static beam configurations and later to generate swept beam parameters to properly contour the dose to the suspect tumor volume. A dose verification scheme utilizing multiwire proportional counters to visualize the pion stopping region must be developed in conjunction with the swept beam system.

As the physicists, biologists, and physicians learn to apply these unique beams, the problems and advantages of pions in radiotherapy will become more clear. The interplay of the different physical characteristics of pion beams of different energies, spatial distribution, and energy spread (e.g., the problems of scattering, neutron production in the stopping volume, star fragment type, range straggling, and a multitude of other considerations) will yield optimum characteristics for the therapy beams required. There is probably no way to determine the optimum beams without extensive experience in clinical situations.

An unexpected delay in the start-up of the LAMPF beam has necessitated a postponement of critical beam development work. However, critical theoretical studies have progressed well and little long-term delay is expected in the overall program to achieve clinical trials with pions.

(2) Radiation Therapy Clinical Investigations. Fifty-five percent of the Cancer Center's radiation therapy patient load is from outside of the city of Albuquerque. Our objective is to expand participation in the protocols of the RTOG. We believe this can be accomplished by the addition of an assistant for Ms. Carol Selheimer, Protocol Coordinating Nurse, who was largely responsible for the increase in accessions during calendar year 1975. We also believe that with the number of out-of-town patients, a social worker will be invaluable.

For over two years, experience has been gained in assisting with patients receiving hyperthermia on the Surgical Service under the NCI Grant #2-R01-CA-15833-03 held by Dr. Sterling Edwards. Dr. Charles Sternhagen has been the radiation therapist associated with this group. The uniqueness of combination hyperthermia-radiotherapy at the CRTC lies in the close association with Dr. James D. Doss at the Los Alamos

Scientific Laboratory. Dr. Doss, in our view, has the best system for localization of heat by means of radiofrequency energy. Animal experimentation has been carried out and two patients have been treated with combination hyperthermia and radiotherapy. A separate grant request is being submitted by Dr. Sternhagen for support of this project; however, we feel that funds from this operational grant should be allocated to Dr. Sternhagen to continue his pilot studies while his own grant is being processed.

The Committee for Human Trials of Pion Radiotherapy UNM/LASL had its last meeting on December 1, 1975 in conjunction with the Radiological Society of North America meeting in Chicago. At that meeting, the report of the initial human biology trials was made. New dose schedules were decided upon for the definitive tests. The x-ray dose will be at 50, 66, 75, and 83 percent of 5200 rads, 15 fractions in 19 days. The comparable peak pion doses, to be certain that there would be an overlap in at least one level for calculation of RBE, will be one-half of 55, 75, 83, and 91 percent of 5200 rads, 15 fractions in 19 days. There will be at least six nodules for each dose level, for a total of 48 nodules. To qualify, a patient must present a minimum of four treatable nodules. Any type of metastatic tumor is acceptable. In addition, the group agreed with the recommendation of Drs. Kligerman, Knapp, Kelsey and Yuhas that three static peak beams be selected to look at the response of normal tissues other than the skin. It is felt that with a static peak pion beam of 5x5x5 cm, and a second of 8x10x6 cm that many far advanced tumors of the head and neck could be treated to observe the response of the normal intraoral and pharyngeal mucosa as well as the response of tumor. In addition, cervical and superficial masses could be observed. Though not presented at the December 1975 meeting, recurrent masses of the pelvis (previously untreated by radiation) could be included. The response of the rectum and vaginal tissues could be observed. Even at 100 microamps, which should be available within two months after the beam is restarted, the dose rate in the peak of the 5x5x5 cm beam would be 40 rads a minute; in the 8x10x6 cm peak, 12 rads a minute. These all appear to be in the range where the possibility of recovery during treatment would be minimal or non-existent. However, Dr. Yuhas and Dr. Kligerman will be doing dose-rate tests on mammalian normal and tumor tissues to determine the minimal dose rate which is acceptable to eliminate significant recovery during treatment for peak pion beams. When the higher dose rate becomes available, another static beam 12x16x12 will be introduced. This will greatly increase the number of tissues that can be tested.

At the time of preparation of this annual renewal request, the refurbished proton accelerator has been operating efficiently and smoothly since August 1975. However, getting Area A, the main experimental area immediately preceding the biomedical channel, shielded and reconstructed for safe operation had taken twice as long as expected. It is predicted that pions will be available to the biomedical channel on or about February 1, 1976. The channel will start operating at 10 microamps but it is estimated that within two months this will be raised to 100 microamps. The decision has been made to have the physicists do all the work they need using the three shifts available in the 24-hour period for the first two months so that when 100 microamps are available the biologists and physicians will be able to start their studies.

The pilot human radiobiology studies leading to the determination of an RBE for late skin effects with the pion beam as compared to x-rays will be undertaken with the dose schedule as described above. Before collimation, the pion peak will be spread to a 4 cm diameter and will be 2 cm thick so that the dose rate with 100 micro-

amps will be 200 rads a minute in the peak period. A comparative experiment will probably be done with dose rates of 30 rads in the peak to see if there is any variation in response over this dose range, although none is expected.

While the difficult problem of inhomogeneities in the beam is being solved for definitive therapy, we believe that we can proceed with studies of the radiobiological response of the mucosa of the mouth, rectum and vagina, by using a relatively broad peak pion mode. The peak volume will be large enough so that the interoral, pharyngeal or pelvic tumor and the normal mucosa surrounding it will all be in the peak pion beam. Any attenuation of the beam passing through bone or going through air (acceleration) will not prevent peak pions from falling on tumor and normal tissues alike because the depth of the peak will be large enough to cover the tissues even if partially attenuated. This situation will be similar to treatment with photons where an entire area gets relatively similar high doses. Information on normal tissue response and tumor response is needed before definitive treatments are instituted. By taking advantage of the information we have on attenuation of electron beams, an area in which Dr. Alfred Smith of our Biomedical Physics Group is an expert, we feel that we will be prepared to start definitive treatments as soon as the current is raised above 100 microamps to the 500 microamps level:

Although an annual radiotherapy caseload in excess of 500 patients is projected for the coming year, an effort is being made to increase the available caseload, so that both the pion patients and the conventional controls could be treated at the Cancer Center. It should be appreciated that the type of material on which we want to test the pion beam would utilize many patients who are not now treated by radiotherapy. Since we are seeing approximately 500 new cancer cases per year in the Center, and a good number of these are the types of advanced cases on which we wish to test the pion beam but which are now treated by chemotherapy, an additional number of patients is available to us over and above those who are now accepted by radiotherapy. Furthermore, as far as the controls are concerned, a number of the protocols dealing with advanced cases do not require controls since their current cure rates and cure rates over the last number of years have not risen above 10 percent. However, the following is being accomplished:

(a) Dr. Gary West (Lt. Col. U. S. Air Force) has completed training in radiation oncology at the University of New Mexico. He has been appointed Chief of Radiation Therapy at Wilford Hall Air Force Hospital, San Antonio, Texas. Currently, that institution is accessing 600 new cancer patients in a year there. Also, Dr. Charles Coltman, Chief of Medical Oncology, is extremely interested in the pion program. Dr. West participated in some of the basic preclinical studies of pion therapy and was the principal investigator's close associate in the human radiobiology studies. Dr. West plans to put 100 percent of his appropriate patients into the pion protocols. Secondly, we are exploring ways of sending controls as well as the pion treatment cases to the CRTC. In any case, since Dr. West's training was at the CRTC, we can depend on the controls being treated the same.

(b) Dr. Kligerman and Dr. West will explore involving the other Defense Department hospitals with large radiotherapy loads in this program. It is believed there is a good chance that this will occur since it will provide part of the much needed academic stimulus that physicians in military hospitals lack.

(c) Mortland Hospital of the New Jersey Medical College has approximately 200 new cancer patients a year, but they are mainly Stage III and IV. A large portion of them are head and neck cases. Since it would help that county

hospital to refer those types of cases, Dr. J. T. Mallams believes he will be able to send both pion and control cases to New Mexico.

In summary, the outlook for ensuring an adequate caseload for radiobiology and pilot studies of the clinical trial treatment plans is vastly improved. If pilot studies go well, there will be no difficulty in accessing the patients we need for clinical randomized trials.

(3) Cancer Chemotherapy Clinical Investigations. New studies in chemotherapeutic agents for multiple myeloma and acute leukemia have been initiated as described in the progress report and preliminary results are expected in the coming grant year. Data should also begin to emanate from the sarcoma tissue repository. Continued expansion of the Leukemia-Lymphoma Program and other SWOG activities is anticipated, particularly as UNM and community physicians become more active in SWOG.

(4) Diagnostic Radiology and Nuclear Medicine. Research efforts will concentrate mainly on support of the pion project, particularly on improved tumor localization for conventional control and pion radiotherapy cases. The ultrasonography unit will be linked with the treatment planning computer, so that information on body inhomogeneities can be taken into account in treatment planning. A whole-body computerized axial tomography unit has been requested in the renewal application for 5-P01-CA-14052-03, and, if approved, will also be linked with the treatment planning computer. The Diagnostic Oncologic Imaging Section will use this unit for improved diagnosis and tumor localization necessary for testing of pions in cancer therapy. Study of tumor regression during and after therapy will also be undertaken. These efforts will also benefit patients on other research protocols at the CRIC.

(5) Biomedical Physics. Several modifications of the Clinac 18 are planned to allow more efficient use of the unit and to lead to possible computer verification of treatment parameters. The first step will be to indicate on a panel near the control console the actual gantry position and collimator jaw position. Next to this will be displayed the desired or "correct" parameters. Computer verification of these parameters will then be instituted.

In radiation treatment planning we will begin to attempt to calculate the effects of body inhomogeneities in treatment planning for pions, x-ray and electron treatments. The inhomogeneities will be determined by conventional radiographic techniques and ultrasonic scanning until a whole-body computerized axial tomography unit is obtained (if approved).

Installation of and development of control systems for the treatment and simulation couches and the simulator system for the LAMPF Biomedical Facility will also be undertaken in the coming year.

c. Tumor Registry

Cancer mortality and morbidity for counties and areas can now be based on six years of death records and seven years of Tumor Registry data, as well as population counts for 1970 and estimates for 1975.

These mortality and morbidity rates will be analyzed for New Mexico and the Navajo Reservation in detail by ethnic group, as subdivided, and by a series of environmental measures, including, but not limited to altitude, occupational patterns,

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etc. The analyses will be prepared as a series of brief papers, around the central topic of the ethnic variation in cancer.

Understanding cancer causation is, of course, a long-term objective. New Mexico can contribute unique observations toward this objective. Subdivisions, by site of cancer, by ethnicity, and by other factors, increase the specificity of the problem. Each time a specific interaction between a disease and some non-disease factor is identified, we pose smaller and more specific minor questions, which contribute to a greater understanding of the larger, global questions related to cancer causation.

3. SIGNIFICANCE

The significance of this program lies mainly in two areas:

(1) The CRTC is conducting at LASL the first therapeutic tests of negative pi mesons in the world, and are beginning to generate a body of knowledge that will be valuable not only in treatment of cancer patients (in the event pi mesons prove advantageous), but which in any case will be valuable to other installations in the world which are investigating or proposing to investigate the use of subatomic particles in cancer therapy. The CRTC is also contributing to the body of knowledge of the efficacy of conventional radiation through participation in national cooperative study groups.

(2) The establishment of the CRTC to plan, support, and implement the pion trials has also provided a medium for establishing a Center designed to serve as a model for delivery of cancer diagnosis, treatment, and follow-up services to the citizens of a sparsely settled state.

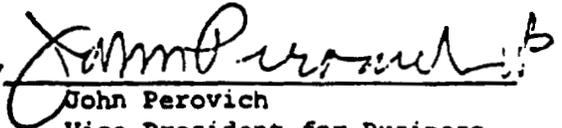
The medical and scientific interest around the country in the pion clinical trials, and the active participation of radiation therapists and scientists from various other institutions, have helped to infuse interest in cancer research programs of all types in New Mexico and are creating opportunities for other kinds of cancer research at the CRTC and LASL not necessarily related to radiation therapy. Similarly, this interest has carried over to the medical community and the citizens of our state. Their acceptance of the CRTC, as evidenced by our rapidly expanding case-load and invitations to expand our outreach program, is helping to ensure participation by New Mexico cancer patients in the pion clinical trials and other clinical research programs directed at improved cancer management.

Dr. Francis J. Mahone,
January 13, 1976
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The parties see no obstacle to effecting this Modification promptly upon receipt of firm information as to the terms of the NCI continuation grant awards.

REGENTS OF THE UNIVERSITY
OF NEW MEXICO

Dated: January 20, 1976

By 
John Perovich
Vice President for Business
and Finance

THE REGENTS OF THE UNIVERSITY
OF CALIFORNIA

Dated: January 13, 1976

By 
M. M. Agnew
Director, Los Alamos Scientific
Laboratory