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J. A. BERNARD, JR.
Director of Reactor Operations

January 24, 1995

U.S. Nuclear Regulatory Commission
Washington, D.C. 20555
Attn: Document Control Desk

Subject: Status of Neutron Capture Therapy Trials

Gentlemen:

As you are aware, the Massachusetts Institute of Technology initiated trials of Neutron Capture Therapy on 6 Sept. 1994 under a Phase I protocol that is required by the U.S. Food and Drug Administration. A second irradiation series was initiated on 10/24/94 and a third on 12/05/94. The protocol stipulates that a review is to be done following each group of three patients. If no adverse effects are noted, then the dose can be increased by 250 RBE-cGy. Enclosed is a summary of the review for the first three patients. We are providing this to you as an item of information. Its submission is not required. We wish to call your attention to two items in the summary. First, the normal tissue response for all three subjects (the word "subject" is used in lieu of "patient" because it's a Phase I study) was graded as "0". That is, no adverse effects occurred to healthy tissue. Second, the third subject's tumor module was markedly reduced in size. Uptake of boron varies substantially from patient to patient and the third subject had a much higher uptake of boron than the first two. Each subject received the same dose (1000 RBE-cGY) to healthy tissue. Hence, a subject with a higher boron uptake would get more dose to tumor. This explains the tumor reduction observed in the third subject.

Sincerely,

John A. Bernard, Ph.D.
Director of Reactor Operations
MIT Research Reactor

JAB/CRM

cc: USNRC - Project Manager,
NRR/ONDD

USNRC - Region I - Project Scientist,
Effluents Radiation Protection Section (ERPS)
FRSSB/DRSS

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TECHNICAL PROGRESS REPORT - *UPDATE*
DE-FG02-87ER60600

******UPDATE TO JANUARY 23, 1995******

BRIEF REVIEW OF THE FIRST THREE EXPERIMENTAL IRRADIATIONS OF HUMAN SUBJECTS UNDER THE APPROVED BNCT MELANOMA PROTOCOL

Robert G. Zamenhof, Ph.D., NEMC,
and Otto K. Harling, Ph.D., MIT

The first three subjects have completed their BNCT irradiations under the approved melanoma protocol. This constitutes the subjects in the first--lowest dose level group, requiring 1,000 RBE-cGy maximum dose to normal tissues. The following is a very brief review of these clinical trials.

General

Test dose of BPA 400 mg/kg, biodistribution (blood) and (punch) biopsies before irradiations.
Four (4) fractions with 400 mg/kg of BPA.
Blood samples before and after irradiation, punch biopsy before start of first fraction.
Each fraction ~ 250 RBE-cGy.
Total dose 1,000 RBE-cGy to normal tissue, delivered over 1-2 weeks.
No problems were experienced.

1. Subject No. 94-1 - 66-year-old male, first fraction September 6, 1994

Melanoma on plantar surface of right foot. BPA and neutron irradiation administered as per protocol: Foot phantom constructed and dosimetry measurement made before first irradiations, retrospectively the CT based Monte Carlo treatment plan completed; ^{10}B blood timecourse study completed; tissue biopsies analyzed for ^{10}B; clinical exams completed; 2,000 mg/kg total oral 1,BPA administered as 400 mg/kg x 5; combined with four fractions of epithermal neutron delivery to selected tumor site. No untoward events related to subject.

Follow-up: Normal tissue reaction graded as "O". No visible tumor response.

2. Subject No. 94-2 - 61-year-old male, first fraction October 24, 1994

Melanoma on medial surface of left lower leg. BPA and neutron irradiation administered as per protocol: CT based Monte Carlo treatment plan completed before first fraction and compared to experimental dosimetry; ^{10}B blood timecourse study completed; tissue biopsies analyzed for ^{10}B; clinical exams completed; 2,000 mg/kg total oral 1,BPa administered as 400 mg/kg x 5; combined with four fractions of epithermal neutron delivery to selected tumor site. No untoward events related to subject.

Follow-up: Normal tissue reaction graded as "0". No visible tumor response.

3. Subject No. 94-3 – 81 year-old female, first fraction December 5, 1994

Melanoma on outer surface of left lower . BPA and neutron irradiation administered as per protocol: CT based Monte Carlo trea nt plan completed before first fraction and compared to experimental dosimetry; ^{10} ood timecourse study completed; tissue biopsies analyzed for ^{10}B; clinical exam npleted; 2,000 mg/kg total oral l,BPA administered as 400 mg/kg x 5; combine h four fractions of epithermal neutron delivery to selected tumor site. No untow events related to subject.

Follow-up: normal tissue reaction graded as 0". Visible tumor response involving redness and blistering of tumor nodules in radiation field (but not those outside) one day after final treatment. Subject reported diminished size of tumor nodules in field 4 days after final treatment with resolution of redness and blistering. First follow-up by NEMC clinicians, one month after last fraction, showed tumor nodules in radiation field markedly reduced in size, but one of those outside radiation field somewhat increased in size.