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OAK RIDGE, TENNESSEE

November 24, 1962

Dr. H. D. Bruner, Assistant Director
for Medical and Health Research
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington 25, D. C.

Dear Dr. Bruner:

The review of the work in neutron therapy on September 24 and 25 was a most profitable one for me since I had not previously had occasion to become familiar with any of the details of this work. As I mentioned to you earlier, I have delayed giving you my impressions of the status of this work, as requested by your letter of October 4, because I felt the need to discuss some aspects of the work more closely with Drs. Bond and Frigerio, and others and also to look into my own situation to decide whether I could do anything useful for the program.

My general feelings after the meeting might be summarized as follows:

1. I do not consider it advisable to attempt further clinical treatments of brain tumor by thermal neutron therapy until there is a sounder basis for the dosimetry of the exposures.

2. There does seem to be some evidence from the animal experiments, and even, in part, from the human exposures, that this method of treatment may ultimately be valuable for certain types of tumor, e.g., if the tumorous tissue is diffuse or branches in a complicated fashion through the brain tissues.

3. Speaking entirely from outside the field, the studies directed toward obtaining a higher concentration of B^{10} in the tumor seemed to offer some hope. At least, those reporting seemed to feel many compounds and modes of administration remain to be tried which were worth exploring. A differential concentration factor of 3 or 4 between tumorous and healthy brain tissues seems in hand, and much higher ratios have been achieved in some cases. It may be possible to discover what produces these exceptional cases and thus be able to increase the efficacy of the therapy.

4. Work on dosimetry is both feasible and indispensible. I believe it possible, within a year, to have good theoretical answers to any practical question the experimenters wish to pose. I have a neutron code which is functional and will estimate the dose from the neutron captures and recoil nuclei. This code does not handle the photons, either those incident or those produced by neutron capture, but, the Mathematics Panel tells me, a general photon code is practically complete here at the Laboratory which could be used for this problem. These studies could give dose distribution in an idealized homogeneous phantom for head and tumor and could take into account the higher concentration of B^{10} in the tumor.

   These studies will never give an extremely accurate estimate of dose since there are many idealizations involved, but we will never have enough detailed information on the configuration of the tumor, the distribution of B^{10} in the tissues, or nonhomogeneity of the tissues to give an estimate of dose down to the last rad. What the theoretical studies can do is give the dose distribution for several idealized cases, assuming different simple shapes for the tumor, different concentrations of B^{10}, etc., and explore these as a function of neutron energy. The advantage of epithermal beams, if there is such an advantage, can be easily demonstrated for these idealized cases. These idealized cases are quite good enough approximations for a decision to be made. Even the anthropomorphic phantom, or even measurements in a cadaver, will not give a precise dose estimate for a patient since his head will undoubtedly differ from both. But these small differences are not the important thing. The dose estimate cannot be more accurately known than the distribution of the B^{10}, and in a clinical case this will be known only roughly. Thus the theoretical studies can give the experimenter or the clinician all the dosimetric information he has a right to expect in a clinical case, for, in that case, the accuracy of the imput data will not be great.

   Experimental measurements should go along with the theoretical work, or anticipate it if possible. The accelerators mentioned at the meeting may make the experimenter's work easier than it has been. Above all, before clinical exposures are begun, there should be some experimental dosimetric studies using the proposed facility and setup for the treatment. If they are not conclusive, one may try to resolve this by both theoretical and practical studies.

I talked with Dr. Frigerio at the meeting about some intercomparison studies using his code and mine. Since his code involves a far more elaborate physical model (Maxwellian distribution of neutron velocities,

etc., vs. the monoenergetic model), this would be illuminating, but neither code should be in error by any amount significant for the clinician. I also have discussed the problem with Ralph Fairchild, and we are planning to work on the problem - he by measurement, and I by calculation. I see no major difficulty which should prevent us from giving as good a dosimetric picture as the input data will permit. Usually, one of the greatest uncertainties is in the energy spectrum of the neutron flux and the γ-rays that are present. That is why I think any answer obtained by calculation should be checked against a measurement on the facility as it will be used.

I do not plan to ask for any additional support for the work I propose to do. This does mean that I do not plan to go ahead on a "crash-program" basis, but I will be producing some dosimetric answers from time to time. Since there is no immediate and pressing need so far as any clinical program is concerned, I suppose this is satisfactory. I would prefer to work on this problem at the slower pace, as I would be reluctant to lay aside my work in internal dose, high-energy proton dosimetry (NASA), etc., and I believe the results will be better as more thought is given to the problem.

Very truly yours,

Walter S. Snyder
Assistant Director
Health Physics Division

WSS:ss

cc: K. Z. Morgan

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON 25, D.C.

October 4, 1962

Dr. Walter Snyder
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Dear Dr. Snyder:

On behalf of Dr. Dunham and members of the Division of Biology and Medicine staff, may I thank you for participating in the Neutron Capture Therapy Conference in Washington, September 24 and 25. Our impression is that valuable realistic consideration was given to many perplexing aspects of the general problem. We would be pleased to receive a letter from you giving thoughts or ideas about points you feel may have been omitted or passed over too lightly, and particularly any conclusions which emerged from the meeting.

While the first attempts at brain-tumor therapy have proved disappointing, the diversity of conditions with respect to differential distribution of target materials of different kinds and the application of neutrons with differing energies are so vast that investigation of potentialities for therapy leave open many avenues of investigation. We would especially ask whether benefit would come from a scientific meeting of the work-shop type convened perhaps shortly after the first of the year.

Please feel free to comment frankly and in detail.

Sincerely yours,

H. D. Bruner, M. D.
Assistant Director for
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