RADIOBIOLOGY

A Fast-neutron Source for Radiotherapy

In a recent note, Lomer and Greene[1] have recommended the development of a 14-MeV fast-neutron source for radiotherapy. We feel that there are disadvantages to this approach. The relative biological effectiveness of fast neutrons is related to their linear energy transfer, which in turn varies inversely with the energy of the neutron[2,3]. It has been shown that cell-killing by 1–2-MeV neutrons (linear energy transfer, 50–60 keV/μ) is relatively independent of oxygen[3]. As the energy of the neutrons is increased, the effect becomes more oxygen-dependent[4]—30-MeV neutrons would have a linear energy transfer similar to 250-kV X-rays, and hence a similar oxygen-dependence. If one is to expect an improvement in the results of radiotherapy due to the relative oxygen-independence of the effect of fast neutrons, then one must attempt to use those neutrons the effects of which are relatively oxygen-independent; this cannot be claimed for 14-MeV neutrons (linear energy transfer 20 KeV/μ). A useful increase in effective linear energy transfer with depth of penetration in tissue has yet to be demonstrated: the neutrons will lose energy and become more densely ionizing but the γ-ray component of the total dose rises.

Lomer and Greene concede that in the *D–T* reaction, 14-MeV neutrons are produced isotropically and do not suggest how they intend to collimate a useful beam of neutrons for localized radiotherapy without introducing extensive γ contamination and lowering the average linear energy transfer of the beam. By contrast, the bombardment of a thick target in a cyclotron produces a beam of fast neutrons projected mainly forwards, and this demands less collimation[5]. Any desired neutron energy may be obtained by appropriate choice of cyclotron size to produce the required energy of bombarding particle. Since fast-neutron irradiation seems to offer the promise of improved tumour response[6], it deserves to be carefully tried using equipment which produces the energy of particle most likely to give this improved response. The choice of a machine which only produces the less-effective 14-MeV neutrons solely because it is less costly, would be a disservice both to the radiotherapist and to clinical science in general.

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[2] Bateman, J. L., Rossi, H. H., Bond, V. P., and Gilmartin, J., *Radiation Research*, **15**, 694 (1961).
[3] Berry, R. J., and Andrews, J. R., *Brit. J. Radiol.*, **36**, 49 (1963).
[4] Hornsey, S., and Silini, G., *Intern. J. Rad. Biol.*, **4**, 135 (1961).
[5] Bewley, D. K., *Brit. J. Radiol.*, **36**, 81 (1963).
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Berry, Oliver and Porter have ably restated the facts we attempted to summarize in the second paragraph of our letter, but do not appear to have grasped the need for a compromise between the desirable high linear energy transfer associated with low-energy neutrons and the desirable penetrating power associated with high-energy neutrons. We do not suggest that 14-MeV neutrons give the best compromise of this type, but merely that since they are obtainable from a relatively cheap and compact source, their usefulness is worthy of experimental evaluation.

We do not dispute that a cyclotron is a more versatile neutron source than a *D–T* generator, but we do claim that the merits of low cost and compactness of the latter are very relevant to radiotherapy. We would certainly not agree that economic consideration can be entirely dismissed, as Berry, Oliver and Porter seem to suggest, though their imputation that cost is our sole consideration is, of course, incorrect.

It is perhaps worth enlarging a little on the importance of compactness. In radiotherapy accurate direction of the beam at the tumour is a primary consideration, and this is best achieved by using a flexibly mounted radiation source so that the beam may be moved with respect to a comfortably placed patient, rather than the patient 'lined up' to the machine: compactness is thus important because it facilitates accurate treatment.

We are, of course, well aware that designing a neutron collimator is a problem, and the solution of this problem is naturally an important part of our development programme.

Furthermore, even if 14-MeV neutrons prove to have no biological advantage over megavoltage X-rays, the *D–T* source may still be competitive with high-energy X-ray units, in so far as there are reasonable grounds for believing that they will produce similar dose distributions inside a patient.

For these reasons, to talk of a "dis-service to science" (as in their last lines) displays an emotional reaction which, when speaking of a research project, is scarcely justifiable.

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Lomer and Greene have recently proposed the development of a source of monoenergetic 14-MeV neutrons for radiotherapy[1]. Berry, Oliver and Porter have commented in the foregoing communication that such neutrons would have too high an energy to give the advantage over X-rays of independence of the biological effect on oxygen concentration which has been found with lower energy neutrons.

There are two distinct aspects to this discussion. One is the discussion of the 'biological' properties of such a beam compared with those of X-rays. The other is a possible 'economic' advantage if simple, cheap apparatus could produce a beam of penetrating radiation, even if the biological properties are not different from those of X-rays.

I agree with Berry, Oliver and Porter's comment that 14-MeV neutrons would have too high an energy, and consequently would give rise to proton tracks in tissue having too low a linear energy transfer, to give a significant advantage over X-rays in respect of the oxygen independence[2]. There is little doubt that the optimum neutron energy for obtaining the best compromise[3] between oxygen-independence[4–6], requiring low neutron energies, and good penetration of tissue[7], requiring high energies, is (giving wide limits) between 3 and 10 MeV mean energy. The small doubt that remains is due to the lack of information about the degradation of neutron energy with penetration into tissue, but rough estimates make this appear extremely unlikely to give a useful gain in ionization density with depth in tissue for neutrons of higher energies. There would be no 'biological' advantage in using neutrons which are too fast to give an oxygen-dependence significantly different from that of X-rays. Indeed, there may be some dangers in doing so until further investigations have been carried out on the effects of fast neutrons on cartilage, connective tissues, and other structures[8]: such work is in progress on the Medical Research Council cyclotron at Hammersmith.

It is true that an 'economic' advantage over cobalt-60 or linear electron accelerator sources would arise if a beam of radiation having penetration and output similar to that of 4-MV X-rays could be generated from simple, cheap