CYCLOTRON PRODUCTION OF THERAPY NEUTRONS

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ABSTRACT

A brief review of the historical development of the production of fast neutron beams for therapy, with special reference to the author's contribution, is presented. Different nuclear reactions and target systems have been critically examined regarding their suitability for cyclotrons of different sizes. A few current problems in this field, where the nuclear and accelerator physics communities can greatly contribute, are highlighted. Specific recommendations are made as to what sort of information needs to be acquired/compiled that would be most useful in the neutron therapy programme

1. Introduction

The interest in neutron therapy, and the number of centres around the world using this form of cancer treatment, have grown considerably since the late sixties when there were only a couple of centres seriously involved with this programme. There are now around 17 centres throughout the world (Table 1) who are routinely applying neutrons for therapeutical applications. More than 10,000 patients have so far been treated with neutrons either as the sole modality of irradiation or in combination with photons. The general conclusion, after reviewing the results on these patients, are that:

- For certain types of tumour (Salivary glands, Paranasal sinuses, Head and Neck tumours, soft tissue sarcomas, Prostatic Adenocarcinomas and Melanomas) neutrons are better than photons.

- For certain other types (Uterine cervix, Bladder and Rectum) conflicting and/or incomplete results have been reported on the comparison of neutron and photon therapies.

- For some tumours (Brain, etc.) there are no benefits, and in fact disadvantages of using neutrons in comparison to photons.

In the second group there are several types of tumour for which results are inconclusive and further studies are necessary. This has been mainly due to the fact that in many centres neutron treatments have been applied by using sub-optimal (e.g. poor penetration, fixed geometry, etc) neutron beams. These technical shortcomings would definately affect the conclusion regarding the value of fast neutron therapy.

However, from the results obtained so far, it can be concluded that neutrons are superior to photons for at least 10-20% of the radiotherapy patients. These percentages are probably at the lower limits because they were often obtained using "sub-optimal" neutron beams - produced by low energy cyclotrons. It is therefore quite likely that with "better" beams (more penetrant and rotating) these percentages could be improved upon.

An examination of Table I would indicate that out of the 17 Centres listed only about 5-6 (Clatterbridge, Louvain-la-Neuve, Fermilab, Seattle, Faure and Seoul) have the accelerators, and neutron producing methods, which could generate fast neutron beams approaching some sort of an "optimum". The remaining centres have to be content with "sub-optimum" neutron beams if they persist with their current neutron producing practices. The 5-6 " privileged Centres have large and expensive machines which only a handful of medical centres around the world can afford. On the other hand more centres are required to carry out neutron therapy programmes with something like "optimum" beams in order to quickly accumulate data on adequate numbers of patients in order to assess the real potential of neutron therapy.

TABLE 1

THE NEUTRON THERAPY FACILITIES IN THE WORLD

Centre	Neutron Producing Reaction	Remarks
UNITED STATES		
M D Anderson - Houston, Texas	p(42)+Be	Rotational Gantry Variable Collimator
Cleveland, Ohio	p(43)+Be	Horizontal Beam
UCLA - Los Angeles	p(46)+Be	Rotational Gantry Variable Collimator
Seattle, Washington	p(50)+Be	Rotational Gantry Multileaf Collimator
Fermilab, Batavia, Illinois	p(66)+Be	Horizontal Beam
EUROPE		
MRC - Clatterbridge, (Liverpool) U.K.	p(62)+Be	Rotational Gantry Variable Collimator
Orleans, France	p(34)+Be	Verticle Beam
UCL - Louvain-la-Neuve, Belgium	p(65)+Be	Verticle Beam
Hamburg, Fed. Rep. Germany	(d + T)	Rotational Gantry
Heidelberg, Fed. Rep. Germany	(d + T)	Rotational Gantry
Munster, Fed. Rep. Germany	(d + T)	Rotational Gantry
Essen, Fed. Rep. Germany	d(14)+Be	Rotational Gantry
ASIA		
National Institute of Radiological Sciences (NIRS) - Chiba, Japan	d(30)+Be	Vertical Beam Multileaf Collimator
Institute for Medical Sciences (IMS) - Tokyo, Japan	d(14)+Be	Horizontal Beam
Korea Cancer Centre Hospital (KCCH) - Seoul, Korea	d(50.5)+Be	Rotational Gantry
King Faisal Hospital - Riyadh, Saudi Arabia	p(26)+Be	Rotational Gantry
AFRICA		
National Accelerator Centre (NAC) Faure, Rep. South Africa	p(66)+Be	Rotational Gantry Variable Collimator

From ICRU (1) and Tsunemoto et al.(2)

As it seems quite likely that there is not going to be additional funding for a large number of big cyclotrons for neutron therapy purposes, alternative possible methods for improving the neutron beams from existing cyclotrons would have to be seriously examined. This is exactly what we have been doing since the late sixties by examining alternative nuclear reactions and target technology for the production of therapy neutrons, and have achieved considerable degree of success. A brief review of this work, with special reference to our own contribution, is presented in this paper. A few current problems in this field, where the nuclear and accelerator physics communities can contribute significantly are highlighted. Some specific recommendations are made as to what sort of information and basic data are still needed for the neutron therapy programme.(3)

2. NEUTRON BEAM REQUIREMENTS

2.1 Dose rate

It is generally regarded that a treatment time per fraction of more than 5 minutes or so would be unacceptable from the patients' comfort point of view. A typical neutron dose delivered per fraction ranges between 100-200 cGy (rad). Therefore the therapy neutron sources must be able to deliver at least 20cGy/min at the patient's position. Of course higher dose rates would be advantageous. The patient is normally located at about 1 - 1.5m distance from the neutron producing target because of the relatively large physical size of the Collimating head.

a. Deuteron reactions

The intensity of neutrons produced by a thick Be-target under bombardment with deuterons is given by

$$D = 2.12 \times 10^{-4} E^{2.97} \text{ rad/min/}\mu\text{A} \quad ....(1)$$

where E is the energy of the incident deuterons in MeV(4). From equation 1 it can be seen quite easily that even a small cyclotron, capable of accelerating deuterons to 10 MeV and having external beam currents of 100 μA (which are quite feasible in modern machines), could produce neutrons with dose rates of about 20/rads/min at 1 m distance from the target. This figure is naturally greater for higher incident deuteron energies available from larger machines. Similar or even larger dose rates are obtained by deuteron bombardment of other light elements, such as deuteron gas and heavy water (5,6), and Li-7 (7).

b. Proton reactions

Similarly, with proton induced reactions on Li-7 and Be-9 targets, using modern cyclotrons, adequate dose rates are produced for therapeutic applications (7 - 15)

Therefore, as far as dose rates are concerned there does not exist any problem with modern cyclotrons irrespective of whether protons or deuterons are used for the production of therapy neutrons. On the other hand, with D - T Generators, it is the intensity of the neutrons produced and hence the deliverable dose rates, along with the limited life of the target, that has discouraged the use of such generators for neutron therapy programmes.

2.2 Depth dose charateristics

This is a function of the neutron energy spectra and its mean energy. In radiological terms, the 50% - depth-dose (the depth in patient, at which the incident beam drops to 50% of its value) of a usable neutron beam should be around 15 cm or better. This compares favourably to the depth-dose characteristics of a modern 8 MeV linear accelerator and is slightly better than Co-60 gamma rays. In terms of neutron energy spectrum this would correspond to a mean energy of neutrons of around 20 MeV or so. This sort of neutron energy is required in order to be able to compare the efficacy of neutron therapy with modern conventional radiotherapy (x-rays) facilities.

Now let us examine how these energy requirements are met by neutron beams produced by cyclotrons of various sizes.

2.2(a) Deuteron Reactions

The average energies of forward direction neutrons produced by the bombardment of thick Be and Li targets, with different energy deutrons, are respectively given by (16)

$$\overline{En} = 0.42 \text{ Ed} \quad \text{(for Be)}$$
$$= 0.44 \text{ Ed} \quad \text{(for Li)}$$

These equations show that using thick targets of Be or Li-7 even a 30 MeV deuteron cyclotron would produce only a sub-optimum, although usable, neutron beam for therapy.

As early as the late 1960s, we started an extensive programme of examining alternative nuclear reactions and targets for producing neutrons with higher mean energies than produced by the d + Be reaction. For this purpose, we made extensive use of available forward direction (zero-degree) absolute cross-sections, and angular distribution of the (d,n) and (d,np) reactions on deuterium. We calculated the zero-degree yield and thick target neutron spectra, and the corresponding neutron dose at 100 cm from the deuterium target, for different incident deuteron energies of up to 16.7 MeV (the energy of the Hammersmith cyclotron). It was on the basis of these calculations that we were able to demostrate in 1969, for the first time ever, that deuterium could be a practical proposition as a neutron producing target in cyclotrons and that it would produce neutrons with higher mean energies and intensities than those produced with a Be target under similar bombardment conditions. For example, a 10 MeV deuteron beam would produce neutrons with a mean energy of about 9MeV from a deuterium target, which is higher than that of neutrons from 16 MeV deuterons on Be (5-6). Tbis indicates that even a small cyclotron, with a maximum energy of only 10 MeV, could produce a neutron beam comparable to that of the Hammersmith cyclotron in penetration and higher in intensity.

The results of our calculations have since been verified both experimentally and theoretically (3) and a number of institutions have used deuterium gas as a neutron producing target in their cyclotrons. The use of a deuterium gas target is, however, technically more complex than using thick Be target. Cells containing high pressure gas to act as thick targets, but still having thin entrance windows to minimize the energy loss by the incoming beam, have to be designed for long and reliable operation. In order to make this apparently difficult task easier, we suggested the use of a 20cm long gas cell with only a few atmospheres of deuterium pressure in it (6, 17). We demonstrated by extensive calculations that by absorption of only a few MeV's from the incoming beam into the target, instead of completely stopping it, one could still produce a therapeutically acceptable beam (17). For example, a 16 MeV deuteron beam would lose 2 or 3 MeV in the gas target with 3.19 or 5.26 atm pressure, respectively, and produce neutron dose rates of 36 and 63 rads/min at a distance of 100 cm from the target (17). Also, it is much easier to construct a cell for holding 3 0r 5 atm of deuteron gas, rather than one for 20 atm which would be required to stop the 16 MeV beam completely.

It was also shown by us theoretically (5) and experimentally (18) that a heavy water target would produce a more penetrating neutron beam than a Be taget at the same bombardment energies, and that a limited neutron therapy programme could be conducted with small cyclotrons (deuteron energy of around 10 MeV) using such a target (19).

During our investigations we also calculated the neutron spectra and intensities form the deuteron bombardment of a thick tritium target at different incident energies. We found that the neutron intensity from a thick tritium target was almost identical to the neutrons from a deuterium target. However, what surprised us most was the result that, in spite of the difference in the Q values of d + D and d + T reactions (3.8 and 17.6 MeV, respectively), there was little difference between the average neutron energies from the two targets, especially at higher energies (5-6). For example, the average neutron energies from thick deuterium and tritium targets at deuteron energies of 8, 10, 12 and 16 MeV were 8.2, 9.1, 9.5 and 11.3 MeV (for deuterium) and 12.3, 12.6, 13.3 and 14.8 MeV (for tritium), respectively.

The similarity between the neutron mean energies from the two targets is attributed to the role of (d,np) neutrons which are produced by the breakup of the deuteron in the coulomb field of the target. The thresholds for this reaction from deuterium and tritium are 4.4 and 3.7 MeV, respectively. Its cross-section increases rapidly with increasing deuteron energy. These netrons have much less energy than the (d,n) neutrons and, owing to their large number, would bring down the mean energy of the entire spectum irrespective of the Q value of the (d,n) reaction. On the basis of this finding, we were able to point out catergorically, for the first time ever, that tritium has no advantage (but some disadvantages) over deuterium as a neutron producing target in cyclotrons, especially at higher deuteron energies (5).

It is also as a reult of these breakup neutrons that the average energies of neutrons produced by thick Be and Li targets, 0.42E and 0.44E , respectively, are very similar, in spite of a large difference in the Q-values of the reactions Be(d,n) and Li(d,n) (4.4 and 15.0 MeV, respectively) (16). Moreover, this breakup phenomenon also provides a possible explanation as to why the shapes of the neutron spectra from a number of targets, from Be to Au, appear to be similar, especially at higher deuteron energies (20). This shows that at higher incident energies, the neutron spectra from most of the elements, with the exception of very light ones such as D and T, would be similar, irrespective of the Q value of the reaction or the level structure in the daughter nucleus.

2.2 Proton induced reactions

In the early 1970s, we started investigating proton induced reactions as possible sources of therapy neutrons, mainly for two reasons: (1) the available proton energy from a modern isochronous cyclotron is about twice that of the deuterons and is, therefore, likely to yield neutrons with higher mean energies; (ii) we presumed that the contribution of the "three-body breakup" neutrons might not be as significant as in the case of deuteron induced reactions.

At the time there were no thick target neutron spectra available in the literature for proton induced reactions on light nuclei such as Li, Be, etc., in the energy range of our interest. Therefore, using the thin target Li(p,n) neutron spectra of Jungerman et al. (21) and the available cross-section data, we empirically constructed the thick target neutron spectra of this reaction at different bombardment energies (8).

We were the first to suggest the use of a Li-7 target for production of neutrons with cyclotrons and to demonstrate, for the first time ever (as far as we are aware), that a Li target would produce neutrons with much higher mean energies when bombarded with protons form a cyclotron than any reaction using deuterons from the same machine at similar beam currents (8). We calculated that incident proton beams of 39, 35, 32, 28, 23, 17, and 10 MeV would produce, from a thick Li-7 target, neutrons with average energies of 19.7, 17.2, 16.7, 15.1, 13.0, 7.2, and 4.5 MeV, respectively (8). It was extremely pleasing to note that these average energies, which had been derived using our "crude" empirical methods, are in good agreement with those measured by Lone et al (7) and with his extrapolated data. The neutron intensities from this reaction, at all the incident energies, were also found to be adequate for therapy. In addition, we showed that, by using a moderatley thick (not stopping the beam completely) rather than a thick Li target, one could further increase the mean neutron energy and obtain a much cleaner (fewer lower energy neutrons) neutron spectrum, and still retain adequate neutron intensity (8). We verified this result experimentally using the Melbourne University cyclotron (22).

Since our results were published, a number of groups around the world have started using proton instead of deuteron induced reactions on light nuclei, especially Be, for producing therapy neutrons with cyclotrons (Table 1). Extensive measurements have been carried out on the intensity and spectra of these (p,n) neutrons (9-15). Most of the experimental arrangements used by these authors have a neutron energy threshold of about 10 MeV (viz. they could not measure neutrons of less than 10 MeV), with the exception of Graves et al. (13), who could measure neutrons of as low as 1.4 MeV. It is quite likely that there are many low energy neutrons which could not be observed by them experimentally (11). Keeping in mind this limitation in the experiments, their results indicate that (11):

a) Li and Be targets of equivalent thicknesses would produce neutron beams of almost similar characteristics (Li being slightly better) when bombarded with protons;

b) protons from a cyclotron incident on a Be target would produce a more energetic, more penetrating, more skin sparing and more intense neutron beam than that produced by the deuterons from the same cyclotron at the same currents from a Be target.

The authors (11) advocate the use of a Be target, as it is easy to handle, has a high melting point, adequate heat conduction and is chemically inert. However, Li has advantages too. It is more readily available, cheaper and less hazardous than Be. Moreover, owing to its low melting point, it should be quite feasible to design a liquid Li target for cyclotron use.

As we pointed out by our calculations (8), the experimental results also demonstrate that, using proton induced reactions on Li and Be, even small cyclotrons (maximum proton and deuteron energies of 20 and 10 MeV, respectively) should produce neutrons of therapeutically acceptable intensity having a penetration equal to or better than that of the Hammersmith neutron beam (7, 12).

A quick glance at Table I wuld show that some of the centres are producing therapy neutron beams by bombarding 60-66 MeV protons on semi-thick Be targets (absorbibg about 40 MeV). This set-up provides adequate dose rates and penetration and seem acceptable. However, the following questions still remain;

1. Could the 60-66 MeV protons on Be (40-MeV thick) neutron beam be further improved or beams with similar characteristics obtained with smaller and hence cheaper cyclotrons/accelerators?

2. What can be done about neutron therapy facilities who are using smaller cyclotrons and therefore, sub-optimum beams - could their neutron beams be improved to somewhat acceptable, although not necessarily optimum, penetrations?

These questions are still very much current and answers would greatly benefit the neutron therapy community.

3. IMPROVEMENT IN THE MEAN ENERGY (AND PENETRATION) OF NEUTRON BEAMS

There are various possible methods for increasing the mean energy of neutrons from a nuclear reaction without changing the bombardment conditions. One method involves the use of a "thin" (or only moderately thick) rather than a thick target and suitable backing material.

We demonstrated by our calculations for the Li(p,n) reaction that a "thin" target, which reduces the energy of 28 MeV protons to 23 MeV, would produce a neutron spectrum with a mean energy of around 19 MeV, instead of about 15 MeV from a thick target (8). Of course, the neutron intensity from these targets would be correspondingly lower. Similar results have been experimentally observed for the Be(d,n) reaction and different thicknesses of Be. Parnell obtained neutron mean energies of 7.7 and 8.2 MeV, respectively, when he used thin Be targets, 101 mg/cm^2 and 51 mg/cm^2 thick (which reduced the 16 MeV deuterons to 11 and 13.5 MeV, respectively) instead of a thick one, which would have given him a mean energy of only 7.0 MeV (23). In the same way, Meulders et al. (20) were able to increase the mean energies of the neutrons produced by 33 MeV deuterons from 15.3 MeV (for a thick target) to 17.9 and 17.5 MeV by using 1.1 mm thin Be targets on copper and gold backing, respectively. Their results also demonstrated the role of the backing material on the resultant neutron mean energy. This material should ideally produce as few neutrons as possible in order to have the least influence on the mean energy of neutrons produced by the target. We have provided a systematic method for selecting the optimum target thicknesses of Be and Li, for producing therapy neutrons, under bombardment with protons and deuterons of different energies specifying cyclotrons of different sizes (24).

The second method for improving the mean energy of neutrons and, hence, their penetration is to attempt to filter the low energy neutrons without affecting the high energy ones to any great extent. The obvious choice for the filter material would seem to be polyethelene or any other hydrogenous substance. Copper filters have also been tried, but without success (13). By using polyethelene filters of different thicknesses, various authors have improved their neutron beams (13-15, 23, 25). However, it must be mentioned that, as expected, there is a certain loss of neutron intensity as a result of filtration (12-15, 25), but this loss would not be drastic and would not affect the usefulness of various neutron beams. The third method would be the choice of another nuclear reaction and target material for producing therapy neutron beams with proton (and/or even deuteron bombardment).

4. CURRENT PROBLEMS AND INFORMATION REQUIRED

There are still a number of problems in the field of therapy neutron production, where the nuclear physics and accelerator communities can substantially contribute and help their medical colleagues. Some of these problems are now discussed.

4.1 Accurate measurements of (d,n) thick target spectra

A great discrepancy still exists regarding the correct shape of thick target neutron spectra from the Be(d,n) reaction. On the one hand, the data of Parnell (23) for a deuteron energy of 16.7 MeV show a single, broad, high energy maximum in the neutron yield, with a monotonic decrease down to about 1 MeV. On the other hand, the data of Lone et al. (7) show, in addition, a very steep rise in the yield below 2 MeV. The data of Meulders et al. (20), which extend down to 2.5 MeV, also show what could be interpreted as the beginning of a rise at lower energy. This low-energy peak has also been observed by Weaver at 22 MeV deuteron energy (26). So the important question arises as to whether this intense low energy shoulder exists in the spectrum or not. Similarly, most of the spectral data on (d,n) and (p.n) reactions extend only down to about 5-10 MeV, and very little information is available on the low energy neutrons. From the shapes of various spectra, and from the depth-dose characteristics, it is expected that the flux of these low energy neutrons will be quite substantial, but this needs experimental verification. From a therapy point of view, these neutrons are very important, as they would be quickly absorbed in the first few millimeters of the body (i.e. in the skin, etc.) and impart large unecessary doses. Furthermore, an accurate knowledge of the entire therapy neutron spectrum is also needed for exact dosimetry calculations.

4.2. (p,n) nuclear reactions

As mentioned above, protn induced reactions on light nuclei offer the possibility of producing the most suitable neutron beams for therapy. Therefore, accurate measurements and compiliation are needed on the cross-sections, angular distributions and thick target spectra of proton induced reactions on Be, Li, C, deuterium and H_2O, for proton energy of up to 100 MeV. As already mentioned, it would be necessary to extend the neutron spectrum measurements from thick targets down to a few hundred KeV's. Information is also needed on the production cross-sections of the accompanying gammas from different target materials.

4.3. Target designs

Information is also required on the practical design of thick and semi-thick targets of the above-mentioned nuclei which would produce the most suitable therapy neutron beam, and of the corresponding backing material.

4.4. Transport calculations/measurements

Calculations, and possible measurements, of the transport of neutrons produced from different elements through tissue equivalent media are of basic importance in neutron therapy. We believe that calculations, using appropriate transport codes and cross-sections, should be a lot easier and more convenient than experimental measurements. In fact, for the neutron beam produced by 16.7 MeV deuterons on Be, we have demonstrated that different transport codes can provide results which are in good agreement with the existing experimental data (27). Therefore, it could be possible to calculate the transport of higher energy neutron beams through the tissue equivalent media using the same or improved codes. Of course, relevant neutron cross-sections on tissue constituents H, C, N, O, P, Ca, etc. would need to be compiled or measured.

4.5. Filtration

It has already been mentioned that the use of certain "filters" removes some of the low energy neutrons and thus "hardens" the neutron beam. However, a great deal of work still needs to be done here in order to find out the optimum composition and thickness of the "filters" for neutron beams produced through different nuclear reactions, target systems and bombarding energies. One could study the effect of different materials and/or their combinations, and of various thicknesses, on thee above-mentioned neutron spectra, either experimentally or by transport calculations.

4.6. Design of the collimator and the "neutron head" shielding

The cross-sections and angular distributions of neutrons and the associated gammas from the (n,xn) reactions on C, Fe, Cu, and W for neutron energies of up to 100 MeV are urgently needed. This information is necessary for the design and improvement of the collimator and "neutron heads", especially for high energy beams (Seattle, Clatterbridge, Faure, etc.) which are already being used for therapy.

To this end we would like to make the following recommendations regarding the requirements of the neutron therapy programme. These were presented to the I.A.E.A. Advisory Group Meeting on Nuclear and Atomic Data for Radiotherapy and Related Radiobiology, Rijswick, Netherlands, 1985 (3).

5. REQUIREMENTS FOR NEUTRON THERAPY PROGRAMME

OBJECTIVES

1. To produce well defined, high intensity fast neutron beams with mean energies in excess of 20 MeV from light element targets of different thicknesses, when bombarded with protons and He-3 particles of up to 100 MeV energy and deuterons of up to 50 MeV.

2. To design a suitable neutron producing target capable of withstanding beam currents of the order of 100 A, with appropriate backing material for beam "dumping" and/or for cooling purposes.

3. To design neutron collimators and "swinging" neutron head with appropriate shielding.

4. To measure and/or calculate the transport of different neutron beams produced by the above-mentioned targets and nuclear reactions through a tissue equivalent medium.

5. To calculate and/or measure the filtering effects of different materials, and their combinations, on the above-mentioned neutron beams. This information would assist in the design of appropriate filters which could harden the neutron beams by selectively removing the low energy neutrons.

NUCLEAR DATA REQUIREMENTS

1. Absolute excitation functions at 0, 15, 30, 45, and 60 degrees (laboratory), from threshold to up to 100 MeV in steps of a couple of Mev's for the production of neutrons and the associated gammas from protons, He-3 and deuteron induced reactions on Be, Li, D_2, C, H_2O and Cu.

2. Complete angular distribution of neutrons and the asssociated gammas from the above-mentioned reactions at different energies up to 100 MeV.

3. Neutron spectra from the above-mentioned nuclear reactions from targets of various thicknesses at 0, 15, 30, 45 and 60 degrees at different bombardment energies (at energy intervals of a few MeV's).

4. Development/compilation of suitable transport codes and the necessary neutron cross-sections on H, C, N, O, P and Ca in oder to be able to calculate the transport of the above-mentioned neutron beams through tissue equivalent media.

5. Absolute cross-sections and angular distribution of the secondary neutrons and the associated gammas from the (n,xn) reactions on Fe, C, W, Cu, etc. for neutron energies up to 100 MeV.

This information is necessary for

designing the neutron collimators, the neutron head and the associated shielding.

REFERENCES

1. ICRU. International Commission on Radiation Units and Measurements, Clinical Neutron Dosimetry, Part 1. Bethesda, MD 20814, USA (1989)

2. H. Tsunemoto, et al., Strahlentherapie und Onkologie (in press)

3. M.A. Chaudhri, Nuclear and Atomic Data for Radiotherapy and Radiobiology, Int. Atomic Energy Agency, Vienna (1987) p. 155

4. J.B. Smathers, V.A. Otte, A.R. Smith and P.R. Almond. Med. Phys. 3 (1976) 45

5. M.A. Chaudhri and G.J. Batra in the Int. Conf. Use of Cyclotrons in Chemistry, Metallurgy and Biology, Oxford, Sept. 1969

6. G.J. Batra, D.K. Bewley and M.A. Chaudhri Nucl. Instr. and Meth. 100(1971)135

7. M.A. Lone, et al., Nucl. Intr. and Meth. 143(1977)331

8. M.A. Chaudhri, S. Zuberi, A.J. Chaudhri and Q.J. Chaudhri. Eur. J. Cancer 10 (1974)260

9. R. Madey, F.M. Waterman and A.R. Baldwin, Med Phys. 4(1977)322

10. S.W. Johnsen, Med. Phys. 4(1977)255

11. H.I. Amols et al., Med Phys. 4(1977)486

12. W.M. Quam, et al., Phys-Med Biol. 23(1978) 47

13. R.G. Graves, et al., Med. Phys. 6(1979) 123

14. G.H. Harrison, E.K. Balcer-Kubiczek and C.R. Cox, Med. Phys. 7(1980)348

15. D.K. Bewley, et al., Phys. Med. Biol. 25(1980)887

16. J.F. Fowler, in Nuclear Particles in Cancer Treatment, Adam Hilger, Bristol (1981)51

17. M.A. Chaudhri, Nucl. Instr. and Meth. 120(1974)357

18. C.J. Parnell, B.C. Page and M.A. Chaudhri, Br.J. Radiol. 44(1971)63

19. M.A. Chaudhri, J.C. Clark and J.C. Parnell, Proc. 9th Int. Conf. Cyclotrons and their Applications, Caen, 1981 (G Gendreau, Ed.), Les Editions de la Physique, Les Ulis (1982)679

20. J.P. Meulders, et al., Phys. Med. Biol. 20(1975)235

21. J.A. Jungerman, et al., Nucl. Instr. and Meth. 94(1971)421

22. M.A. Chaudhri, J.L. Templer and J. Rouse, Int. J. Appl. Radiat. Isot. 30(1979)504

23. C.J. Parnell, Br. J. Radiol. 42(1972)452

24. M.A. Chaudhri, Proceedings of this Conference

25. S.W. Johnson, Phy. Med. Biol. 23(1978)499

26. K.A. Weaver, Rep. UCRL-51310, Lawrence Livermore National Laboratory, Livermore, California (1973)

27. M.A. Chaudhri and B. McGregor, in Proc. II Int. Symp. Radiation Physics, Universiti Sains Malaysia (1983)492