# PRODUCTION OF SECONDARY NEUTRONS FROM PATIENTS DURING THERAPY WITH CARBON IONS, THEIR DOSE CONTRIBUTIONS AND POTENTIAL RISKS

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*Abstract*

By making use of the experimental neutron production data from different elements, under bombardment with carbon ions of 100 to 400 MeV/u energies, we have estimated the flux and energy distribution of secondary neutrons produced in patients during therapy with C-ions.
Our results indicate that at least 4 neutrons, with energies greater than 5 MeV, are produced for every C-ion of 400 MeV/u energy incident on tissue; which reduces to 3, 1.4 and 0.3 respectively at incident C-ion energies of 300, 200 and 100 MeV/u. For a typical therapy C-ion dose of 20 Gy (physical), the effective whole body dose due to the secondary neutrons is estimated to be about 1 Sv, that is about 5% of the incident C-ion dose for 400 MeV /u energy. The doses to 22 Organs from these neutrons have also been estimated and ranges up to 230 mGy cm ^2 at an incident C-ion energy of 400 MeV/n. These figures could be higher if neutrons with energies less than 5 MeV, about which we do not have any experimental data, were also included.
In our opinion these neutron doses are large enough to potentially cause secondary cancers and induce other harmful effects into patients. Therefore, this matter of secondary neutrons from patients during therapy with C-ions must be even more thoroughly investigated before continuing therapy with C-ions.

## INTRODUCTION

Radiotherapy treatment of different types of cancers with carbon ions is being conducted at the National Radiological Centre in Chiba (Japan), at the Heavy Ions research Facility at Darmstadt, Germany by the German Cancer Research Centre and the University of Heidelberg and at Particle Accelerators for Therapy, Radiology and Oncology Centre at Hyogo, Japan [1]. So far more than 2025 patients have been treated with C-ions at these centres [1]. Further facilities to conduct carbon- ion therapy are under construction at Heidelberg and Lanzhou (China) and being planned in Italy and Austria [1]. However, in spite of all this activity and interest in carbon-ion therapy, it is surprising that the matter of secondary neutron production from patients, and its potential implications, has been practically ignored.

## METHOD AND MATERIALS

There appear to be no measurements or calculations in the literature, on neutron production from tissue under bombardment with carbon ions,. However, experimental data is available where neutron yields from thick- targets of C and other heavier elements have been studied for carbon ion incident energies of up to 400 MeV / u [2], which covers the energy range being actually used in therapy . It is shown that the secondary neutrons produced have energies ranging from 5 MeV to twice the incident carbon- ion energy per nucleon with a abroad peak, at about 60-70 % of the incident carbon-ion energy, in the forward direction.
Furthermore, it is also pointed out by the authors, Kurosawa et al [2], that the dependence of the yield of neutrons with energies greater than 5 MeV (apparently the minimum neutron energy which they could measure), integrated for a hemisphere from 0 to 90°, on the target mass is very small compared with the difference of neutron numbers of the targets. For example the differences in the total yields of neutrons with energies greater than 5 MeV, from thick targets of carbon and aluminium, bombarded with carbon ions of 100, 180 and 400 MeV / u, are only 11.6, 13.0 and 13.6 % respectively, while the differences in the neutron yields from thick carbon and lead targets, are 10.8, 22.4 and 4.4 % respectively at incident carbon ion energies of 100, 180 and 400 MeV / u.. This means that the intensity of the secondary neutrons produced from thick targets of H, C, N and O would be similar, and at the most no more than around 10-15 % different from each other, under bombardment with C-ions in the energy range being presently considered.
Therefore, based on these observations, one may be justified to use the secondary neutron production yields from a thick target of carbon in order to approximately estimate the numbers of such neutrons produced within patients (tissue), undergoing therapy with carbon ions, as the major constituents of tissue are H, C, N and O.

## RESULTS AND DISCUSSION

Our results clearly show that 4.2, 3, 1.4 and 0.3 neutron, with energies greater than 5 MeV, are produced for every C-ions with energy of 400, 300, 200 and 100 MeV /u respectively. Besides these secondary neutrons, there would also be a considerable number of slower neutrons of energies lesser than 5 MeV for which there is no experimental data and therefore could not be included in the present estimation.

Typically, the medium dose per treatment of skull base tumours is around 20 Gy (physical) in the Darmstadt-Heidelberg programme [3].The numbers of C-ions required to impart a dose of 1Gy in tissue in the Bragg Peak are 6.9 x $10^{6}$/ $cm^{2}$, 8.8 x $10^{6}$ / $cm^{2}$ and 18.7 x $10^{6}$/ $cm^{2}$ at carbon ions energies of 100 , 200 and 400 MeV / u. respectively [4]. This means that the total numbers of secondary neutrons, with energies > 5 MeV produced from tissue at incident carbon ions energies of 100, 200 and 400 MeV /u would be 4.1 x $10^{7}$ / $cm^{2}$, 2.5 x $10^{8}$ / $cm^{2}$ and 1.6 x $10^{9}$ / $cm^{2}$ respectively.
These very large number of neutrons could potentially cause new secondary cancers and could also have other side effects, especially when the high radiobiological effectiveness (RBE) of neutrons is taken into consideration [5].
Kurosawa et al (5) also measured the energy distributions of neutrons produced from thick-carbon-target under bombardment with C- ions of 100, 180 and 400 MeV / u. By making use of the arguments already given one may also be justified to regard these energy spectra as similar to those which would be coming from a tissue target under bombardment with carbon ions. Therefore, from these energy distributions we have been able to estimate the mean-energy of the neutron spectrum to be 29, 50 and 125 MeV respectively at C-ions energies of 100, 200 and 400 MeV /u respectively. We used these values for estimating the "effective whole body dose" as well as doses to a number of organs. The energy spectra are "smooth and slowly varying" and one is, therefore, justified to take the mean-energy of the secondary neutrons spectra in order to estimate the dose contributions, rather than calculating doses at all the energies.
In order to estimate the radiation doses to the whole body and to different organs we made use of the tabulations of Bozkurt et al [6] which give fluence- to- dose conversion coefficients, at different neutron energies, based on their VIP-Man (Visible Photographic Man).

Our results show that for a physical dose of 20 Gy in the Bragg peak, the effective whole body doses due to these secondary neutrons are 18, 114 and 955 mSv cm ^2 respectively at C-ion energies of 100, 200 and 400 MeV/u. Furthermore, we have also estimated the doses to 24 body organs due to these secondary neutrons for different incident geometries, again by using the tabulations of Bozkurt et al [6].The results are shown in table 1 for three different incident geometries ; anterior-posterior (AP), posterior-anterior (PA), and isotropic (ISO).
It can be seen from our results that the effective whole body doses of around 18, 114 and and 955 mSv $cm^{2}$, are imparted by these secondary neutrons coming from patients' tissue at incident C-ion energies of 100, 200 and 400 MeV /u respectively. The corresponding doses to different organs range from 2-5, 15-30 and 130-230 mGy $cm^{2}$ at incident Carbon-ion energies of 100, 200 and 400 MeV /u , respectively. These doses are definitely not insignificant, especially when the radiation weighting factor for neutrons is taken into consideration for estimating the absorbed doses to different organs.
According to Brenner et al [3] " good evidence exists of increased cancer risks in humans for acute exposure of 10-50 mSv ". Therefore, the secondary neutrons produced by patients' tissues at incident carbon-ion energies of 200 MeV / u and above have the real potential of causing new cancers.

## CONCLUSIONS

Our estimation clearly show that a very large number of secondary neutrons are produced by patients undergoing therapy with C-ion beams, especially at energies of 200 MeV / u and higher. The estimated whole body effective dose and the doses to different organs are not insignificant and have the real potential to cause new cancers in the patients. It is therefore strongly recommended that, in the interest of safety of patients undergoing therapy with C-ions, comprehensive calculations and measurements should be conducted as soon as possible in order to:

(a) determine accurately the yields and energy distributions of the secondary neutrons, down to thermal region, produced from the patients
(b) to estimate the radiation doses imparted to various organs
(c) to assess the risks of new cancers and other side effects

An accurate knowledge of the fluence and energy distributions of the secondary neutrons is also necessary in order to assess their contribution to the "observed" RBE of C-ions.
It is further recommended that most serious and careful consideration should be given before deciding to treat a patients with C-ions, especially children and younger people who still have many years to live. After all, in our opinion, almost all the advantages of charged particle therapy can be achieved with proton beams which produce only 0.2-0.3 neutron per proton at incident energies of 200-250 MeV / u [8] and are therefore a lot less hazardous.

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| Carbon ion energy | 200 MeV / u | | | 400 MeV / u | | |
|---|---|---|---|---|---|---|
| | Radiation doses mGy cm^2 | | | Radiation doses mGy cm^2 | | |
| Incident geometry | AP | PA | ISO | AP | PA | ISO |
| ORGAN | | | | | | |
| Adrenals | 23 | 23 | 21 | 214 | 200 | 208 |
| Bladder walls | 26 | 24 | 20 | 205 | 205 | 198 |
| Bone | 15 | 15 | 13 | 136 | 147 | 137 |
| Brain | 23 | 24 | 23 | 187 | 181 | 184 |
| Breast | 20 | 24 | 22 | 105 | 208 | 163 |
| Esophagus wall | 26 | 24 | 22 | 205 | 203 | 190 |
| Eye lenses | 24 | 17 | 21 | 128 | 168 | 152 |
| Heart wall | 26 | 25 | 21 | 201 | 211 | 200 |
| Kidney | 24 | 26 | 21 | 211 | 222 | 202 |
| Liver | 24 | 24 | 21 | 205 | 211 | 198 |
| Lower large intestine | 27 | 24 | 21 | 206 | 216 | 195 |
| Lungs | 25 | 25 | 21 | 197 | 200 | 190 |
| Muscle | 24 | 24 | 21 | 186 | 184 | 182 |
| Pancreas | 24 | 23 | 21 | 203 | 211 | 197 |
| Prostate | 25 | 26 | 21 | 229 | 216 | 213 |
| Red bone marrow | 22 | 23 | 19 | 200 | 200 | 189 |
| Skin | 19 | 19 | 18 | 137 | 140 | 140 |
| Small intestine | 26 | 23 | 21 | 203 | 213 | 194 |
| Spleen | 22 | 25 | 22 | 210 | 198 | 192 |
| Stomach wall | 24 | 23 | 21 | 203 | 214 | 192 |
| Testes | 25 | 22 | 21 | 132 | 220 | 179 |
| Thymus | 24 | 21 | 19 | 173 | 190 | 186 |
| Thyroid | 30 | 23 | 21 | 162 | 224 | 184 |
| Upper large intestine | 26 | 23 | 21 | 189 | 213 | 195 |

Table 1. Radiation doses to different organs of a VIP-man, under various geometries, from secondary neutrons produced from patients' tissues after 20 Gy (physical dose in the Bragg-peak) irradiation with C-ions of different energies.