Secondary Neutron production from patients during hadron therapy and their radiation risks: the other side of hadron therapy

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- Hadron therapy has been reported to have many successful treatments in many patients. However, in some patients it does not work though theoretically it should. One possible cause could be the secondary neutrons which might cause this sort of failure. We must keep this in mind.

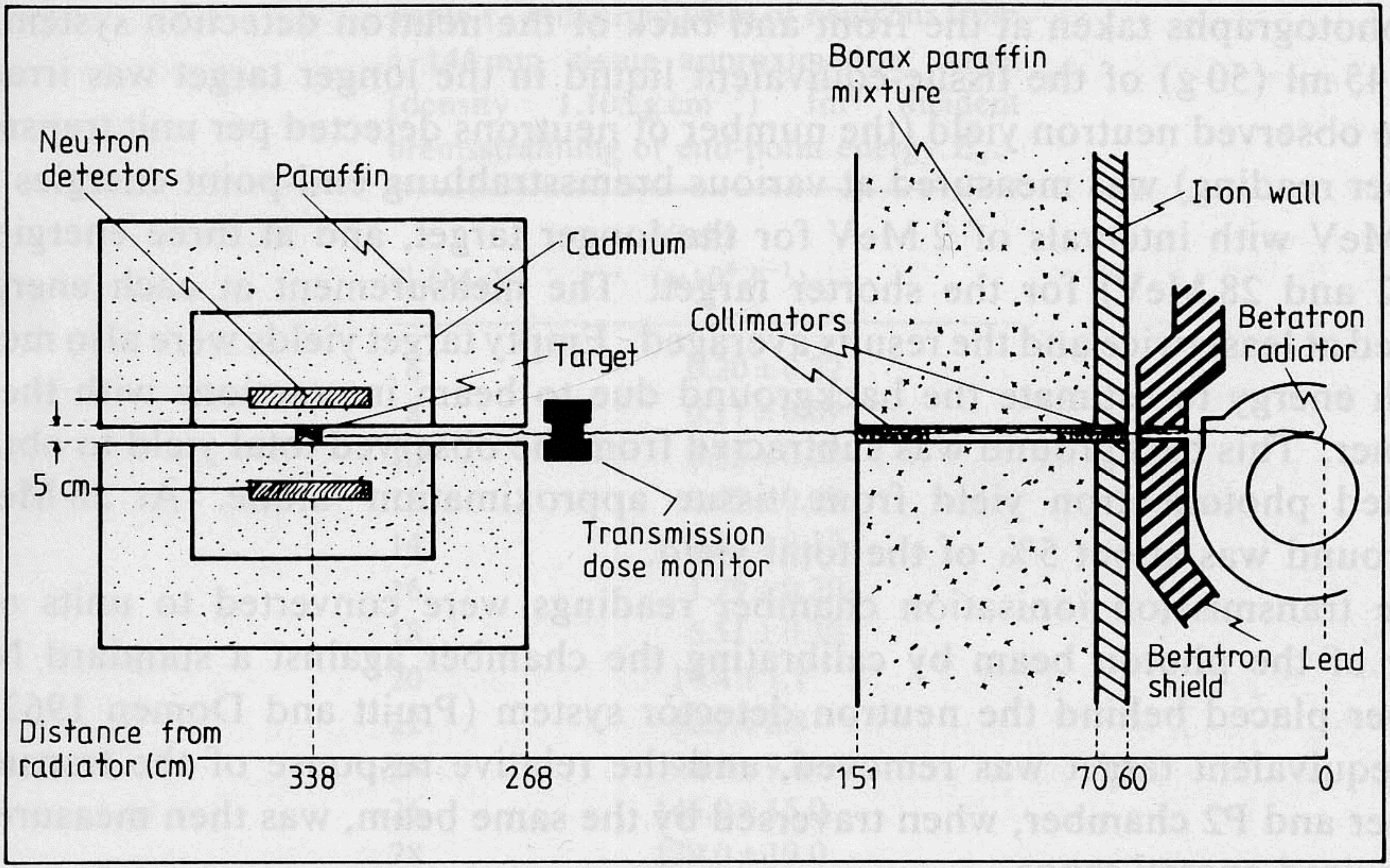
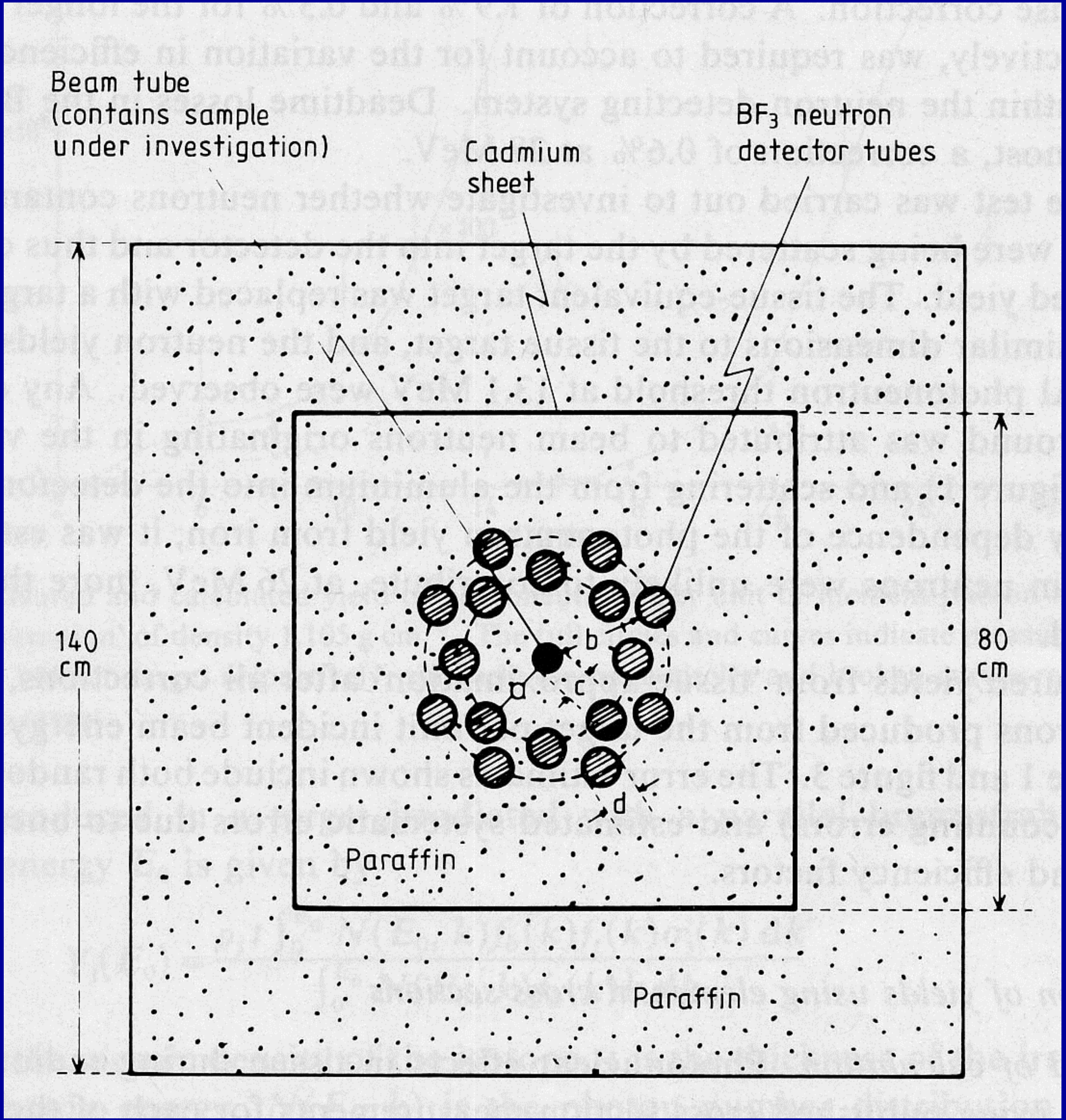
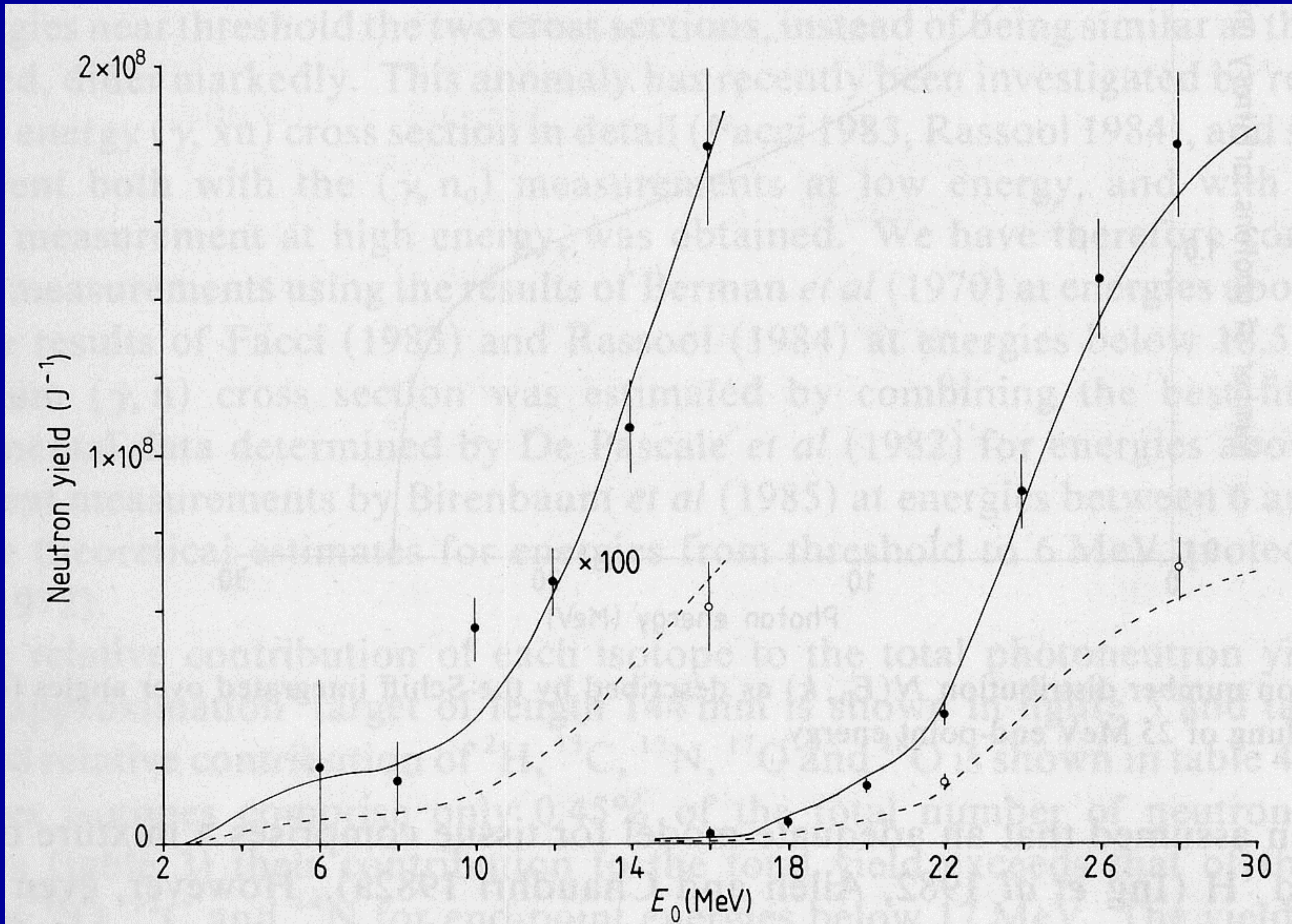


Figure 1. Experimental arrangement for the measurement of photoneutron yields.

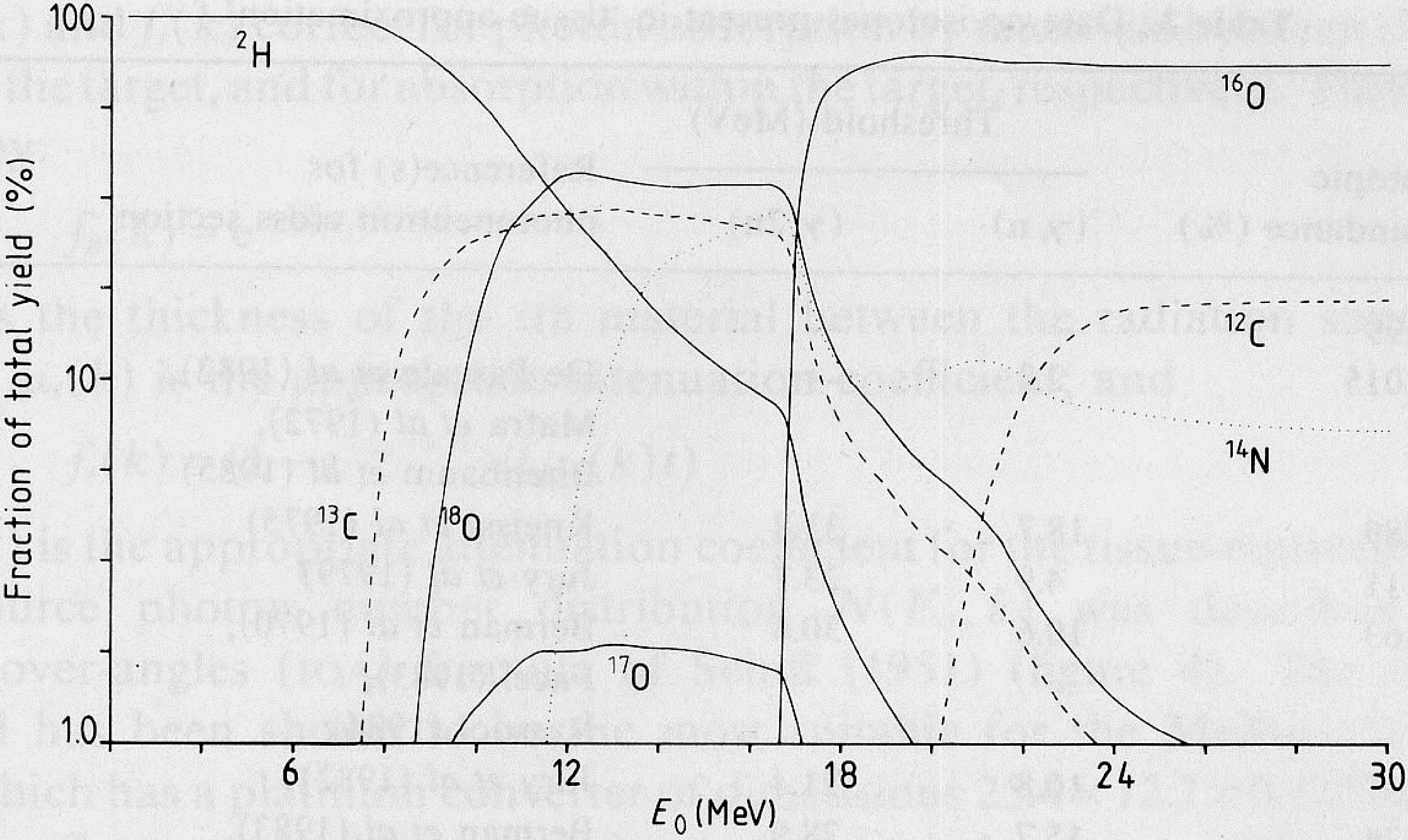

Beam tube
(contains sample
under investigation)
Cadmium
sheet
BF3 neutron
detector tubes
140
cm
80
cm
b
c
a
d
Paraffin
Paraffin



2×10^8
1×10^8
0
Neutron yield (J^-1)
×100
2
6
10
14
18
22
26
30
E0 (MeV)

Table 2. Data on isotopes present in 'tissue approximation'.

Isotope	Isotopic abundance (%)	Threshold (MeV) (γ, n)	Threshold (MeV) $(\gamma, 2n)$	Reference(s) for photoneutron cross section
^{1}H	99.99	—	—	
^{2}H	0.015	2.2	—	De Pascale *et al* (1982), Mafra *et al* (1972), Birenbaum *et al* (1985)
^{12}C	98.89	18.7	31.8	Kneissl *et al* (1975)
^{13}C	1.11	4.9	23.7	Jury *et al* (1979)
^{14}N	99.63	10.6	30.6	Berman *et al* (1970), Facci (1983), Rassool (1984)
^{15}N	0.37	10.8	21.4	Jury *et al* (1982)
^{16}O	99.76	15.7	28.9	Berman *et al* (1983)
^{17}O	0.04	4.1	19.8	Jury *et al* (1980a)
^{18}O	0.20	8.0	12.2	Woodworth *et al* (1979)



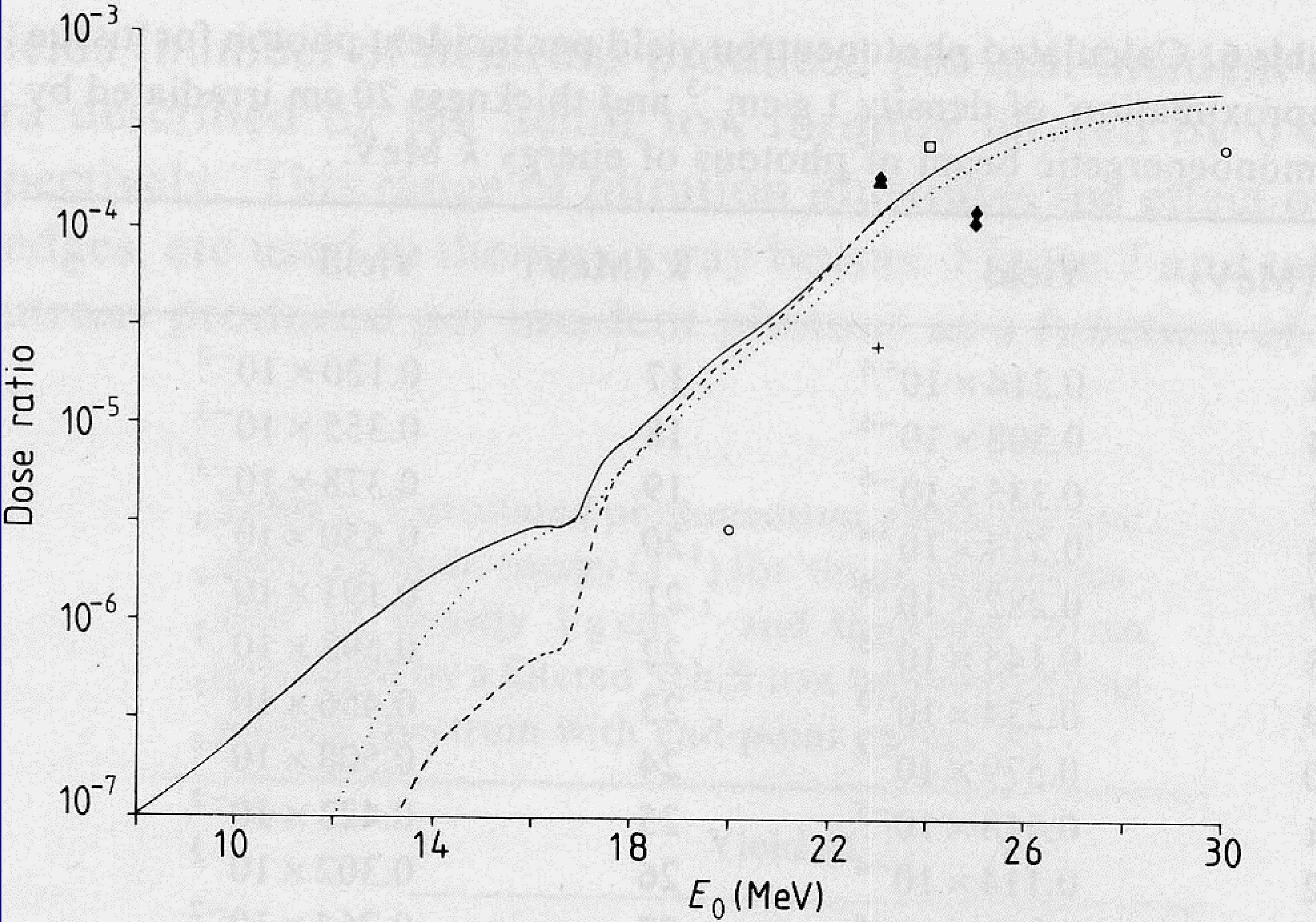
100
10
1.0
Fraction of total yield (%)
^{2}H
^{16}O
^{12}C
^{14}N
^{13}C
^{18}O
^{17}O
6
12
18
24
30
E_0 (MeV)

Table 3. Percentage contribution of each constituent isotope to the total photoneutron yield from 'tissue approximation' as a function of bremsstrahlung end-point energy E_0.

Isotope	Relative atomic abundance excluding ^{1}H(%)	Percentage of total yield E_0(MeV) 6	12	18	24	30
^{2}H	0.025	100.0	29.5	2.2	0.1	0.1
^{12}C	20.60	—	—	—	15.4	16.7
^{13}C	0.233	—	28.8	7.6	0.9	0.5
^{14}N	4.15	—	3.2	10.9	8.2	7.3
^{15}N	0.017	—	0.2	0.2	0.0	0.0
^{16}O	74.80	—	—	67.6	73.9	74.6
^{17}O	0.029	—	1.8	0.5	0.1	0.1
^{18}O	0.150	—	36.6	11.0	1.3	0.7

Table 4. Percentage contribution of the isotopes ^{2}H, ^{13}C, ^{15}N, ^{17}O and ^{18}O to the total photoneutron yield from 'tissue approximation', as a function of bremsstrahlung end-point energy E_0.

E_0(MeV)	Percentage of total yield
<10	100
12	97
14	80
16	72
18	21
20	10
22	5.4
24	2.5
26	1.8
28	1.5
30	1.4



10^{-3}
10^{-4}
10^{-5}
10^{-6}
10^{-7}
Dose ratio
10
14
18
22
26
30
E_0 (MeV)

Introduction

When patients are irradiated with hadrons, especially with heavier ions such as C, Ne, etc., a large number of secondary neutrons are produced from patients' tissue. These neutrons, from which no part or organ of the patients can be shielded, have the potential to cause harmful effects, such as induction of new primary cancers; life-shortening; chromosomes aberrations and genetic effects, etc, [1]. It is therefore essential to estimate the fluence and energies of these neutrons in order to calculate their dose contributions and to have an idea about their harmful effects.

Method of Estimation I

- There appears to be no measurements or calculations on secondary neutron production from tissue under bombardment with hadrons, especially ions heavier than protons (alphas, C and Ne-ions, etc.).
- However, there are measurements available on the fluence and energy distributions of the secondary neutrons from thick targets of carbon and other heavier elements, under irradiation with alphas, C and Ne-ions of up to 400 MeV / nucleon [2]. This range coves the energies which are currently being used for therapy with these ions.

•*It is shown by the authors that*:

The neutron spectrum in the forward direction spreads to upto twice the energy of the incident particles, with a broad peak at about the 60-70 % of the incident energy

• the difference in the out puts of the secondary neutrons, with energies greater than 5 MeV, from different elements, under bombardment with alphas, C and Ne ions is very little compared to the difference in the neutrons in the target nuclei.

- This means that the neutron out put from neighboring elements would be very similar, especially from C, N and O, etc, the main constituents of tissue.

- Therefore, for estimation purposes the neutron production from tissue would be similar to that from a carbon target under irradiation with alphas, C and Ne-ions.

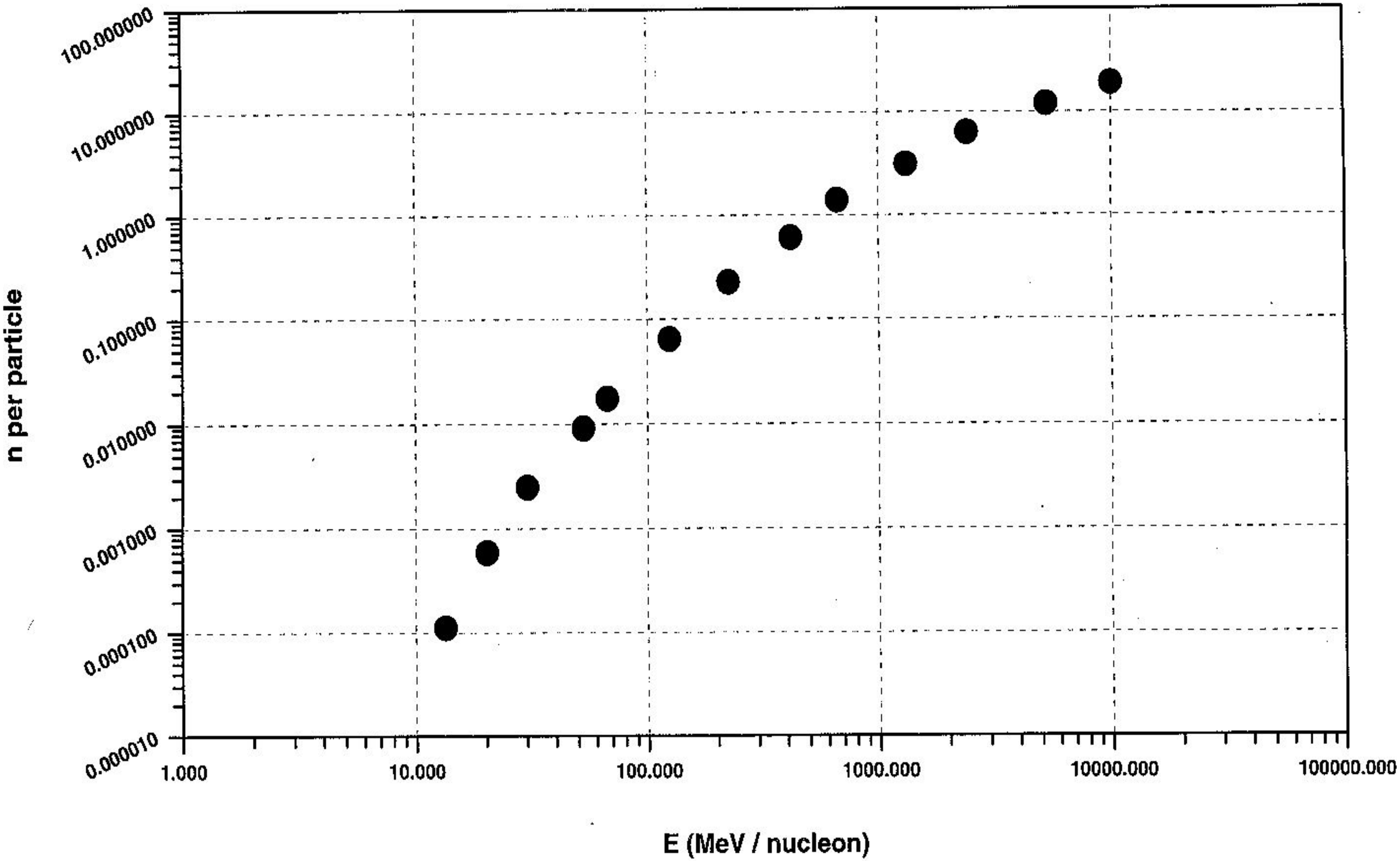
Results and Discussion

Estimated yields of secondary neutrons, of energies greater than 5 MeV, from tissue under irradiation with alphas, C and Ne ions are shown in fig. 1-3, respectively.

It should be noted that due to the non-availability of data from Kurosawa et al [2] for neutrons of energies lesser than 5 MeV, these could not be included in our estimation.

However, it should also be pointed out that this low-energy range is most important for the patient's safety purposes and every effort should be made to estimate the fluence and energies of these neutrons.

Protons on tissue



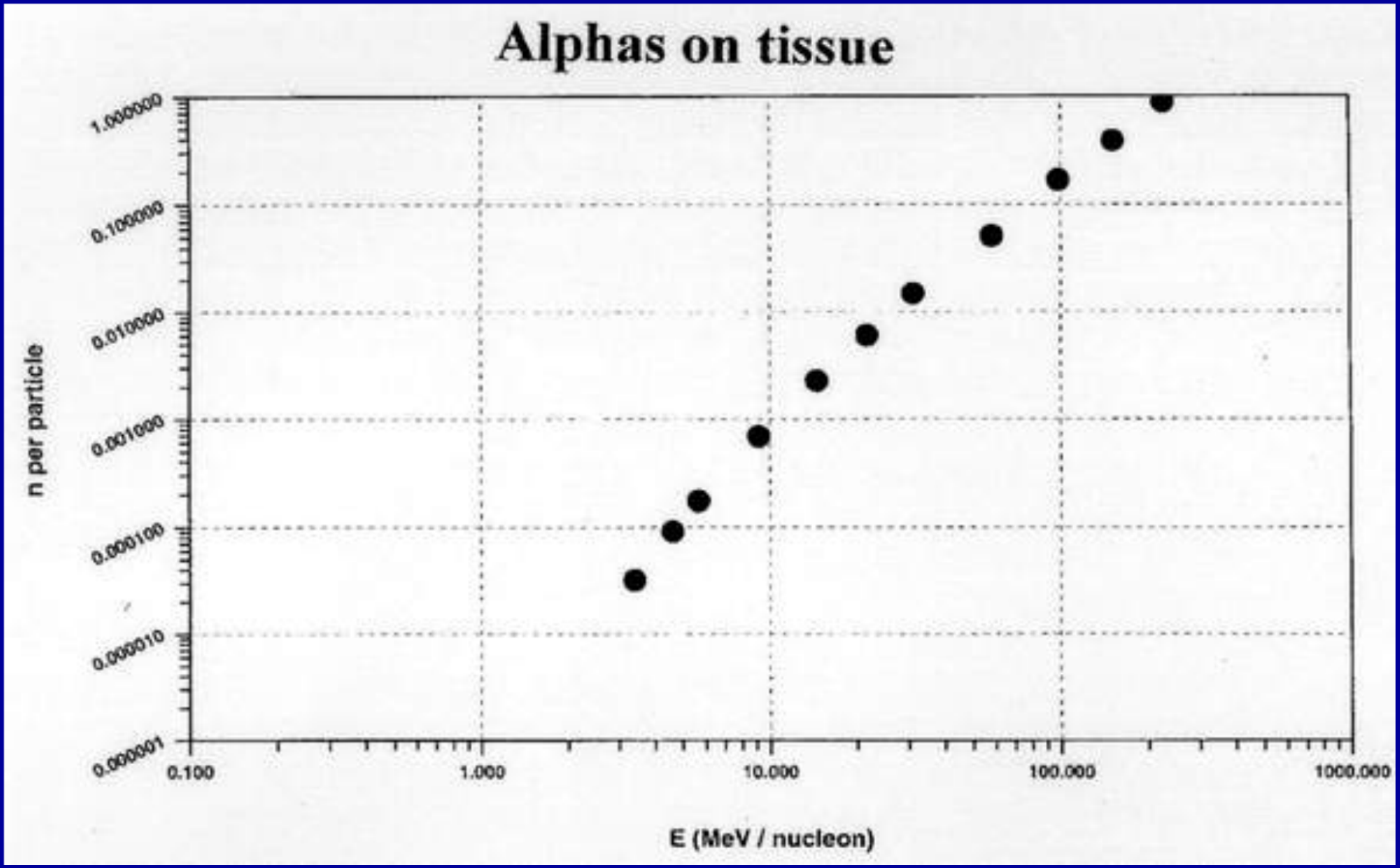


Fig. 1: Estimated yield of secondary neutrons, of energies greater than 5 MeV, produced from **tissue under irradiation with alpha particles.**

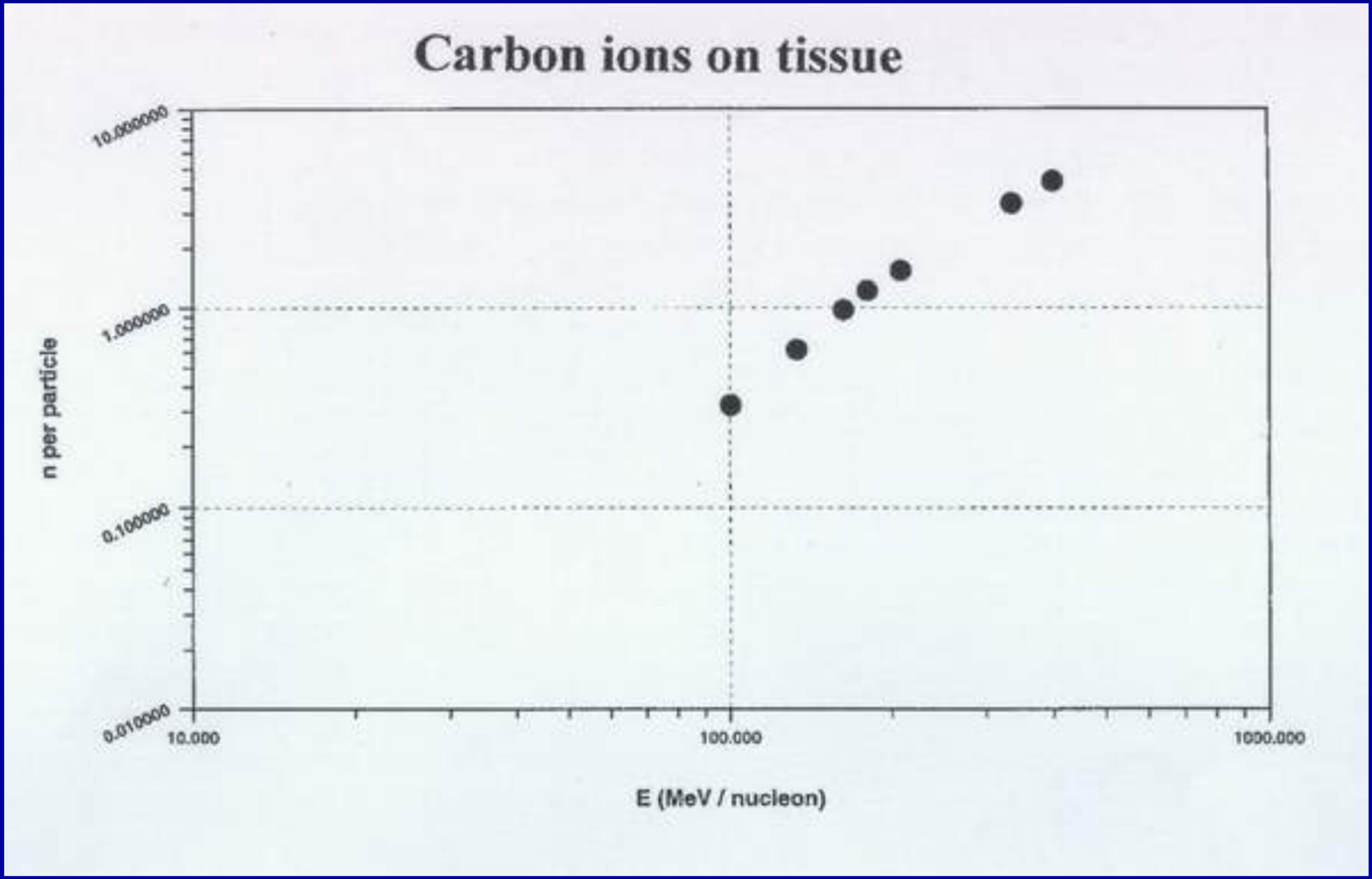


Fig. 2: Estimated yield of secondary neutrons, of energies greater than 5 MeV, produced from tissue under irradiation with Carbon-ions.

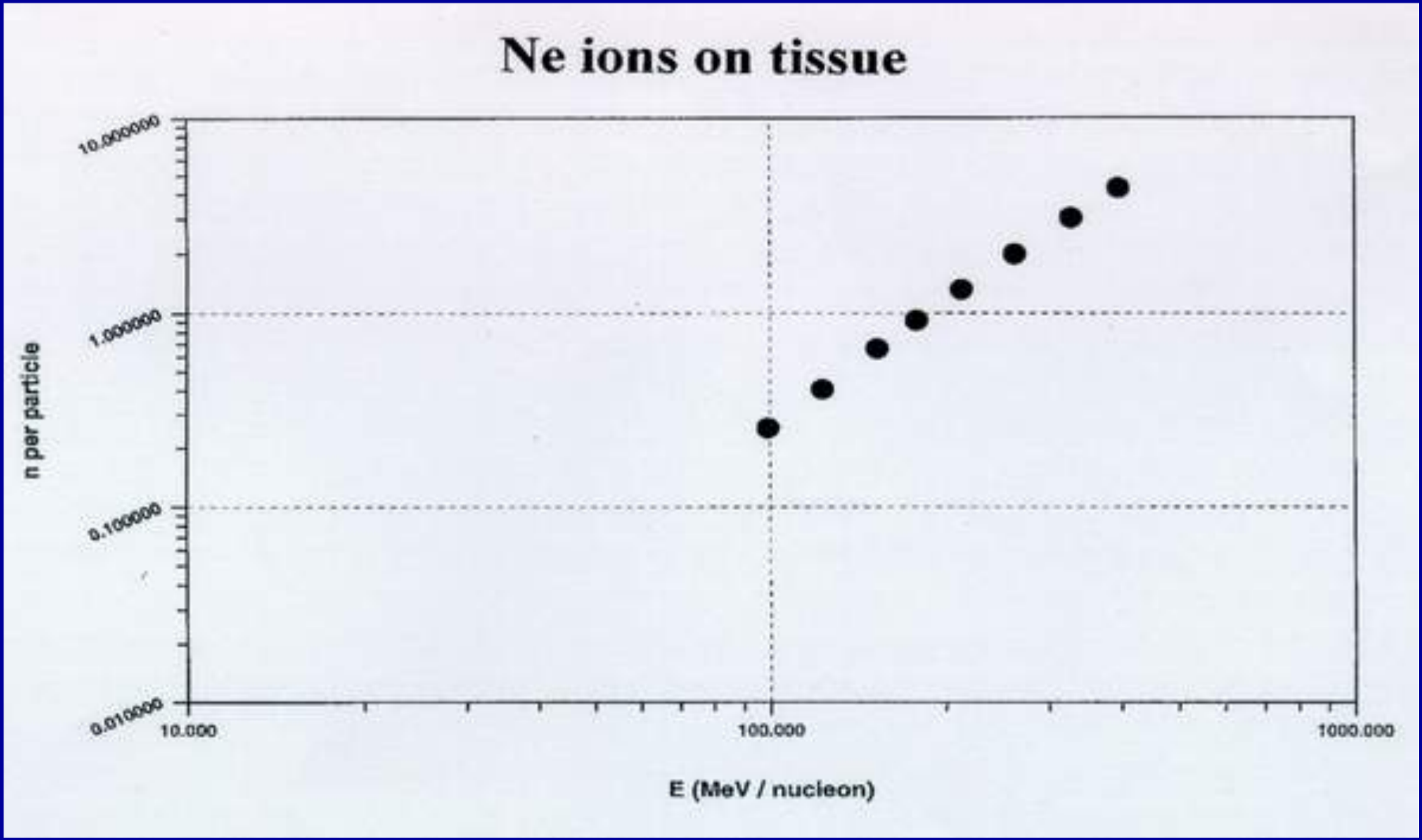


Fig. 3: Etimated yield of secondary neutrons, of energies greater than 5 MeV, produced from tissue under irradiation with Neon-ions.

incident energy of protons (MeV)	no of protons / cm² to impart 1 Gy in the Bregg Peak	everage nutreon energy (MeV)	no of secondary nutreons produced per proton	total number of secondary nutreons produced by a physical proton dose of 20 Gy in the Bregg Peak	estemated effective dose due to secondary nutreons (mSv) (ref. 4)		
					AP	PA	ISO
70	1.04 x 10^8	12	0,02	4,17 x 10^7	18	13	11
160	2,08 x 10^8	28	0,1	4,17 x 10^8	238	194	179
200	3,125 x 10^8	37	0,2	2,00 x 10^9	1094	1011	893

Proton energy	70 MeV			160 MeV			200 MeV		
geometry / organs	AP (mGy)	PA (mGy)	ISO (mGy)	AP (mGy)	PA (mGy)	ISO (mGy)	AP (mGy)	PA (mGy)	ISO (mGy)
adrinals	1,4	2,2	1	30,5	35,2	28	171	182	156
bledder wall	2,1	1,8	1,1	41,7	34,6	26,2	206	184	152
bone	1,2	1,1	0,9	20,2	90,8	17,3	111	235	100
brain	1,6	2	1,9	34,9	36,9	34,4	179	185	178
breast	3,4	1	1,9	43,4	30,5	35,6	172	179	175
esophagus wall	2,1	1,9	1,4	39,1	36,1	28,9	200	184	161
eye lense	2,8	1,1	1,3	39,3	23	39,8	189	129	183
heart wall	2,5	1,7	1,3	40,2	35,4	30,1	200	189	159
kindney	1,6	2,1	1,1	34,3	38,8	27,6	184	199	158
liver	1,9	1,8	1,2	36	35,2	28,6	186	184	157
lower large intestine	2,1	1,6	1,2	39,7	35,6	29,2	202	186	161
lungs	2,2	2,2	1,4	38,8	39,4	30,6	196	199	160
muscle	2	2,1	1,4	37	37,6	31,1	186	189	164
pancreas	1,9	1,6	1,2	36	35,3	27,2	187	180	154
prostate	1,8	2	1,1	38,3	39,3	27,4	196	199	158
red bone marrow	1,9	2,3	1,5	32,2	34,9	26,1	169	177	147
skin	2,5	2,4	2	33	31,8	29,9	156	152	152
small intestine	2,4	1,3	1,2	39,7	32,6	28,7	200	175	157
splean	1,3	2,4	1,2	30,8	39,4	29,3	167	196	164
stomach wall	2,2	1,5	1,4	36,9	32,6	28,4	192	175	154
testes	2,6	1,2	1,5	44,6	33,3	31,6	203	172	162
thymus	3	1,6	1,3	37,9	28,1	29,5	189	157	146
thyroid	2,5	1,5	1,4	48,3	32	31,5	235	173	164
upper large intestin	2,4	1,2	1,2	41,6	32,2	29,6	207	174	162

Proton ener	70 MeV			160 MeV			200 MeV		
geometry									
organs	AP (mGy)	PA (mGy)	ISO (mGy)	AP (mGy)	PA (mGy)	ISO (mGy)	AP (mGy)	PA (mGy)	ISO (mGy)
adrinals	1,4	2,2	1	30,5	35,2	28	171	182	156
bledder wal	2,1	1,8	1,1	41,7	34,6	26,2	206	184	152
bone	1,2	1,1	0,9	20,2	90,8	17,3	111	235	100
brain	1,6	2	1,9	34,9	36,9	34,4	179	185	178
breast	3,4	1	1,9	43,4	30,5	35,6	172	179	175
esophagus v	2,1	1,9	1,4	39,1	36,1	28,9	200	184	161
eye lense	2,8	1,1	1,3	39,3	23	39,8	189	129	183
heart wall	2,5	1,7	1,3	40,2	35,4	30,1	200	189	159
kindney	1,6	2,1	1,1	34,3	38,8	27,6	184	199	158
liver	1,9	1,8	1,2	36	35,2	28,6	186	184	157
lower large	2,1	1,6	1,2	39,7	35,6	29,2	202	186	161

Proton ener	70 MeV			160 MeV			200 MeV		
geometry									
organs	AP (mGy)	PA (mGy)	ISO (mGy)	AP (mGy)	PA (mGy)	ISO (mGy)	AP (mGy)	PA (mGy)	ISO (mGy)
lungs	2,2	2,2	1,4	38,8	39,4	30,6	196	199	160
muscle	2	2,1	1,4	37	37,6	31,1	186	189	164
pancreas	1,9	1,6	1,2	36	35,3	27,2	187	180	154
prostate	1,8	2	1,1	38,3	39,3	27,4	196	199	158
red bone ma	1,9	2,3	1,5	32,2	34,9	26,1	169	177	147
skin	2,5	2,4	2	33	31,8	29,9	156	152	152
small intesti	2,4	1,3	1,2	39,7	32,6	28,7	200	175	157
splean	1,3	2,4	1,2	30,8	39,4	29,3	167	196	164
stomach wa	2,2	1,5	1,4	36,9	32,6	28,4	192	175	154
testes	2,6	1,2	1,5	44,6	33,3	31,6	203	172	162
thymus	3	1,6	1,3	37,9	28,1	29,5	189	157	146
thyroid	2,5	1,5	1,4	48,3	32	31,5	235	173	164
upper large	2,4	1,2	1,2	41,6	32,2	29,6	207	174	162

The results of the secondary neutron production from tissue under bombardment with C-ions are described in more details in Table 1, due to the fact that these particles are currently being used in Germany and Japan for the treatment of patients and a number of other institutions are also contemplating of using C-ions for cancer treatment.

Incident energy of C-ions (MeV/n)	Number of C-ions to impart one Gy dose in the Bragg-Peak / cm^2	Average energy of the seconda ry neutrons (MeV)	Number of neutrons, with energies greater than 5 MeV per C-ion	Total number of neutrons, with energies greater than 5 MeV produced for a physical C-ion dose of 20 Gy in the Bragg-Peak	Estimated Effective dose due to secondary neutrons [ref. 4] (mSv)
100	6.9×10^{6}	29	0.3	4.1×10^{7}	18
200	8.8×10^{6}	50	1.4	2.5×10^{8}	114
300	12.2×10^{6}		3	7.3×10^{8}	
400	18.7×10^{6}	125	4.2	1.6×10^{9}	955

The relatively large number of neutrons produced per C –ion , especially at 300 and 400 MeV / n, and their effective dose contributions which is about 2.5 and 5 % of the incident primary C-beam dose respectively, could be a cause of concern, especially when treating younger patients.

Furthermore, it should also be kept in mind that there are many more neutrons of energies lesser than 5 MeV, which are not included in our estimation, especially when the very high RBE of lower energy neutrons is taken into consideration for new tumor induction.

Our preliminary calculations show that the number of these low energy secondary neutrons is at least as much if not higher than the neutrons of energies greater than 5 MeV [4].

Carbon ion energy	200 MeV / u			400 MeV / u		
Incident geometry	Radiation doses mGy					
ORGAN	AP	PA	ISO	AP	PA	ISO
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

- We are introducing or repeating the concept of „Compromise ideal Incident Energy“. It should be the lowest energy to reach the tumour and producing lowest amount amount of neutrons, even if we have to irradiate the patients from different sides and angles.

References

[1] H. Engels et al. Strahlentherapie und Onkol. 175, Suppl. II (1999) 47.

[2] T. Kurosawa et al. Private communications.

[3] A. Bozkurt et al. Health Physics 81 (2001) 184.

[4] A. Sosnin et al. Private communications.

[5] Brenner DJ, Doll R, Goodhead DT, et al. Cancer risks attributable to low doses of ionizing radiation: Assessing what we really know. PNAS 2003; 100: 13761-13766