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^{11}C AND ^{15}O INDUCED IN THE MOUSE BY 175 MeV PROTONS

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The primary yield of nuclides from high energy radiation passing through tissue may be estimated with fair accuracy from empirical formation cross sections and the elemental composition of the tissue. The chemical behaviour of the nascent radiating products in the living body has, however, been almost completely neglected. Some investigations of the chemical fate of nuclides induced in aqueous solutions have been reported (e.g. STENSTRÖM 1970), but it appears hazardous to extrapolate from such simple systems to the complexity of living tissue. The behaviour of nuclides induced by high energy α particles in human beings was reported by SARGENT (1961), who found production of ^{11}CO and $^{11}CO_2$. LARSSON et coll. (1964) irradiated blood in vitro with high energy protons and found a considerable attachment of ^{11}C to blood corpuscles. Neutron activation of living material has been analysed by BIGGIN & MORGAN (1972) and others but has little bearing on the present work.

From the estimated production yield it may be shown that for high energy protons the radiation dose given by the decay of the induced nuclides may be ignored, compared to the primary proton dose, provided a rather drastic accumulation of the nuclides to small, radiation sensitive organs does not occur. That this is not the case has not been strictly proved, however.

There are also other reasons for analysing the behaviour of induced nuclides. One

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is the possible use of induced activity for dosimetry in the therapy and following radiation accidents (GRAFFMAN & JUNG 1964, MILLER & PATTERSON 1972), another that the behaviour of induced activity reflects the physiologic state of irradiated tissue such as oxygen tension, vascularity, water content, membrane permeability, etc. It is also conceivable that the chemical behaviour of the recoiling nuclides in nascent state elucidates the radical processes that precede the radiation injury (STENSTRÖM 1970). The aim of this communication is to present some basic information for an evaluation of these possibilities.

The investigation was concentrated on the behaviour of 20.5 min ^{11}C, which is the dominating nuclide with respect to activity during the interval from 10 min to 4 h after high energy proton irradiation of tissue. During earlier periods, ^{15}O dominates, but its short half-life, 2.0 min, prevents its analysis in greater detail. The following factors were primarily considered: (a) fractional amount of induced nuclides remaining close to the production site, (b) fractional amount excreted through the lungs and the kidneys, and (c) the chemical composition of mobile activities.

Material. White mice of the NMRI strain, weighing 18 ± 2 g, of both sexes, were used. Ascarite (NaOH on asbestos, A. H. Thomas Co., Phil., USA) was used to absorb CO_2, and Dehydrite ($MgClO_4$, A. H. Thomas Co., Phil., USA) to dehydrate respiration gases. Hopcalite ($CuO_2 + MnO_2$, B. Karlsson Co., Stockholm, Sweden) is a catalyst which facilitates the oxidation of CO to CO_2 at room temperature. It was used to transfer CO to CO_2 before absorption on Ascarite. Nembutal (Abbott Laboratories) was given intraperitoneally (0.04 mg/g body weight) for anaesthesia. Sephadex G-25 (Pharmacia, Uppsala, Sweden) was used to separate urine ^{11}C activity according to molecular size. Dowex 50W-X8 cation exchange resin on H_3O^+ form and Dowex I-X8 (Feinbiochemia, Heidelberg, BRD), 75 to 100 mesh, anion exchange resin on F^- form were used in the search for the chemical form of urine activities.

Methods

The irradiation was performed in the external, 185 MeV proton beam from the synchrocyclotron of the Gustaf Werner Institute. The beam was shaped with collimators and sweeping magnets to a laterally sharply defined field with a transverse homogeneity better than ± 5 per cent. The dose was measured with a nitrogen-flushed ionisation chamber of transmission type to an estimated accuracy better than 5 per cent. The dose rate was normally 100 rad/min. The stopping power in animal tissue for 185 MeV protons is about 5 MeV/cm. The mean proton energy was thus about 175 when a mouse was irradiated. The general layout of the irradiation facility was described by LARSSON (1961).

Activity was measured in lead-shielded 7.5 cm $\times$ 7.5 cm and 4.5 cm $\times$ 5 cm NaI(Tl) crystals with wells measuring 3.8 cm $\times$ 6.4 cm and 2.5 cm $\times$ 3.8 cm, respectively. Both crystals were equipped with conventional electronics, including single channel

analysers and printers. The larger crystal was used for wholebody animal measurements. In a special test it was found that the counting efficiency for positron annihilation quanta was constant (within ± 1 %), irrespective of the size of the source provided this did not extend outside two thirds of the height of the well. Most measurements were made as activity ratios for samples of similar physical form which should reduce any remaining counting efficiency variations to a negligible level. The absolute counting efficiency of the crystals was determined by ^{22}Na and ^{60}Co samples from the National Bureau of Standards, calibrated to an accuracy of ± 3 per cent (LARSSON & SARBY 1974). All nuclides under investigation are pure positron emitters.

The total production of ^{11}C, ^{13}N and ^{15}O was determined by measuring the induced positron activity in a dead mouse irradiated for 27 s over the whole body. The absorbed dose in animal tissue was 11.6 rad. The initial disintegration rate of the three nuclides was determined by least squares techniques assuming three components of half-lives 2.0 min (^{15}O), 10 min (^{13}N) and 20.5 min (^{11}C).

Expiration of ^{11}C activity was determined by measuring the remaining wholebody ^{11}C activity in mice killed after prescribed intervals after irradiation. Animals killed before irradiation served as standards. Five animals, placed on a turntable, were irradiated simultaneously. The experiment was repeated several times. Measurement of the ^{11}C activity was made when ^{13}N and ^{15}O had decayed to negligible levels. The turntable arrangement secured that the groups of five animals received the same dose.

The chemical composition of expired ^{11}C activity was analysed with a gas chromatograph (Aerograph 202 B, Varian) with a packing of the molecular sieve type (5A, Waters Ass. USA). A mouse, placed in a sealed, 100 ml syringe, filled with pure oxygen, was exposed to the proton beam for 5 min. After irradiation, half of the syringe volume was injected repeatedly at about 15 min intervals into the chromatographic column. Following injection, the remaining gas volume was washed several times with pure oxygen for about half a minute and the syringe filled with O_2 and kept closed until the next sample was drawn. The effluent gas from the chromatograph was led through a glass spiral with 2 ml volume placed in the small NaI(Tl) crystal. The relative amounts of the various ^{11}C activities were obtained by adding the counts registered under the peaks. In some experiments macro-amounts of CO and CO_2 were added for identification of expired gas ^{11}C activities. The macro-amounts were detected with the thermal conductivity detector of the instrument and were registered in parallel with the well-crystal counting-rate on a two-pen strip-chart recorder.

The elimination rate of $^{11}CO_2$ and the ratio between induced ^{11}CO and $^{11}CO_2$ as well as between these gases and total induced ^{11}C activity were determined in experiments in which a mouse was placed in a 60 ml glass chamber through which air was sucked by a membrane pump at a constant rate of 200 to 400 ml/min. The air flow was controlled by a conventional flow meter. Two alternating, identical absorber-

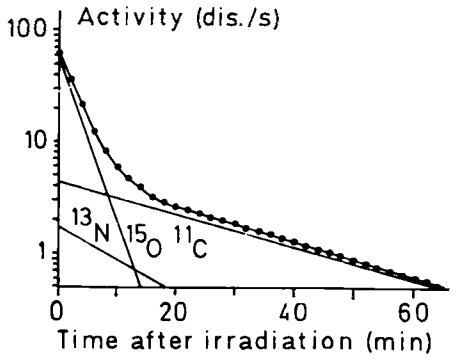

Fig. 1. Disintegration rate of induced nuclides per g-rad in a mouse after whole body irradiation with 175 MeV protons. The composite decay curve was decomposed in three components, with half-lives corresponding to ^{15}O, ^{13}N and ^{11}C, by the method of weighted least squares. Points indicate experimental data, lines the result of analysis.

catalyst chains were inserted in parallel between the chamber and the pump. The chains consisted of eight exchangeable tubes, containing, in order from the chamber, Ascarite, Ascarite, Dehydrite, Hopcalite, Ascarite, Dehydrite, Hopcalite and Ascarite. The animal was exposed to the proton beam for 2 to 6 min and the absorber system shifted repeatedly after intervals equal to the irradiation time. The first interval was counted from the irradiation mean time. New Ascarite tubes were replaced for old ones after each shift of absorber chain. The activity of the tubes was measured in the large crystal when short-lived activities (^{15}O and ^{13}N) had decayed sufficiently to be negligible.

The gas chromatograph was also used to obtain pure samples of ^{11}CO from proton-irradiated tap water. The gas was given to several mice either through venous injection of blood shaken with the gas or through inhalation by keeping the animals for 10 min in a 100 ml syringe containing the gas. The elimination rate of ^{11}C from the animal was followed with measurements of the whole-body activity in the large crystal. The small plastic bottle containing the mouse in counting position was ventilated at a rate of about 2 l/min by normal air from a pump or by a mixture of O_2 95 % and CO_2 5 % from an anaesthetic stand.

Table 1

Production of ^{11}C, ^{13}N, ^{15}O in mice irradiated with 175 MeV protons

	Initial disintegration rate (dis/s g-rad)			Production (nuclei /g-rad)		
	^{11}C	^{13}N	^{15}O	^{11}C	^{13}N	^{15}O
Experiment	4.9	1.7	78	8 200	1 500	14 000
Theory*	4.4	1.7	59	7 800	1 500	10 000

* Assumed composition (ICRP 1959): 18 % C, 3 % N and 65 % O by weight
Assumed production cross section (JUNG 1964): ^{16}O (p, 3p3n) ^{11}C 11 mb, ^{12}C (p, pn) ^{11}C 45 mb, ^{14}N (p, 2p2n) ^{11}C 7 mb, ^{16}O (p, 2p2n) ^{13}N 4.5 mb, ^{14}N (p, pn) ^{13}N 14 mb, ^{16}O (p, pn) ^{15}O 45 mb

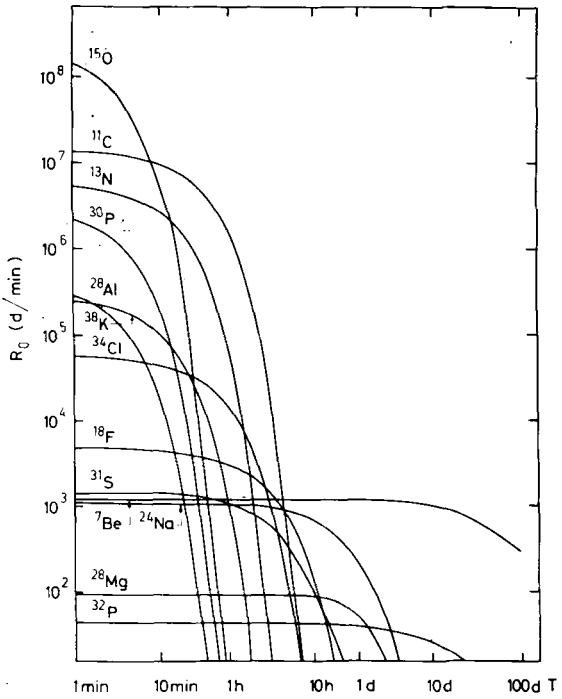

Fig. 2. The disintegration rates, R_0, of the most important nuclides as a function of time after irradiation of 1 g/cm² with the elemental composition of the human body (ICRP 1959) with 6×10^{11} protons during 1 min (from HÄLLER & JUNG 1963).

^{11}C activity in urine was measured in animals irradiated over the upper part of the body. Before irradiation the animals were anaesthetized and the urethra ligated. The animals were killed after different intervals after irradiation and the total amount of urine in the bladder was collected. The urine was measured in the large well crystal and the activity related to the total remaining activity in the carcass plus urine. Correction for expired ^{11}C activity was performed.

Attempts to characterize the chemical composition of ^{11}C activity in urine were made on some 30 min urine samples. The urine was boiled for five minutes in neutral and strong acid and alkaline solution. Neutral urine was separated on a Sephadex G-25 column. Urease was added to some samples in a search for active urea. Boiling with concentrated sulphuric acid was performed in order to test for active formic acid. Ion exchange with cation exchange and anion exchange resins was also tried.

The activity remaining at the irradiation site in muscle and bone was measured in several mice irradiated over their right hind leg. The irradiated volume did not exceed 5 per cent of the total body volume. Some mice were killed before, others at various times after irradiation. Samples of muscle and bone were extirpated, weighed and measured for ^{11}C activity.

The course of ^{11}C activity in blood after irradiation was determined by irradiating, on the turntable, one blood sample and four mice. At preselected intervals following

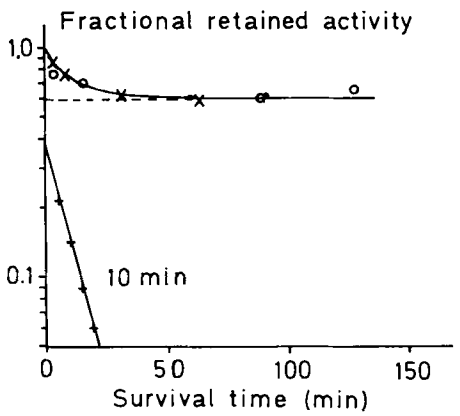

Fig. 3. Fractional retained ^{11}C activity in mice irradiated over the whole body as a function of survival period after mean time of irradiation. The elimination rate through respiration corresponds to a half life of 10 min. Corrections for physical decay performed.

irradiation the heparinized mice were partially exsanguinized through decapitation. The blood samples, including that irradiated in vitro were weighed and measured for activity. The activity concentrations in the samples were related to the ^{11}C activity of the mice.

The loss of ^{15}O from irradiated animals during the first minutes after irradiation was determined by measuring the whole-body activity of mice killed at preselected intervals after irradiation. Irradiated dead mice served as controls.

The redistribution of ^{15}O activity during and after irradiation was determined following irradiation of the upper or lower halves of mice. At 1, 3 and 5 min after irradiation the animals were submerged in liquid nitrogen. The frozen bodies were cut into one non-irradiated part and one which had been partially irradiated. The ^{15}O activity per gram body weight of the two halves was determined.

The behaviour of ^{15}O activity induced in irradiated human whole blood was analysed in one model experiment. Blood samples were irradiated for 10 s and two aliquots of 1 ml taken. One of these served as standard, the other was boiled under reduced pressure for 1, 2 or 3 min. Both samples were measured repeatedly for activity and the 2-min ^{15}O component extracted.

Results and Discussion

Results regarding total induced ^{11}C, ^{13}N and ^{15}O activity in the mouse appear in Fig. 1 and Table 1. In the latter, theoretical data on estimated production rate of the three nuclides are included. The data were obtained by assuming the mice to contain (by weight) O 65 %, C 18 % and N 3 % (ICRP 1969). The three nuclides are the dominant ones as is evident from Fig. 2, taken from a report by HÄLLER & JUNG (1963). The close agreement between the empirical and theoretical values is surprising in view of the uncertainties in the elemental composition and in the formation cross sections introduced in the theoretical estimates.

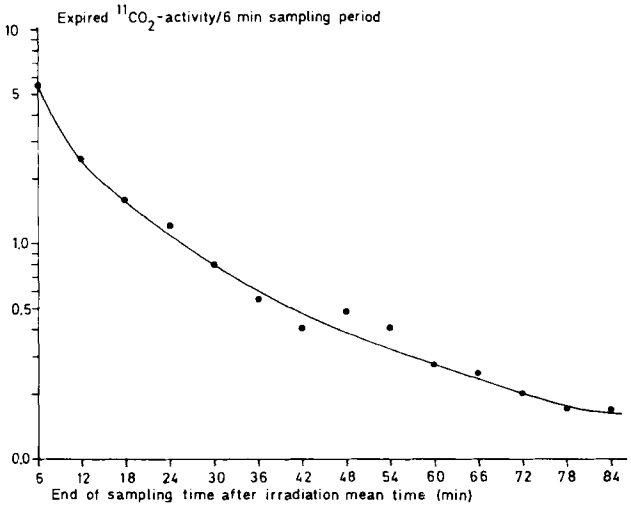

Fig. 4. Elimination curve of $^{11}CO_2$ from a mouse irradiated over the whole body. Corrections for physical decay performed.

The expiration loss of ^{11}C activity was characterized by a rapid initial fall in retained activity followed by a more gradual decrease to an asymptotic value of about 0.60 (Fig. 3). The loss of ^{11}C through expiration followed a time course which is compatible with a single half-life of about 10 min.

Only two, well separated, active peaks were obtained by gas chromatography of expiration gas. These could be ascribed unambiguously to ^{11}CO and $^{11}CO_2$ in the experiments with added macro-amounts of these gases. Also metabolic CO_2, which was always present, followed the $^{11}CO_2$ peak. Other active gases were not found in amounts larger than 1 per cent of ^{11}CO. Due to inevitable gas recirculation in the syringe in which the mouse was kept, elimination rates could not be determined in this experiment.

The elimination of $^{11}CO_2$ from irradiated mice, as found in the experiments with the absorber—catalyst chains, appears in Fig. 4. The collection efficiency of Ascarite for $^{11}CO_2$ was excellent and the second Ascarite tube contained only about 1 per cent of the activity of the first tube.

Table 2

Expiration of ^{11}C activity from mice irradiated over the whole body

Irradiation period (min)	Total collection period (min)	Total expired fraction of total induced ^{11}C activity (corrected for physical decay)		Ratio between expired ^{11}CO and $^{11}CO_2+^{11}CO$
		^{11}CO	$^{11}CO_2$	
2	30	0.210	0.135	0.61
4	52	0.237	0.121	0.66
6	84	0.320	0.145	0.69

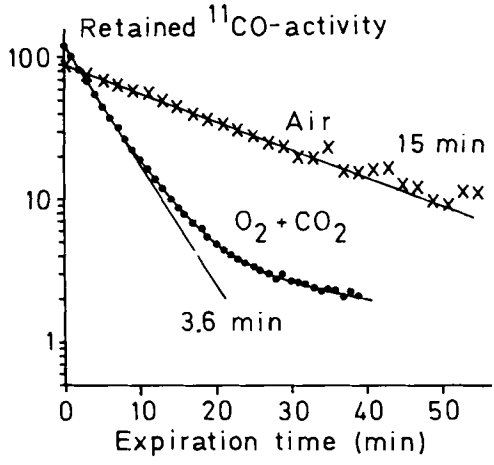

Fig. 5

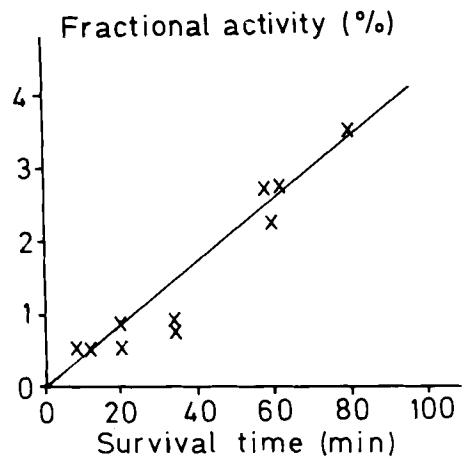

Fig. 6

Fig. 5. Retained activity in a mouse given ^{11}CO by intravenous injection as a function of time. The labels air and O_2 95% + CO_2 5% indicate the respiration gas used in the two experiments. Corrections for physical decay performed.

Fig. 6. The fraction of the total induced ^{11}C activity in whole-body irradiated mice collected in urine at different times after irradiation. Corrections for physical decay performed.

The ^{11}CO elimination rate was difficult to determine by the chain, however, since it was found that ^{11}CO to a non-negligible degree was absorbed by Hopcalite, possibly after conversion to $^{11}CO_2$. This did not influence the estimate of the total ^{11}CO activity eliminated during the experimental periods, which is given in Table 2.

From the experiments with ^{11}CO administered in breathing gas or in blood by venous injection it was found that essentially all ^{11}CO was eliminated at a rate corresponding to a single half-life of 15 min when the animal was breathing ordinary air (Fig. 5). A half-life of about 3.6 min was found when the animal was breathing the O_2–CO_2 mixture. A similar increase in elimination rate has been found in human beings treated for carbon monoxide poisoning (Root 1965). A small component eliminated at a lower rate was found in the O_2–CO_2 experiment. It may be due to ^{11}CO absorption on myoglobin or a conversion of ^{11}CO to $^{11}CO_2$ (Tobias et coll 1945, Allen & Root 1957). The two types of administration gave similar results. It is presumable that expiration of ^{11}CO from an irradiated animal follows a time course that closely simulates that for injected or inhaled ^{11}CO. A rapid accumulation in blood of ^{11}CO induced in the irradiated mouse is indicated by the results appearing in Fig. 9.

The ^{11}C activity in urine increased linearly with time during the first hour after irradiation (Fig. 6). About 2.5 per cent of the totally induced ^{11}C activity was collected in urine after 1 h. The relative amount of ^{13}N was found to be higher in urine than in whole body and correction for ^{13}N activity had to be carried out although the measurements were made after a considerable decay period.

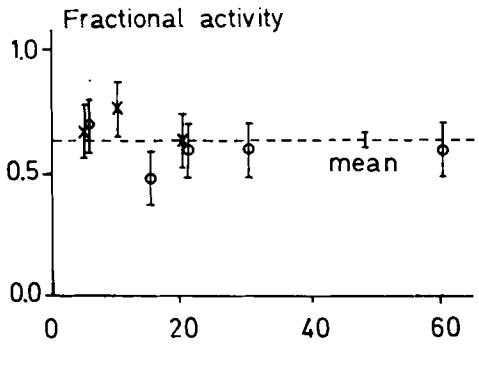

Fig. 7

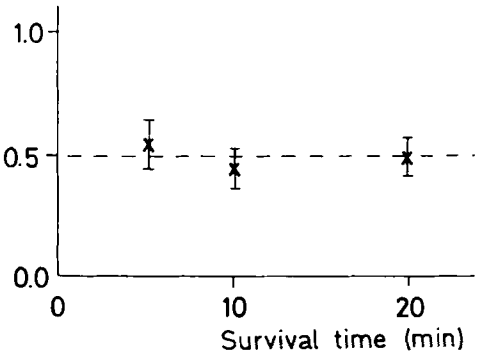

Fig. 8

Fig. 7. Remaining ^{11}C activity in muscle after localized irradiation. The fractional activity (corrected for physical decay) is given as the ratio between activity concentrations in muscle extirpated from mice living or dead during irradiation. Crosses and open circles refer to two different experiments.

Fig. 8. Fractional ^{11}C activity remaining in bone after localized irradiation.

From the attempts to characterize the chemical composition of ^{11}C activity in urine it may be reported that the activity could not be made volatile by adding acids or alkalines and that most activity was bound to compounds of molecular weights less than 1 000. Tests for active urea and formic acid gave negative results. No activity was absorbed from neutral urine on cation exchanger, while about 60 per cent was retained by anion exchange resin when the eluent was distilled water. In view of the apparent variety of the chemical forms of ^{11}C activity in urine no further tests were made.

Muscle, representating about 40 per cent of total body weight, and bone, in which blood circulation is comparatively low, were taken as representatives of the whole body in measurements of stationary activity. The results are given in Figs 7 and 8. The observed stationary activity represents the relative amount of nuclides which remained at the production site, i.e. nuclides which were bound to chemical compounds which did not migrate rapidly in the body and which were not transformed to such compounds at a high rate. It may be noted that JOHANSON et coll. (1974) have found ^{11}C bound to nucleic acids and protein isolated from proton irradiated mouse liver. Non-stationary ^{11}C activity disappeared from the irradiated site at such a high rate as to prevent its time-course being determined with available techniques. From the measurements it cannot be excluded, however, that a small fraction, 5 per cent at most, of the stationary induced ^{11}C activity disappeared at a slow rate, possibly secondary to metabolic processes.

The course for ^{11}C activity in blood appears in Fig. 9. Initially, the relative activity concentration in the blood increased rapidly to a value six times the one found for blood irradiated in vitro. Subsequently, there was a gradual decrease to about 0.7

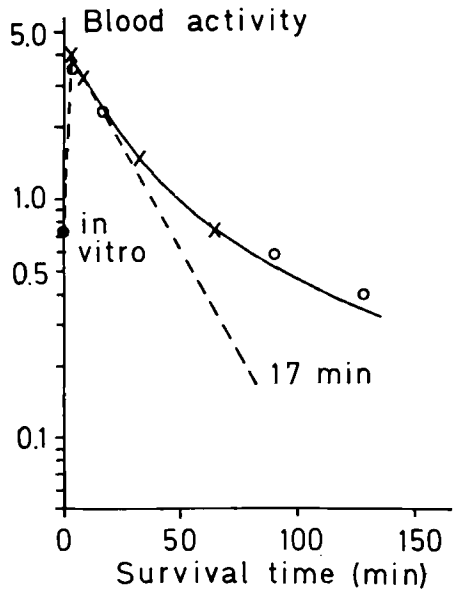

Fig. 9. ^{11}C concentration in blood related to total ^{11}C concentration in a mouse irradiated over the whole body as a function of sampling time after mean time of irradiation. Crosses and open circles refer to two separate experiments. Correction for physical decay performed. The in vitro point gives the ^{11}C concentration in a blood sample irradiated simultaneously with the mice.

times the in vitro value. These findings may suggest a nearly momentary accumulation in the blood of almost all induced ^{11}CO, followed by expiration of ^{11}CO. Under this assumption, and correcting for 60 per cent stationary activity in the blood, the elimination constant for ^{11}CO was found to correspond to a half-life of about 17 min, in fair agreement with other measurements of this rate, reported here. (The change in blood content of $^{11}CO_2$ can be neglected in this determination.) Also the initial increase to a relative activity concentration in the blood of 4.5 corroborates this suggestion, provided the relative blood content of the mouse and the fraction of induced ^{11}C activity present as ^{11}CO, were 6 and 26 per cent, respectively. Further, it is confirmed by the finding that in blood samples, taken one minute after irradiation, 80 to 90 per cent of the ^{11}C activity was attached to the blood corpuscles whereas for blood irradiated in vitro this figure was about 40 per cent.

The comparison of the ^{15}O activity in irradiated living and dead mice indicated that less than 5 per cent of the ^{15}O activity was lost per minute through expiration and perspiration. The transport of ^{15}O activity from the irradiation site was found to be very fast in the experiments with partially irradiated mice. More than 60 per cent of the induced ^{15}O activity was distributed from the irradiation site throughout the body within 5 min. The results of the model experiment with irradiated whole blood indicate clearly that most of the ^{15}O activity behaved as water (Fig. 10), further supported by the finding that the ^{11}C and ^{13}N activities did not behave in this manner. In preliminary experiments, $H_2{}^{15}O$, administered intravenously, was found not to be homogeneously distributed throughout the body within the first 15 min after injection.

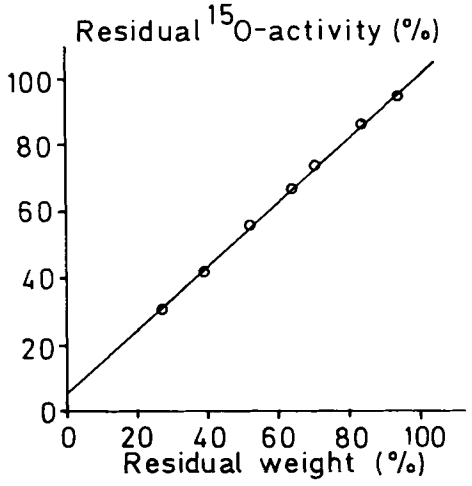

Fig. 10

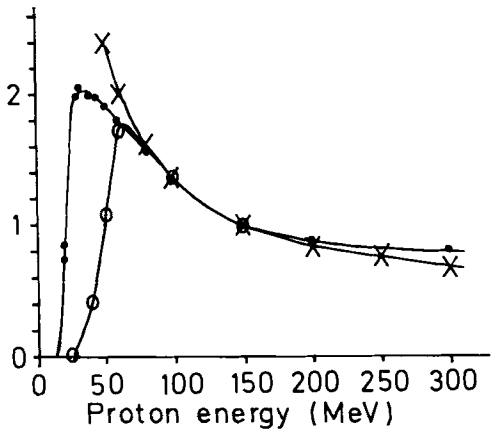

Fig. 11

Fig. 10. Residual ^{15}O activity as a function of residual weight after irradiation of human whole blood in vitro and boiling under reduced pressure. Correction for physical decay performed.

Fig. 11. Production cross section of ^{11}C from carbon (.) and oxygen (o) and the mass stopping power of proton in tissue (x) as functions of proton energy. The data are normalized to 1.0 at 150 MeV (from GRAFFMAN & JUNG 1964).

The observations do not allow conclusions regarding the potential use of induced activity for an analysis of physiologic parameters. The formation cross sections for ^{11}C from ^{12}C and ^{16}O are such, however, that the total amount of ^{11}C per g-rad will depend on the water content of the irradiated tissue. Observations on mice with varying amounts of intraperitoneal fluid irradiated with high energy protons support this hypothesis.

In experiments with mice the ratio between ^{11}CO and total production of ^{11}C was found not to be changed substantially when the animals were kept in low oxygen atmosphere or in hyperbaric (3 atm) pure O_2 during irradiation.

Conclusions

The distribution throughout the body of the additional dose due to the decay of induced ^{15}O is complex. Assuming total absorption of positrons and annihilation photons within the body, it may be calculated from the production values in Table 1, that the additional integral dose from ^{15}O is 3×10^{-4} g-rad per g-rad proton dose. Under the same assumptions and neglecting the elimination from the body the corresponding figure for ^{11}C is 2×10^{-4} g-rad per g-rad. The CO fraction of this activity is rapidly accumulated in the blood which, together with the vessels, will receive some extra dose especially from the positrons. The annihilation photons are

of long range and their contribution to the dose will not be concentrated to blood and vessels. The 2.5 per cent fraction collected in urine in 1 h will not give much dose to bladder tissue and gonads because of the slow rate of accumulation.

Assuming that all nuclides induced by high energy protons in tissue (cf. Fig. 2) decay within the body and that all secondary radiation is absorbed within the body the additional, fractional, integral dose is found to be less than 0.001.

For estimating integral, high energy proton dose from induced activity ^{11}CO and $^{11}CO_2$ probably offer the best means except for, possibly, whole body counting. In tissue, the ratio between ^{11}C production and linear energy transfer is fairly constant for protons above 50 MeV (Fig. 11). There are no reasons to believe that the chemical fate of ^{11}C is strongly dependent on proton energy. Both ^{11}CO and $^{11}CO_2$ are easily sampled from the expired air by absorbers. ^{11}CO is concentrated in red blood corpuscles and blood samples offer an attractive alternative for measuring this activity. It appears that CO is most suitable due to its simple rate of elimination, which can be accelerated by using O_2–CO_2 as breathing gas.

Acknowledgements

This work has been financially supported by grants from the Swedish Cancer Society and the Swedish Atomic Research Council.

SUMMARY

The total production of ^{11}C, ^{13}N and ^{15}O in the mouse by protons with a mean energy of about 175 MeV was found to be 8 200, 1 500 and 14 000 nuclei per g-rad, respectively. About 40 per cent of the total induced ^{11}C activity was eliminated through expiration and about 2.5 per cent with the urine during the first hour after irradiation. The expired gas contained ^{11}CO and $^{11}CO_2$ in the ratio 2/1. The urinary ^{11}C activity was bound to several compounds, the chemical nature of which was not established. The ^{15}O activity behaved as H_2O and was found not to be eliminated from the body during the short observation time available. The additional, fractional, integral radiation dose due to decay of induced nuclides is less than 0.1 per cent, and can be neglected since no accumulation to any small organ was seen. Sensitive means for an estimate of integral dose based on the induced nuclides would be the detection of ^{11}CO activity in expired gas or in blood.

ZUSAMMENFASSUNG

Die gesamte Produktion von ^{11}C, ^{13}N und ^{15}O in der Maus durch Protonen mit einer mittler Energie von etwa 175 MeV wurde mit 8 200, 1 500 bzw. 14 000 Nuclei per g-rad, gefunden. Etwa 40 % der gesamten induzierten ^{11}C-Aktivität wurde nach Bestrahlung durch die Atmung und etwa 2,5 % durch den Harn während der ersten Stunde eliminiert. Das Ausatmungsgas enthielt ^{11}CO und $^{11}CO_2$ im Verhältnis 2/1. Die ^{11}C-Aktivität des Harns war an verschiedene Verbindungen gebunden, deren chemische Natur nicht festgestellt wurde. Die ^{15}O-Aktivität trat als H_2O auf und wurde während der kurzen zur Verfügung

stehenden Beobachtungszeit nicht vom Körper abgegeben. Die zusätzliche, unbedeutende Integraldosis infolge des Zerfalls der induzierten Nukleide beträgt weniger als 0,1 % und kann vernachlässigt werden, da keine Akkumulation in irgende einem der kleinen Organe gesehen wurde. Eine empfindliche Weise zur Bestimmung der Integraldosis, die sich auf die induzierten Nukleide stützt, wäre die Messung der ^{11}CO-Aktivität im ausgeatmeten Gas oder im Blut.

RÉSUMÉ

La production totale de ^{11}C, ^{13}N et ^{15}O chez la souris par les protons ayant une énergie moyenne d'environ 175 MeV est respectivement de 8 200, 1 500 et 14 000 nucléi par g-rad. Environ 40% de l'activité de ^{11}C induite totale est éliminée par expiration et environ 2,5% éliminés par l'urine au cours de la première heure après irradiation. Le gaz expiré contenait du ^{11}CO et du $^{11}CO_2$ dans le rapport 2/1. L'activité ^{11}C urinaire était liée à différents composés dont la nature chimique n'a pas été établie. L'activité ^{15}O se comportait comme H_2O; il semble qu'elle n'ait pas été éliminée du corps pendant la courte période d'observation. La dose de radiation supplémentaire, fractionnaire, intégrale due à la désintégration des nuclides induits est inférieure à 0,1 pour cent et peut être négligée étant donné qu'on n'a pas observé d'accumulation dans aucun petit organe. Les moyens sensibles pour estimer la dose intégrale basée sur les nuclides induits devrait être la détection de l'activité ^{11}CO dans le gaz expiré ou dans le sang.

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