RADIOACTIVE ION BEAMS : RESULTS AND PERSPECTIVES FOR LIGHT ION THERAPY AND DIAGNOSTIC PURPOSES

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Abstract : *An alternative method for the production of intense medium energy beams of radioactive isotopes has been developed by the Centre de Recherches du Cyclotron at Louvain-la-Neuve. Instead of using high velocity secondary beams coming out of a target bombarded by medium energy (up to 400 MeV/a.m.u.) ions, it uses an intense, low energy, light ion beam which is sent on a suitable target to selectively produce the desired isotopes. After extraction and purification, the gas going out of the target is ionized in a high efficiency source for subsequent acceleration to the required energy. The method has already been successfully applied for the production of $^{13}N^{1+}$ beams. The simplicity and relatively low cost of such scheme allows the use of positron emitters like ^{11}C, ^{13}N, ^{15}O, ^{18}F and ^{19}Ne for eventual treatment of locally advanced tumours, as well as for the on-line diagnostic of the irradiated zone with a PET camera. The different production and acceleration schemes are reviewed and their implications in the EULIMA project are discussed.*

Introduction

The treatment of cancer with energetic light ions requires a precise localization of the Bragg peak in the tumour volume. Following the method developed at Lawrence Berkeley Laboratory, this can be verified by using a beam of radioactive positron emitting ions like ^{19}Ne[1]. In this case, the detection of the 511 keV annihilation gamma-rays by a positron emission tomography scanner (PET) allows a precise determination of the beam range[2]. Although these radioactive ions are only used for diagnostic purposes before the treatment with stable ^{20}Ne ions, an irradiation with the same radioactive beam would avoid frequent beam changes and offers the possibility to check the range during the treatment. A possible way to produce high intensity radioactive beams, is to use the nuclear fragmentation of high energy nuclei after interaction with a target. This method has been analysed in detail by A. Bimbot[3]. In this paper, we discuss the possibilities to use an alternative method to accelerate radioactive ions and their implications in the EULIMA project.

Production of high energy radioactive beams

The classical way to produce radioactive beams is to bombard a target with a high intensity (~ 10^{11} pps) and high energy (400 MeV/u) beam. The fragmentation products are then separated from the primary stable beam and, after magnetic purification of the secondary beam coming out of the target, could be used for the treatment. This way, an ^{15}O beam of 2 10^8 pps is expected with a primary beam of 10^{11} pps[3].

The approach followed in Louvain-la-Neuve, uses two accelerators coupled by an on-line ion source. The first accelerator is a small industrial cyclotron which is used to produce a large amount of radioactive atoms by a suitable reaction. They are extracted from the target by a carrier gas and ionized by an Electron Cyclotron Resonance (ECR) source. A second cyclotron brings these radioactive ions to the desired energy. With this scheme, 1.5 10^8 atoms of $^{13}N^{1+}$ have already been accelerated to 8.5 MeV[4,5]. The same method could be used in the EULIMA project, if an intensity of the order of 10^7 to 10^8 pps of fully stripped ions at 400 MeV/u can be obtained. With this intensity, the treatment dose (10^{10} atoms) would require an irradiation time of a few minutes.

Ion choice and targetry problems

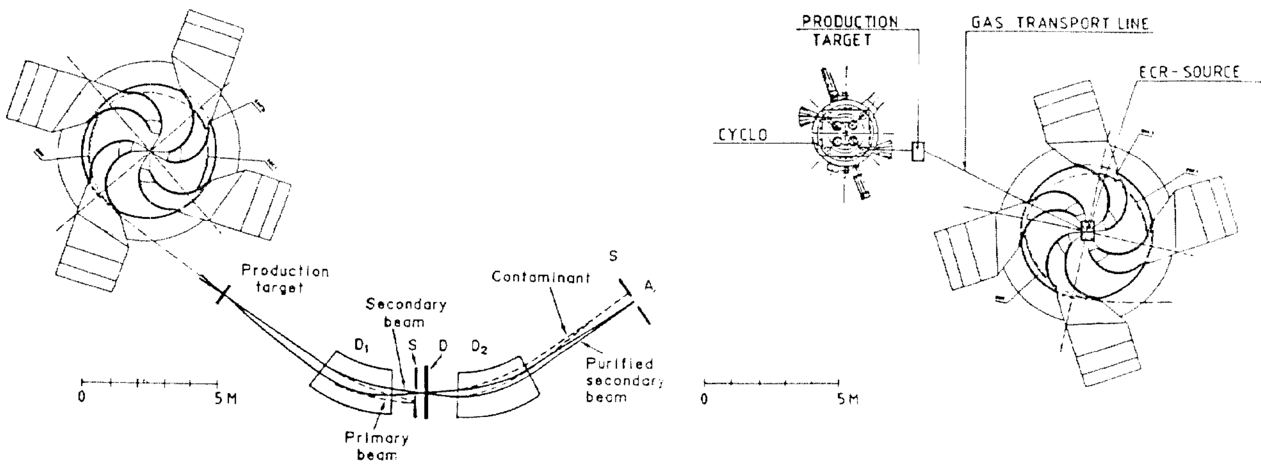
The suitable ions for light ion therapy are in the mass range between carbon and neon, so positron emitters like ^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{19}Ne could be used for the treatment. As shown in table 1, these elements can be produced by (p,n) or (d,n) reactions in dedicated targets, with a beam energy between 15 MeV and 30 MeV. These beams can be accelerated by compact cyclotrons up to 500 μA[6]. The target must display the following properties : the ability to dissipate up to 15 kW of beam power, a high extraction efficiency for the release of the radioactive atoms produced inside the target material, a short term activity induced by the beam around the target and finally a low cost and a high reliability. A graphite target meets all these requirements for the production of ^{13}N. It avoids problems of using high pressure nitrogen gas targets or enriched $H_2{}^{18}O$ liquid targets, which are needed for the production of ^{15}O and ^{18}F respectively. Moreover, as the activity produced in the target has a short lifetime (< 1 h), the activation problem of the target material is kept to a minimum. A compact shielding for the low energy neutrons produced by the reaction is sufficient around the target. With a natural graphite target, ^{13}N can be produced by a (d,n) reaction with a production yield of 0.96 10^{-3} ^{13}N atoms per deuteron at 20 MeV, i.e. with 300 μA, 1.8 10^{12} ^{13}N atoms are produced in the target[7]. The yield for the (p,n) reaction on ^{13}C is slightly higher (1.19 10^{-3} ^{13}N atoms per proton at 20 MeV) but requires an enriched ^{13}C graphite target like it is presently used in the Radioactive Ion Beam project (RIB) in Louvain-la-Neuve[8].

Table 1 : Production of radioactive isotopes for light ion therapy with protons or deuterons [7] [11].

Isotope	Half-life	Reaction	Yield (20 MeV)	Target material
^{11}C	20 min	$^{11}B^*(p,n)^{11}C$	~ 2 10^{-3}	B_2O_3
		$^{14}N(p,\alpha)^{11}C$	~ 1.8 10^{-3}	N_2
		$^{10}B^*(d,n)^{11}C$	< 0.1 10^{-3}	B_2O_3
^{13}N	10 min	$^{13}C^*(p,n)^{13}N$	1.19 10^{-3}	^{13}C
		$^{12}C(d,n)^{13}N$	0.96 10^{-3}	C
^{15}O	2 min	$^{15}N^*(p,n)^{15}O$	1.2 10^{-3}	$^{15}N_2$
		$^{14}N(d,n)^{15}O$	< 0.1 10^{-3}	$^{14}N_2$
^{18}F	109 min	$^{18}O^*(p,n)^{18}F$	2.4 10^{-3}	H_2O^{18}
		$^{20}Ne(d,\alpha)^{18}F$	1.1 10^{-3}	Ne
^{19}Ne	17 s	$^{19}F(p,n)^{19}Ne$	0.7 x 10^{-3}	(LiF)

*Enriched target

Figure : Schematic layout of the two possible schemes for the production of high energy radioactive beams. In the first one (left), the radioactive ions are produced at high energy by nuclear fragmentation, and the contaminants are eliminated by magnetic spectrometers and an energy degrader (drawing extracted from A. Bimbot ref. [3]). In the second one (right), the radioactive atoms are produced in a thick target and are accelerated after ionization in an on-line ECR source.



On-line ionization source

The ^{13}N activity can be extracted from the graphite target as ^{13}N-^{14}N molecules by a small nitrogen gas flow (~ 0.1 cm^3 per hour). An extraction efficiency of 50 % has already been achieved[8]. The molecules are sent to an on-line ECR source with a high ionization efficiency. The present ECR source used in Louvain-la-Neuve for the RIB project has achieved an ionization efficiency of 15 % for the 1+ charge state and 1 % for N^{4+}. It is a single stage ECR source working at 6 GHz and is designed to have its highest ionization efficiency for N^{1+}. Its performance has been described in detail elsewhere[9]. The stable and reliable operation of this type of source allows its use for a medical machine. In order to have a high ionization efficiency for N^{7+}, an ECR source working at 14 GHz or 16 GHz should be constructed. With the actual performance of these sources, an ionization efficiency in the order of $5\ 10^{-4}$ to $1\ 10^{-3}$ is expected for N^{7+}[10]. With these values, an intensity of $5\ 10^8$ to $1\ 10^9$ ions per second could be produced and transported for injection in the main accelerator. Lower charge states like $^{13}N^{4+}$ could be injected in a preaccelerator and stripped to $^{13}N^{7+}$ before injecting in the main machine, but a direct production of $^{13}N^{7+}$ after the ECR source reduces the complexity without loosing too much intensity.

Implication for the EULIMA project

Due to its low duty factor, a synchrotron is excluded for the acceleration of radioactive ions produced at low energy, unless a new device like an ions trap is used to store the ions before injection. However, owing to its 100 % duty factor, a cyclotron, like proposed in the EULIMA project, will accelerate these elements with high efficiency. Taking 10 % of acceleration efficiency, an intensity of $5\ 10^7$ to $1\ 10^8$ pps at 400 MeV per nucleon seems to be technically feasible. With these intensities, an irradiation of three minutes would be enough to give a treatment dose of 10^{10} atoms (table 2).

Table 2 : Expected intensity of radioactive ^{13}N at the different stage of the production process.

20 MeV deuteron	300 μA
Yield $N(^{13}N)/N(d)$	$0.96\ 10^{-3}$
Extraction efficiency	50 %
Ionization efficiency $^{13}N^{7+}$	$0.5\ 10^{-3}$ ... $1\ 10^{-3}$
Acceleration efficiency	10 %
Accelerated intensity	$5\ 10^7$ ... $1\ 10^8$ pps
Treatment time for 10^{10} particles	2 ... 3 min.

Finally this scheme can be compared with the intensities which are produced by the nuclear fragmentation scheme ($2\ 10^8$ pps for a primary beam of 10^{11} pps) but it avoids the possible problems related to the activity produced around the fragmentation target. The schematic layout shown in the figure gives an idea of the relative sizes of both approaches. Shielding requirements in the case of a low energy production cyclotron are far less than in the case when nuclear fragmentation is used. Moreover, the very high intrinsic analysing power of a cyclotron like EULIMA will yield a pure beam without any contamination.

Conclusion

We have proposed an alternative scheme to accelerate radioactive ions. It requires a 20 MeV deuteron cyclotron to produce ^{13}N in a natural graphite target, and a high efficiency ECR source to produce $^{13}N^{7+}$. Intensities of the order of $5\ 10^7$ to $1\ 10^8$ pps can be expected at the output of the EULIMA cyclotron. With such facility, the treatment of tumours, and the precise localization of the ions range, will be possible without any beam change.

References

[1] J.R. Castro et al., "Heavy charged particle therapy at LBL" in Proceedings of the EULIMA Workshop, edited by P. Chauvel and A. Wambersie, 1988, pp. 219-232.

[2] A. Chatterjee and J. Llacer, "Applications of radioactive beams in diagnostic studies" in Proceedings of The First International Conference on Radioactive Nuclear Beam, edited by W.D. Myers, J.M. Nitschke and E.B. Norman, World Scientific, 1990, pp. 403-413.

[3] A. Bimbot, "Production of 400 MeV/u radioactive ion beams for therapy purposes" in Proceedings of the EULIMA Workshop, edited by P. Chauvel and A. Wambersie, 1988, pp. 443-468.

[4] D. Darquennes et al., "Radioactive Ion Beams at Louvain-la-Neuve : production, acceleration and uses" in Proceedings of The First International Conference on Radioactive Nuclear Beam, cfr. [2], pp. 3-12.

[5] P. Decrock et al., "Production of an intense ^{13}N radioactive ion beam" in Proceedings of this conference.

[6] J.L. Bol et al., "Operational experience with 500 μA H^- isotope production cyclotron, CYCLONE 30", in Proceedings of the EPAC Conference, Rome 1988, edited by S. Tazzari, World Scientific, pp. 1488-1490.

[7] Sindano Wa Kitwanga, "Production of ^{13}N radioactive nuclei from $^{13}C(p,n)$ or $^{16}O(p,\alpha)$ reactions", Phys. Rev. C40, 1989, pp. 35 and Ph.D. thesis (unpublished).

[8] M. Arnould et al., "Target development for a radioactive ion beam", Nucl. Instr. Meth. A282 (1989) pp. 99-101.

[9] P. Decrock et al., "An electron cyclotron resonance ion source for efficient production of radioactive nuclear beams" in Proceedings of The First International Conference on Radioactive Nuclear Beam, see ref. [2], pp. 597-602 and Rev. Sci. Instrum. 67, 1990, pp. 279-281.

[10] R. Geller et al., "Upgrading of the multiply charged heavy ion source mini-mafios", Nucl. Instr. Meth. A243 (1986) pp. 244-254.

[11] B.W. Wieland, R.R. Highfill, "Proton accelerator targets for the production of ^{11}C, ^{13}N, ^{15}O and ^{18}F", IEEE NS-26, 1979, pp. 1713-1717.