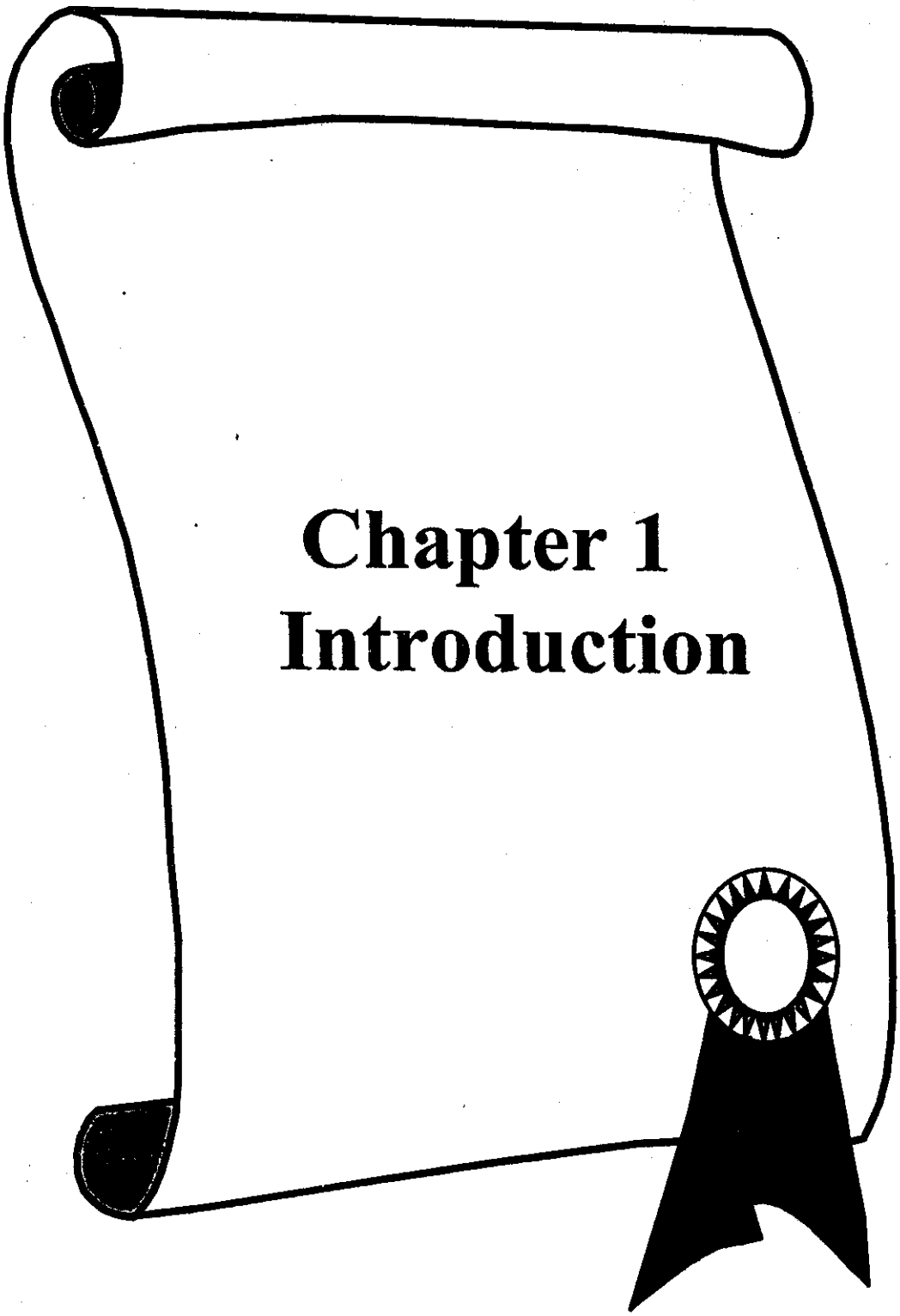

Chapter 1
Introduction

INTRODUCTION

1.1 Introductory Outline

Radioactivity has revolutionized life sciences during the last century. It is still an indispensable tool from the time of its discovery tell now and the human efforts has been devoted to study its characteristic phenomena and applications in many fields of life discipline like industry, agriculture, biology, chemistry and specially in diagnostic and / or therapeutic nuclear medicine [1]. Since the discovery of artificial short- lived radioisotopes with significant decay mode and characteristic emitting energy which meet the requirements of nuclear medicine; and many scientists have done their efforts to improve their methods of production, separation, detection and quality control assessment.

While radioisotopes produced via a cyclotron facility are, mainly, induced by charged particles irradiation; those produced via a reactor facility are, mainly, induced by neutron irradiation [i.e (n, γ) nuclear reactions]. The developments achieved in the field of nuclear reactors makes it one of the most important sources for production of artificial radioactivity because of [2]:

- The ease with which large and thick targets can be irradiated at high fluxes for long periods of time .
- The possibility of simultaneous irradiation of many targets.
- The relatively low costs of irradiation.

However; the cyclotrons remain indispensable sources of production of a lot of radioisotopes. It provide the only means of making most neutron deficient radioisotopes via bombardment with charged particles such as protons, deuterons and alpha particles. These radioisotopes tend to decay by electron capture or positron emission

modes such as the short-lived B^+-emitters: ^{11}C, ^{13}N, ^{15}O used in positron emission tomography (PET) and/or emitting single γ- ray such as ^{67}Ga, ^{111}In and ^{201}Tl used in single photon emission tomography (SPECT). Therefore; cyclotron produced radioisotopes have found increasing favour in diagnostic and therapeutic nuclear medicine applications due to special advantages compared to reactor produced radionuclides [3, 4]:

- Possibility of in vivo qualitative study of regional physiological functions using B^+-emitting organic radioisotopes,
- High specific activity of the product, and
- Low radiation dose to the patient.

In contrast to neutron field that immerses a target in the reactor, charged particle beams are small and focused onto areas of only a few square centimeters. Therefore; one must design a target to present a maximum number of eligable atoms to the beam. The use of separate isotope accelerator targets has several advantages:

-Maximum target atoms concentration in the beam.

-Minimized beam degradation.

-Minimized production of unwanted radioisotopes.

For isotope production with accelerators or reactors it is often desirable to use targets enriched or depleted in certain isotopes to maximize the concentration of eligable atoms per unit space through which the flux of incident particles [projectiles] passes. Thereby, to enhance the probability of interaction and achieve the necessary specific activity with available fluxes and to decrease the contribution of parasitic production of undesirable radiocontaminants. Various types of targets have been designed to meet the radioisotope production conditions and requirements. Primary consideration is given to heat deposition in the target by irradiation in the reactor or cyclotron. The temperature can rise

to 1000^0C and, if the target material is not properly selected and designed, the target is likely to be burned or destroyed. For this reason, water cooling of the cyclotron probe to which the target is attached is commonly adopted. The common form of the target is metallic foils, e.g, copper, aluminum, uranium, vanadium and so on. Other forms of targets are oxides, carbonates, nitrates, and chlorides contained in an aluminum tubing which is then flattened. Aluminum tubing is used because of its high melting point and very short half -life of the product radioisotope [1]. After irradiation, the target is dissolved in an appropriate solvent; either an acid or an alkali; for further chemical processing by precipitation, ion exchange, solvent extraction, distillation and / or chromatography [1].

Through the last twenty years ago many of scientists efforts has done and a lot of methods and ways for the production, separation, purification and quality control assessment of the cyclotron produced radionuclides were more or less well established. Due to the lack of local informations and experience in the field of cyclotron produced radioisotopes, somewhat detailed literature survey on ^{67}Ga, ^{111}In and ^{201}Tl would be considered of great importance in this respect as a preliminary guide for the radiochemists to understand the variable parameters which control the subject of radioisotope production using the cyclotron facility.

1.2 Radioisotopes of Gallium, Indium and Thallium

Among all the isotopes of gallium, indium and thallium, the cyclotron products; ^{67}Ga, ^{111}In and ^{201}Tl, appear to be the most useful radionuclides for medical applications. Their half-lives are considerably sufficient for radiochemical processing. In addition, they have reasonable biological half-lives and easily detectable radiations. Tables 1, 2 and 3

compiles the known radionuclides of gallium; indium and thallium together with their half-lives, mode of decay and principal energies.

Gallium -67 is used mainly in the localization of soft tissue tumours and for detection of acute inflammatory processes; assessment of cardiac viability; inflammation of cardiac muscle and abscess. It has been found on studying its biodistribution that it accumulates in stomach; intestine; bone marrow; liver; spleen; neck and face [32, 33]. ^{67}Ga can undergo extensive hydrolysis, at pH 3 and above if not chelated. At physiological pH the major species for Ga is the gallate $[Ga(OH)_4]^-$ [34].At pH 7.4 gallium forms mostly $[Ga(OH)_4]^-$ (98%)and some $Ga(OH)_3$ (1.6%) with OH- ligands [35].

Table 1. Radioisotopes of gallium and their nuclear characteristics[13,14]

Nuclide	Half-life ($T_{1/2}$)	Mode of decay; E=MeV	Nuclide	Half-life ($T_{1/2}$)	Mode of decay; E=MeV
^{62}Ga	0.116 s	B^+=9.17	^{73}Ga	4.87 h	B^-=1.59
^{63}Ga	32 s	B^+=5.5	^{75}Ga	2.1 min	B^-=3.39
^{64}Ga	2.63 min	B^+=7.16	^{76}Ga	29 s	B^-=6.8
^{65}Ga	15.2 min	B^+=3.256	^{77}Ga	13 s	B^-=5.3
^{66}Ga	9.5 h	B^+=5.175	^{78}Ga	5.09 s	B^-=7.9
^{67}Ga	3.26 d	E.C=1.001	^{79}Ga	2.85 s	B^-=6.8
^{68}Ga	1.13 h	B^+=2.921	^{80}Ga	1.68 s	B^-=10
^{69}Ga	21.1 min	B^-=1.653	^{81}Ga	1.22 s	B^-=8.3
^{70}Ga	21.1 min	B^-=1.653	^{82}Ga	0.607 s	B^-=12
^{72}Ga	14.1 h	B^-=3.99	^{83}Ga	0.31 s	B^-=10.5

However, the solubility of gallate is limited by that of $Ga(OH)_3$ with a minimum value of ~40nM [34], the uncharged $Ga(OH)_3$ would precipitate if its concentration is above this value. For ^{67}Ga this limit is not a concern *in vivo* because for usual initial blood level of ~74 KBq/ml

(6mCi normal dose/~3000ml plasma), the gallium concentration would be 0.05 nM. However, the citrate complex of ^{67}Ga radiopharmaceutical, a weak chelate K_{ML} =~10^{10}, prevents any possibility of hydrolysis and subsequent precipitation [36]. For many years ^{67}Ga citrate was used for the detection of both acute and chronic abscesses and inflammatory processes [40,41]. However, it is now used mostly to identify chronic occult abscess sites and chronic inflammatory lesions in the diseases such as sarcoidosis[43,45]. After injection, ^{67}Ga goes to the iron transport protein transferrin (TF) in the blood and a small percent of non- protein bound Ga remains in equilibrium. In humans, the radioactivity is normally distributed in the liver (5%of injected dose), spleen (1%), kidney (2%), and skeleton (24%) which remains constant as a function of time[35,37,38].

Indium-111 is used in lymphoscintigraphy, infection imaging, cisternography and it has a high potential for use in radioindium immunoscintigraphy. Its 2.83 day haf-life makes it a preferred radionuclide over ^{113m} In ($T_{1/2}$ =1.7 h) obtained from ^{113}Sn-^{113m}In genarators and ^{99m}Tc ($T_{1/2}$=6.0h) obtained from ^{99}Mo- ^{99m}Tc generators for studies which last only 1-3 days .Indium-111 labeled polyclonal human immunogloblin G (^{111}In * Ig G) is designed to image infection. It is a polyclonal human IgG to which are covalentely coupled 2 to 3 DTPA molecules to lysines or argining on antibody in a random process[85]. When injected, ^{111}In *IgG has a long $T_{1/2}$ in the blood [85]. For example, at 12 h post injection, nearly 60% of 2 min value remains in the blood. The major organs; liver, spleen, kidney, and bladder are the sites of radionuclide deposition in normal volunteers. After injection, indium-111 labeled oncoscint has a long terminal $T_{1/2}$ in the blood 56h[95]. In 72 h, only 10% of the injected activity is eliminated.

Table 2. Radioisotopes of indium with their nuclear characteristics[13,14]

Nuclide	Half-life ($T_{1/2}$)	Mode of decay; E=MeV	Nuclide	Half-life ($t_{1/2}$)	Mode of decay; E=MeV
^{102}In	23 s	E.C=9.1	^{119}In	2.3 min	B^-=2.34
^{103}In	1.1 min	B^+=6.04	^{120}In	3.1 s	B^-=5.3
^{104}In	1.84 min	B^+=7.9	^{121}In	23 s	B^-=3.36
^{105}In	5.1 min	B^+,EC=4.85	^{122}In	1.5 s	B^-=6.77
^{107}In	32.4 min	B^+=3.42	^{123}In	6 s	B^-=4.4
^{108}In	40 min	B^+=5.14	^{124}In	3.18 s	B^-=7.18
^{109}In	4.2 h	B^+=2.02	^{125}In	2.33 s	B^-=5.5
^{110}In	1.15 h	B^+=3.9	^{126}In	1.63 s	B^-=8.2
^{111}In	2.8 d	E.C=0.86	^{127}In	1.14 s	B^-=6.5
^{112}In	14.4 min	B^+=2.588	^{128}In	0.8 s	B^-=9.3
^{113m}In	104min	I.T.=0.393	^{129}In	0.63 s	B^-=7.6
^{114}In	1.198 min	B^-=1.989	^{130}In	0.29 s	B^-=10.1
^{116}In	14.1 s	B^-=3.27	^{131}In	0.28 s	B^-=8.9
^{117}In	44 min	B^-=1.45	^{132}In	0.2 s	B^-=13.4
^{118}In	5 s	B^-=4.42	^{132}In	0.2 s	B^-=13.4

The normal biodistribution includes, early localization in liver and spleen [93]. The radiopharmaceutical(^{111}In*OctroScan) is cleared from the blood, for example, at 10 min only 33% of the injected dose remains in the blood and 25% of the injected radioactivity is present in the urine after 3h [94]. After intravenous administration, accumulation of ^{111}In is observed in the thyroid gland, pituitary gland, liver, spleen, kidney, and bladder, gallbladder and intestinal radioactivity are seen at later time points[96]. Indium - 111 *Myoscint remains in the blood with an initial short $T_{1/2}$ of 1.9 h and slower phase washout of 25.6 h [98]. For imaging, it is a must to wait ~24 h in order to let the blood pool radioactivity clear. The ^{111}In radioactivity remaining is usually localized in the liver, spleen, kidneys and bone marrow. [97,99,100].

Thallium-201 is the widely used radionuclide throughout the world in the management and diagnosis of artery diseases because of their rapid uptake and concentration in myocardium. Imaging with ^{201}Tl facilitates a functional assessment of myocardium which directly reflects the blood flow to myocardial tissue. This nuclide provides a polysiological assessment of heart segments which are no longer functioning after heart attack. After injection with $^{201}TlCl$, the radioactivity is rapidly taken up by the normal heart and other muscle tissue achieving maximal concentration of 4-5% of the total injected dose in 10-30 min. About 90% of the radioactivity disappears within 20min. This means that imaging can begin 15-20 min after injection. Thallium is incorporated into the myocardial cell in a similar manner as potassium; since it has a similar crystal radius (1.5A° vs 1.38A° for K^+) and hydrated radii.

Table 3. Radioisotopes of thallium with their nuclear characteristics[13,14]

Nuclide	Half-life ($T_{1/2}$)	Mode of decay; E=MeV	Nuclide	Half-life ($t_{1/2}$)	Mode of decay; E=MeV
^{179}Tl	0.2 s	α	^{196m}Tl	1.41 h	B^+,EC= 4.9
^{183m}Tl	0.06 s	α	^{196}Tl	1.84 h	B^+ =4.4
^{184}Tl	11 s	B^+ = 9.3	^{197}Tl	2.83 h	B^+ = 2.17
^{185m}Tl	1.8 s	α = 5.97	^{198}Tl	5.3 h	EC ,B^+ = 5.3
^{186}Tl	1.8 s	B^+,EC = 8.5	^{199}Tl	7.4 h	EC = 1.4
^{186}Tl	28 s	B^+, EC = 7.8	^{200}Tl	1.087 d	EC = 2.46
^{188}Tl	1.2 min	B^+,EC = 7.9	^{201}Tl	3.038 d	B^- = 0.48
^{189}Tl	2.3 min	B^+,EC = 5.2	^{202}Tl	12.23 d	B^- =1.36
^{190}Tl	2.6 min	B^+, EC = 6.9	^{206}Tl	4.2 min	B^- =1.531
^{192}Tl	9.2 min	B^+, EC = 6.1	^{207}Tl	4.77 min	B^- = 1.43
^{193}Tl	22 min	B^+,EC = 3.6	^{208}Tl	3.05 min	B^- = 4.998
^{194}Tl	34 min	B^+,EC = 5.2	^{209}Tl	2.2 min	B^- = 3.99
^{195}Tl	1.16 h	EC = 2.8	^{210}Tl	1.3 min	B^- = 5.49

1.3 Cyclotrons and Their Utilization

When particle accelerators, and in particular cyclotrons, were first developed during the period-1929 - 1935and their applications in nuclear sciences started a quantum jump. This necessitates ever increasing development of different types of particle accelerators, since the electrostatic generators can not be used to accelerate particles to very high energies because of break down in the electrical insulation and corona discharge. This difficulty was overcome by acceleration using the principle of resonance; by the repeated application of a relatively small voltage. This has led to development of cyclic accelerators or cyclotrons.

E.Lawrence and M.Livingston constructed the first cyclotron in 1932 by making use of the principle of magnetic resonance. A diagram of a typical cyclotron is shown in Figure 1[(4)]. A source, S, of positive ions, such as protons, deuterons or alpha particles is placed in the centeral region of the gap between two hollow metallic boxes, DD', called dees because of their shape. The dees are connected to the terminals of an alternating field in the gap between the dees. When one dee is positive the other is negative, and vice versa .The dees are placed in an evacuated chamber, from which they are completely insulated. A uniform magnetic field is applied perpendicular to the whole cross sectional area of the dees by placing the dees between the pole faces of the large magnet.

Suppose at the instant a positive ion is ejected from the source S and one D is positive and the other D' is negative; the charged ion will be attracted towards D' (-ve) and hence accelerated across the gap. Once inside D', it will not be influenced by the electric field because of the electerical shielding produced by the dees. However, the magnetic field will bend the path of the ion into a circular path. By the time the ion is about to enter the gap again, if the frequency of the alternating voltage is

such that D is negative now and D' is positive, the ion will be accelerated between the gap towards D. This process of acceleration in steps continues every time the ion crosses the gap. As the velocity of the ion increases, the magnetic field makes them move into bigger and bigger orbits. At the end, the ion beam is extracted from the chamber by means of a deflecting magnet [5].

Some small cyclotrons are exclusively devoted to the production of short-lived B^+-emitters. Medium and larger sized machines have often interdisciplinary utilization, they are capable of delivering a variety of radioisotopes. The cyclotrons and accelerators used for medical radioisotopes production can be roughly divided into three groups:

i) Low energy machines (E< 15MeV), including Baby-cyclotrons. These are associated with hospitals and used mainly for the on-site production and application of short -lived B^+ -emitting nuclides like ^{11}C, ^{13}N and ^{15}O.

(ii) Multipurpose, multiparticle medium energy machine (E<200MeV), including compact cyclotrons on the lower energy side of this group. A large variety of radioisotopes are produced using such machines.

(iii) High energy machines (E>300MeV), accelerating mostly protons. They are used basically for high energy physics studies and some radioisotope production activities[16].

A brief summary of the types of accelerators used for radioisotopes production is given in Table 4. This is an updated version of the classification suggested by Wolf and Barcly Jones[4]. The smallest machine (E < 4 MeV) is a linear (single or two particle) accelerator, used

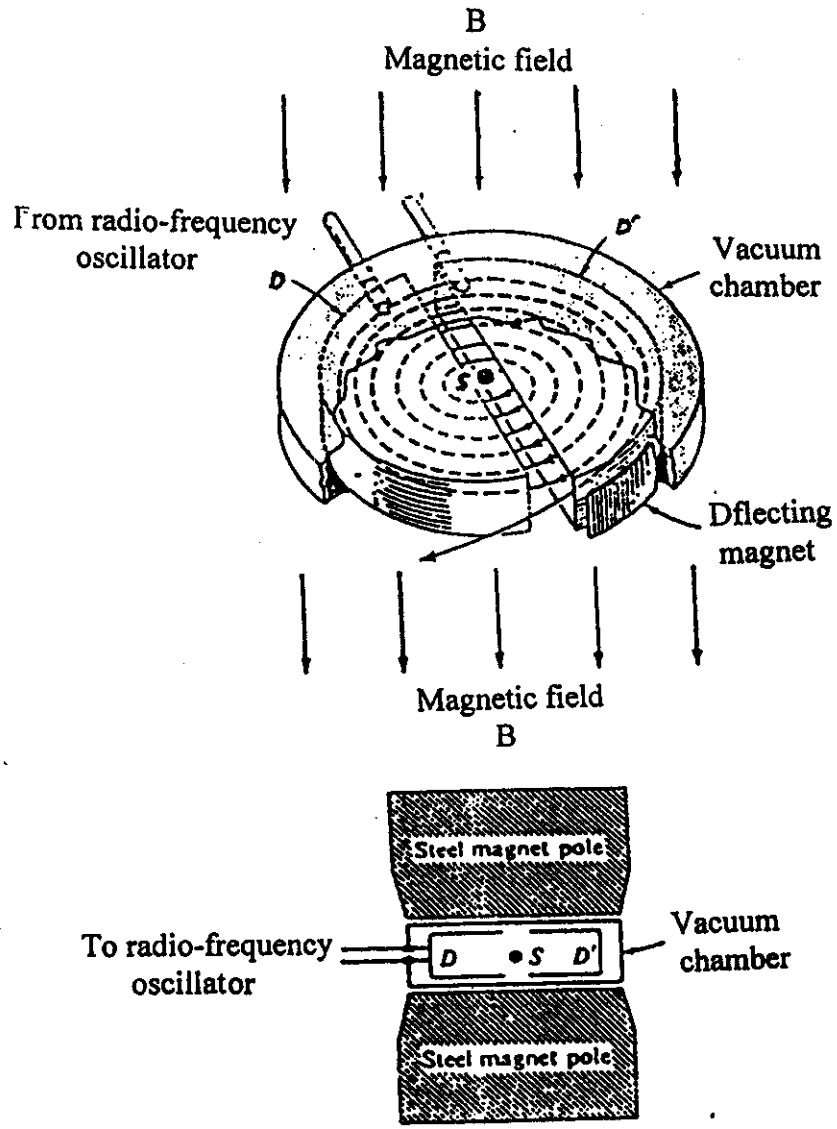

Figure 1. Schematic diagram of cyclotron dees and projectile source[5].

exclusively for the production of the B^+-emitter ^{15}O ($T_{1/2}$=2 min) and possibly also ^{18}F ($T_{1/2}$=110 min). Since it does not need any shielding, it is housed in the hospital environment.

Table 4. Types of accelerators routinely used for radioisotopes production[3,4]

Classification	*Characteristics*	*Energy(MeV)*	*Major produced radioisotope*
Level I	Single particle (d)	≤ 4	^{13}O
Level II	Single particle (P)	≤ 11	^{11}C, ^{13}N, ^{15}O, ^{18}F
Level III	Single or tow particle (P, d)	≤ 20	^{11}C, ^{13}N, ^{15}O, ^{18}F (^{123}I, ^{67}Ga)
Level IV	Single or multiple particle(p, d, ^3He, ^4He)	≤ 40	^{38}K, ^{73}Se, ^{75}Br, ^{123}I, $^{81}Rb(^{81}Kr)$, ^{67}Ga, ^{111}In, ^{201}Tl, ^{22}Na, ^{57}Co
Level V	Single or multiple particle(p, d, ^3He, ^4He)	≤ 100	^{123}I, $^{72}Se(^{72}As)$, $^{82}Sr(^{82}Rb)$, ^{117m}Sn
Level VI	Single particle (p)	≥ 200	^{26}Al, ^{32}Si, ^{44}Ti, ^{67}Cu, $^{68}Ge(^{68}Ga)$, ^{109}Cd

Other larger sized cyclotrons have a wider utility; as far as isotopes production is concerned [3]. The basic fields of activity based on cyclotrons with energies up to 20 MeV proton including the Egyptian MGC-20 Multipurposes cyclotron (under construction) are:

i - Basic research in nuclear and atomic physics .

ii - Production of short-lived cyclotron isotopes such as ^{11}C , ^{13}N , ^{15}O , ^{18}F , ^{43}K , ^{67}Ga , ^{62}Zn , ^{111}In , ^{81}Rb , ^{203}Pb , ^{55}Co , ^{48}Cr , ^{52}Fe .

iii - Material science and solid state physics .

iv - Nuclear data and services .

v - Nuclear analytical methods of analysis .

1.4 Production of Radionuclides

The amounts of radioactivity produced via a cyclotron, or a reactor facility, are submitted to various parameters illustrated by the equation of disintegration rate of the produced radionuclide:

$$D=IN\sigma(1-e^{-\lambda t})$$

Where;

D= number of disintegrations per second of the radionuclide produced,

I = flux of the irradiating particles (number of particles /cm^2),

N= number of target atoms,

σ=formation cross - section (probability) of the radionuclide (cm^2) ;
It is given in units of "barn" which is equal to 10^{-24} cm^2,

λ = decay constant given by 0.693 / $T_{1/2}$, where $T_{1/2}$= half-life of the produced radionuclide, and

t =duration of irradiation in the same units of $T_{1/2}$

It is obvious that the product radioactivity depends upon the intensity and energy of the incident particles, the amount of the target materital, the half-life of the radionuclide produced and the duration of irradiation [1].

1.4.1 Commonly Used Production Methods

The technological methods used for production purposes depend on the type of radionuclide desired. We consider below the routine production methods for positron emitters, photon emitters and therapy related radioisotopes.

- *Positron Emitters:*

A brief resume including the commonly used nuclear reactions, their suitable energy ranges and the target materials employed for the production methods of the four short- lived B^+-emitters, viz. ^{11}C, ^{13}N, ^{15}O and ^{18}F which are commonly used in positron emission tomography (PET) [17] is given in Table 5. All of them can be produced at a small sized two particle (p and d) cyclotrons.

Table 5. Common methods of production of the short-lived organic positron emitters[3,17]

Radioisotope	*$T_{1/2}$(min)*	*Production route*	*Energy range (MeV)*	*Target*	*Target production*
^{11}C	20	$^{14}N(p, \alpha)$	13-3	$N_2(O_2)$	^{11}CO, $^{11}CO_2$
		$^{11}B(p, n)$	10-0	B_2O_3	$^{11}CO_2$
		$^{10}B(d, n)$	10-0	B_2O_3	$^{14}CO_2$
^{13}N	10	$^{12}C(d, n)$	8-0	CO_2,CH_4	^{13}NN, $^{13}NH_3$
		$^{16}O(p, \alpha)$	16-0	$H_2{}^{16}O$	$^{13}NO_2^-$
^{15}O	2	$^{14}N(d, n)$	8-0	$N_2(O_2)$	^{15}OO
^{18}F	110	$^{18}O(p, n)$	16-0	$H_2{}^{18}O$	^{18}F

- *Photon Emitters:*

The number of photon emitters is very large. However, only those radioisotopes of greater interest are which emit either a single or a predominantly single γ -ray. Thus; they find applications in diagnostic nuclear medicine, using either γ-cameras or, in recent years, single photon emission computed tomography (SPECT). Some of the commonly used radioisotopes are listed in Table 6, together with their production routes [6,18]. The radioisotope ^{99m}Tc ($T_{1/2}$=6.0 h) is the work horse of diagnostic nuclear medicine and is obtained via the $^{99}Mo/^{99m}Tc$ generator system. Many of the accelerators, medium-sized cyclotrons,

producing γ-ray emitting radionuclides, like ^{67}Ga, ^{111}In, ^{123}I and ^{201}Tl, are also finding increasingly wide applications. In recent years very high intensity medium-sized and completed automated cyclotrons have been developed with the specific aim of medical radioisotope production. Extracted beams of about 0.5 mA are available; they fall strongly on solid targets. Many methods have also been developed for producing some of those radioisotopes at a small cyclotron, e. g ^{123}I via the ^{123}Te (p,n)[19, 20] , ^{67}Ga via the ^{67}Zn (p , n) [21] and ^{111}In via the ^{111}Cd (p , n) reaction [22] .

Table 6. Routine methods of production of some commonly used photon emitters[3,6,18]

Radioisotope	$T_{1/2}$	*Mode of decay*	*γ-ray energy keV(%)*	*Nuclear process*	*Energy range (MeV)*
^{67}Ga	3.26 d	EC (100)	93(37)	$^{68}Zn(p,2n)$	26-18
^{99}Mo ↓ ^{99m}Tc	2.75 d 6 h	B^- (100) EC(100)	740(12) 141(87)	$^{98}Mo(n,\gamma)$	
^{111}In	2.8 d	EC (100)	173(91)	$^{112}Cd(p,2n)$	25-18
^{123}I	13.2 h	EC (100)	159(83)	$^{123}Te(p,n)$	14-10
^{201}Tl	3 d	EC (100)	69-82(X-ray)	$^{203}Tl(p,3n)^{201}pb$	28-20

1.4.2 Nuclear Data Relevant to Cyclotron Produced Short – Lived Medical Radioisotopes

Choice of a radioisotope for medical applications demands an accurate knowledge of its nuclear structure and decay data. The charged particle induced nuclear reaction cross-section data are needed for optimizing the production of a radioisotope , especially for calculating

the production yield and impurities as well as for target design and chemical processing. The term nuclear data originating from the decay of radioactive nuclei or from the interactions of nuclei with matter fall under this heading [6]. The data can be generally grouped into two classes as shown in Figure 2.

1.4.2.1 Nuclear Structure and Decay Data Importance

These data are needed for selecting and production of a particular radioisotope which is useful or potentially useful for in-vivo medical applications(Figure 2). The selection is determined by two factors, namely:

- The resolution and efficiency of the radiation detecting system used, and
- Radiation dose caused to the patient.

In regard to the first factor, the use of a conventional photon-detecting camera requires an isotope with principle γ -ray energies in the range of 60 to 300 keV with absence of high-energy γ -rays for good quality scans. Similarly, radioisotopes with strong B^+ branching, the energy of the positrons, is also important. High B^+ energies lead to long annihilation path affecting, thereby, the resolution of the detectors adversely [6].

In regard to the second factor, the radiation dose caused to the patient is a very important consideration in the choice of a radioisotope. The radioisotope should preferably not be B^- or α - emitter. The knowledge of the decay scheme of the radioisotope, half- life, the number of particles or photons per disintegration as well as the mean energies of the particles and the photons are essential [7].

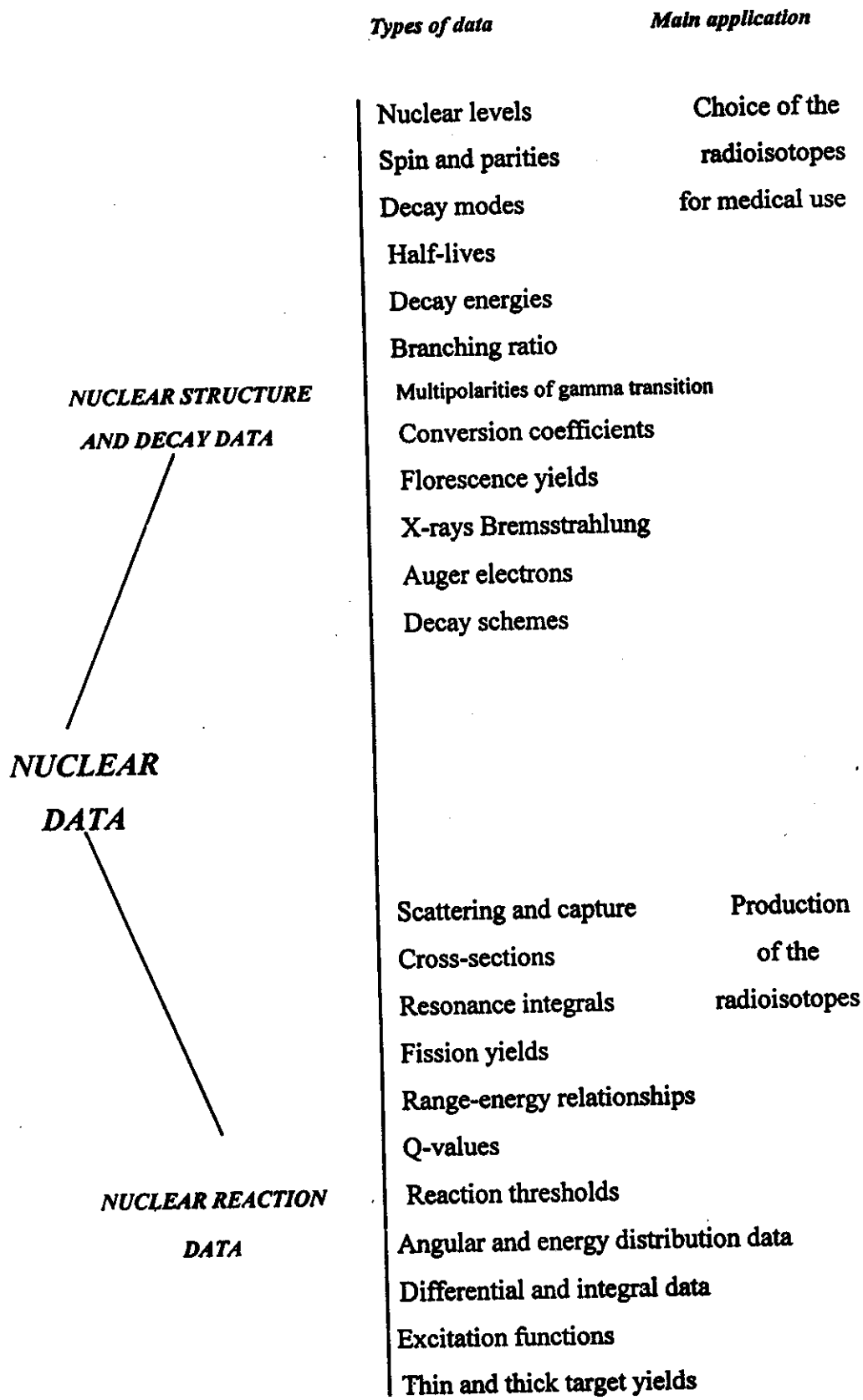

Figure 2: Types of nuclear data and their main applications to medical radioisotopes [6, 13]

1.4.2.2. Nuclear Reaction Data Importance

These data are important in connection with the production of radioisotopes:

- Determining the energy range optimum for the production of a specific radioisotope,
- Calculating the expected thick target yield of the isotope to be Produced, and
- Calculating the yield of radionuclidic impurities for a given thickness and enrichment of the target.

A selection of the projectile energy range that will maximize the yield of the desired product and minimize that of the radioactive impurities is of vital importance in optimizing a production method. At low projectile energies the number of open reaction channels is generally small but with increasing the incident particles energies several competing reactions set in. The level of isotopic impurities can be suppressed only by using enriched isotopes as target materials and/ or by a careful selection of the particles energy range effective at the target [8]. The use of a highly enriched target material may generally yield the desired radioisotope in a high radionuclidic purity. In cases where target technology is not sufficiently advanced another nuclear process on a different target element (of even natural isotopic composition) and careful selection of the optimum energy may be of considerable advantage. For example, high purity ^{201}Tl can be produced via the ^{201}Hg (p,n)^{201}Tl nuclear reaction using highly enriched ^{201}Hg as target. However, since neither elemental mercury nor any of its known compounds are capable of with standing high currents, the route of production of ^{201}Tl is via the process

$$^{203}\text{Tl (p,xn) } ^{201}\text{Pb} \xrightarrow{\text{(EC) 9.4h}} ^{201}\text{Tl}$$

The limiting factor in this process is the impurity level of ^{200}Tl. Excitation function measurements [9,10] (out of the scope of this study) revealed that the optimum incident proton energy is 28 MeV, at which the undesired ^{200}Tl impurity is <1%. At higher energies the ^{201}Tl yield are significantly higher but it is also true for the ^{200}Tl contamination.

The nuclear data are generally well known and have been taken from:

1-Nuclear data sheets, edited by the nuclear data project for the international network for nuclear structure data evolution , Academic press ,New York (periodical issues) [13].

2-Table of isotopes, 7Th Edition, edited by C.M. LEDERER and V.S.HIRLEY, John Wiley and Sons, Inc., New York (1978) [14].

As discussed above the nuclear structure and decay data are well-known and the needs are commonly met by the existing data[15]. Measurements on neutron induced reaction cross-section data are generally motivated by energy research programs. The existing data are sufficient for medical radioisotope production using nuclear reactors.

1.5 Production of Gallium-67

1.5.1 Gallium-67 Production Via Zn Target Irradiation

1.5.1.1 Target Preparation and Cooling System

Enriched zinc target was prepared by electrodeposition. A sketch of the electrolytic cell used for target preparation, excitation function measurements as well as for ^{67}Ga production is shown in Figure 3[21]. Nickel foils of 5μm were used as backing material. For preparing production targets; 250 mg of enriched zinc was electrolytically deposited in cavity of 12 mm diameter previously (Ni) plated copper backing.

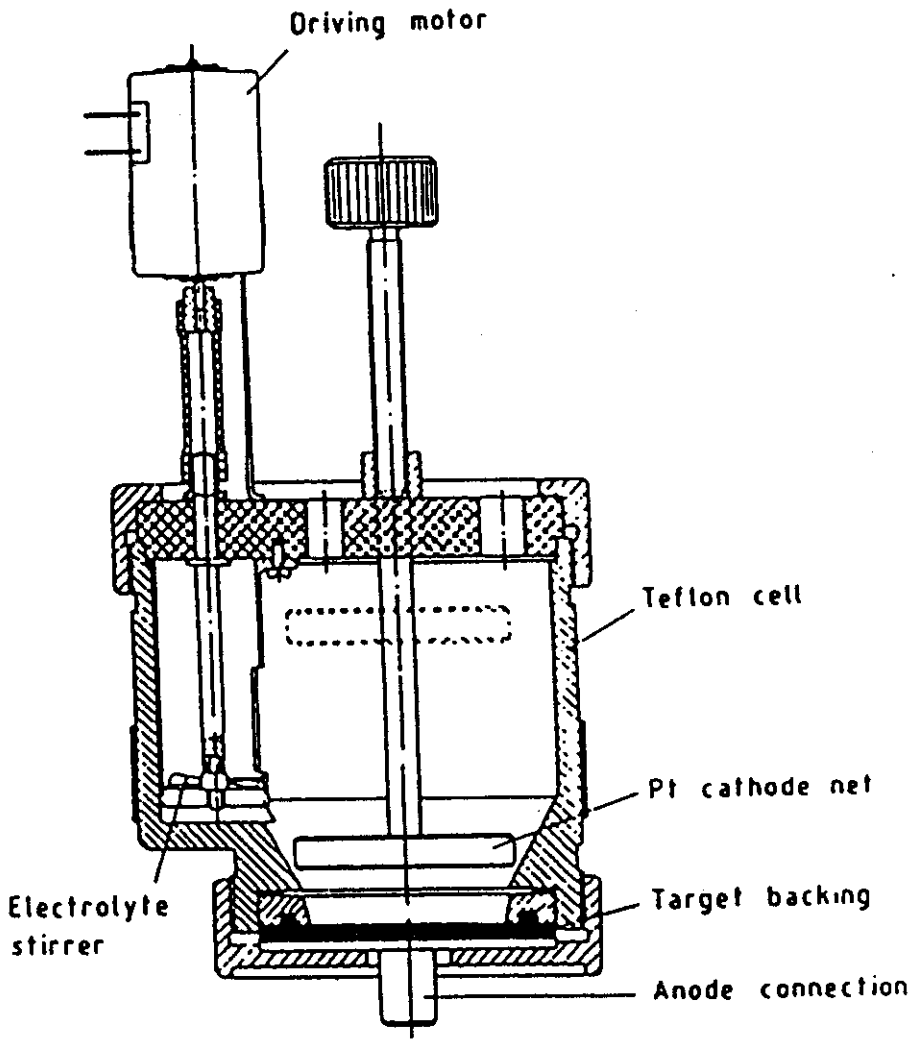

Figure 3. Sketch of electrolytic cell used for preparation of samples excitation function measurements and for routine production of radioisotopes[21].

For production targets, the electrolyte was 50 ml HCl containing 2g enriched $ZnCl_2$. The time of electrolysis was 1h at 600mA constant current and the polarity of copper electrode was changed for 2s every 20 second. To reach higher mechanical stability the layer was compressed with 300 bars. There was no Zn loss from the target during the irradiation.

The main elements of the modular target system for the gallium production are shown schematically in Figure 4. The system is used on a vertical beam line [76] and has a conventional construction. Helium cooling from the front side and water cooling from the backside transfer the heat produced in the target, target backing and the foil window. The foil makes possible the front gas cooling, and serves as a window. The target system is insulated from the beam line with an electrostatic suppressor module, which is used for the most accurate beam current determination. The beam is rotated at high current irradiation to avoid "hot spots" and additional shields are applied in front of the target system for percollimation of the entering beam. A beam stop is used for checking the beam position, intensity and profile before irradiation. A special beam stop equipped with a set of thermometers could be used for measurement of the heat distribution in the target. The second entrance port used for the production target system is remote controlled [21]. For production of ^{67}Ga; 14MeV proton and 35-40μA beam intensity are used. Typically irradiation time is 15-16 h depending on the demands of users. The ^{66}Ga impurity at end of bombardment (EOB) is less than 5%, but at the time of administration (nearly day after EOB) it is lower than 1%[77].

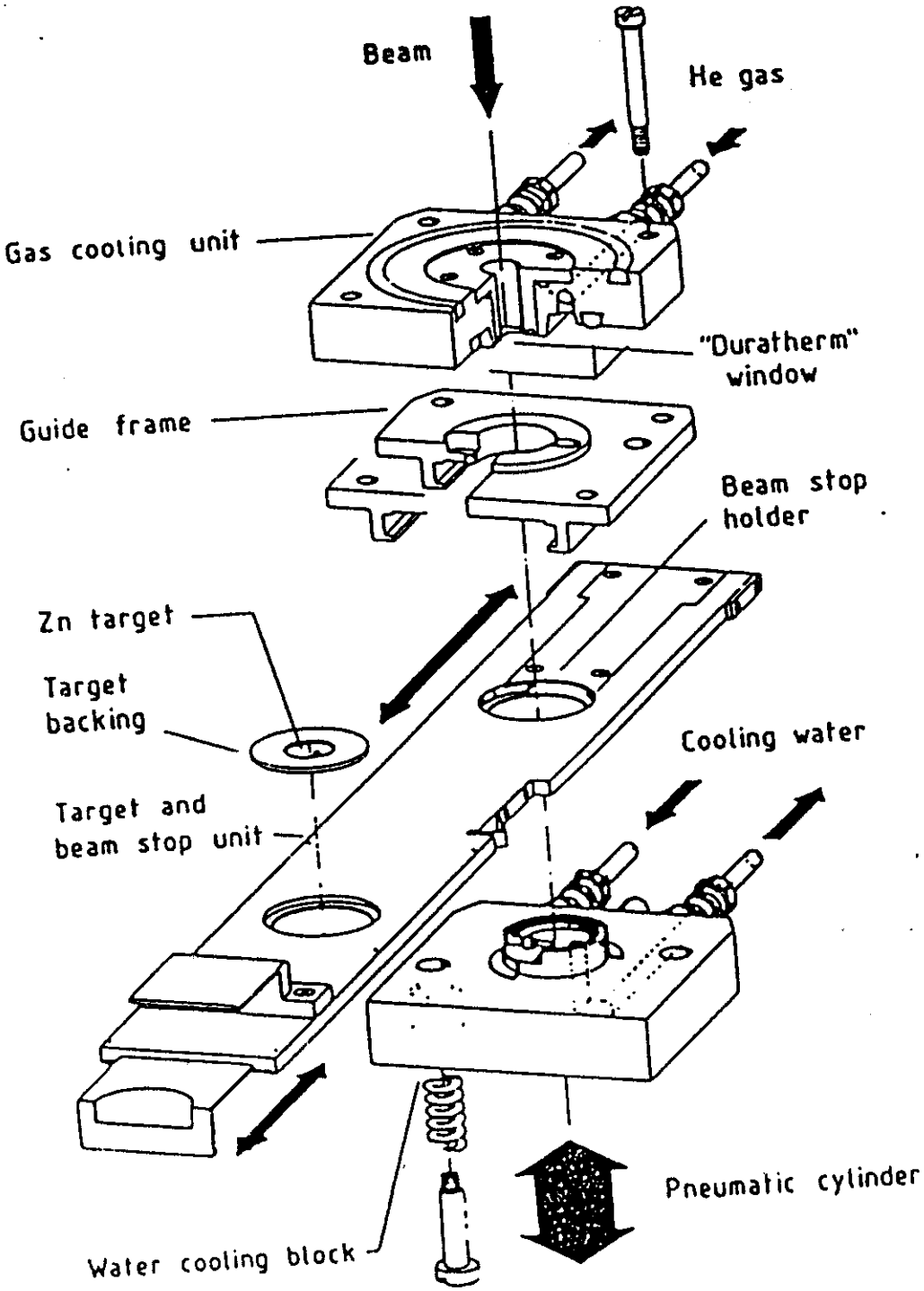

Figure 4. Exploded sketch of production target[21,76].