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COLLEGE ON MEDICAL PHYSICS
AND
WORKSHOP ON
NUCLEAR DATA FOR SCIENCE AND TECHNOLOGY:
MEDICAL APPLICATIONS
(20 SEPTEMBER - 15 OCTOBER 1999)

"Accelerators for Medical Isotope Production and Therapy"

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Accelerators for medical isotope production and therapy

(requirements, cyclic and linear accelerators, new developments and trends)

F. Tárkányi, Debrecen, Hungary

Introduction

Field of medical application of accelerators

Basic layout of an accelerator system

Requirements to the accelerator systems

Basic principles of the accelerators
Cyclic and linear accelerators

Modern trends in different accelerators

Nuclear data connected to accelerator technology

Introduction

Nuclear medicine mostly based on:

Reactors(radioisot, BCNT,analytic)
Accelerators(radioisot, therapy, analytic)

Accelerators

Total about		**10 000**
Medicine/biology(50 %)		**5000**
Radiotheraphy(80 %)		**4000**
	X	**10**
	N	**10**
	P	**10**
	HI	**5**
Others		**1000**
	Isot.prod. (cycl)	**300**

Medical application fields of accelerators

Radioisotope production for:

Diagnostics

Single Photon
Positron

Endotherapy

Principle: radioisotopes are injected to the body. Their radiation is used to detect distribution of labeled compounds(diagnostics) or to destroy tumour cells(endotherapy)

Radiation therapy with:

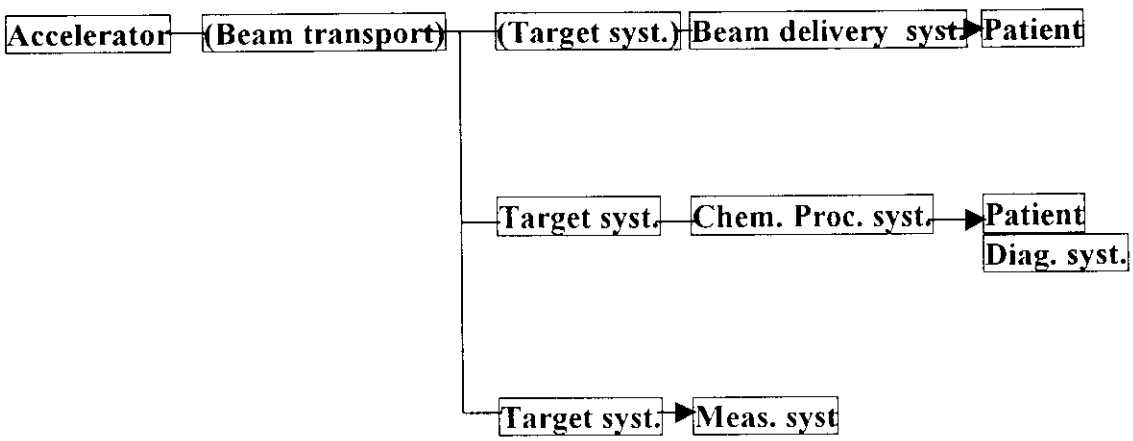
X, e^-

Hadrons
Neutron
Proton
HI

Principle: irradiation with external particles to destroy tumour cells
To perform conformal irradiation
- **Maximal dose in tumour cells**
- **Minimal dose to healthy cells**
- **"limited time" of irradiation**

Different particles, different energy deposition, different intensities, different energies etc.

Basic layout of accelerator systems



(Trieste99-Accelerators-Tarkanyi)

Basic principles of the accelerators
Cyclic and linear accelerators

Constant current accelerators

Principle: Electrical potential difference accelerate ions in linear acceleration tube
Different methods to produce electrical potential

Cocroft –Walton generator(voltage multiplier)
Van de Graaff generator((charged high voltage terminal)
Tandem Van de Graaff(charged high voltage terminal+tandem principle, stripping)

Linear accelerators

Principle: set of linearly arranged electrodes (tubes) with alternatively changing potentials
Different constructions

Drift tube accelerators
Wave guide electron accelerators

Cyclic accelerators

Principle: ions accelerated stepwise by electric fields describing circular path due to magnetic fi
Different magnetic fields, different frequencies of electric field

Cyclotron
Isocrhone cyclotron
Syncrocyclotron
Electron synchrotron
Proton Synchrotron
Microtron
Betatron

(Trieste99-Accelerators-Tarkanyi)

Requirements to accelerators used for therapy

Used (accelerated) particle	Energy accelerated beam(MeV)	Intensity primary beam (μA)	Accelerator	Aux. equip.
X(e^-)	40	10 000	el. linear acc., betatron	fixed head, or isocentric gantry
e^-	40	10	el. linear acc., betatron	fixed head, or isocentric gantry
π-	100	0.2	synchrotron	fixed head, or isocentric gantry
Fast neutron (p,d)	70	50	cyclotron, linear acc.	fixed head, or isocentric gantry
^1H	200(70)	0.2	cyclotron, linear acc., synchrotron, syncrocyclotron	fixed head, or isocentric gantry
^4He	800	0.2	linear acc., synchrotron	fixed head, or isocentric gantry
^{12}C	4600	0.2	linear acc., synchrotron,	fixed head, or isocentric gantry
^{20}Ne	10 500	0.2	linear acc., synchrotron,	fixed head, or isocentric gantry
Epithermal neutron BCNT(p,d)	2.5	15 000	Linear acc., cyclotron	

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Requirements to the accelerator systems

Physical parameters of the primary beam

- Energy
- Intensity
- Time structure
- Intensity distribution

Physical parameters of the secondary beams

- Energy
- Intensity

Parameters of the irradiation facilities

- Field sizes
- Dose rates
- Target systems

Engineering problems of the effective appl.

- Reliable
- Simple to operate

General requirements of cost effective use

- Low capital and operating cost
- Compact
- Location

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Requirements to therapeutic machines

- The beam must be available to meet clinical requirements, located at hospital
- Short treatment times, not exceeding 5-10 minutes
- Dedicated irradiation and treatment system
- Simple to operate
- Reliable
- Low capital and operation cost
- Compact
- Isocentric gantry
- Multileaf collimation
- Field sizes
- Dose rates
- Penetration

Trends in accelerators used for therapy

- Dedicated machines, not multipurpose
- Commercial products
- Accelerator, beam transport, irradiation facility in complex
- New technical solutions, integrated design, new methods
- Discussion of accelerators used in different fields

X, e^-
n
p
p, Hi

Parameter	Specification
Range in Patient	32 g/cm^2 Max 3.5 g/cm^2 Min
Range Modulation	Steps of < 0.5g/cm^2
Range Adjustment	Steps of <0.1g/cm^2
Avg. Dose Rate	25cmx25cm modulated to 32g/cm^2: 2Gy in < 1min
Spill Structure	Scanning Ready
Field Size	Fixed >40cmx40cm Gantry >40cmx30cm
Dose Uniformity	2.5%
Effective SAD	~2.5m
Distal Dose Fall-off	<0.1g/cm^2
Lateral Penumbra	<2mm

Parameter	Specification
Time for startup from standby	<30min
Cold Startup Time	<2hours
Time for Shutdown to Standby	<10min
Time for 'Manual' Setup in one room	<1min
Time for Auto Setup in one room	<0.5min
System Availability	>95%
Dosimeter Reproducibility	1.5% (Daily) 3.0% (Weekly)
Time to Switch Rooms	<1 min
Switch energy in one room	<2 sec
Radiation Levels	ALARA

Application of radioisotopes

- Basic principle of PET, SPECT and endotherapy

Isotopes and production routes

- Basic principles and steps of production of labelled compounds
- Main characteristics of medical radioisotopes and most important routes for their production

Requirements to accelerators

- Classification of the accelerators used for isotope production.
- Requirements to the main physical parameters of the accelerators.
- Technological requirements to the present day accelerators.

Cyclotrons

- Technological progress in development of cyclotrons.
- Common features of dedicated cyclotrons.
- Comparison of a compact multipurpose and third generation dedicated PET cyclotron.
- Statistics of cyclotrons

Other accelerators

- New types of small accelerators.
- Reactions for PET isotope production at low energies.

Targetry

- Requirements to the targetry (selector + targets).
- Technological progress on developments of targetry.

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Basic principles and steps of production of labelled compounds

The manufacturing process

Production of radioisotope

- production of isotopically enriched row materials
- fabrication of cyclotron bombardment targets
- cyclotron operation for target bombardment
- radiochemical extraction of the radioisotope
- waste disposal of highly radioactive waste

Production of the labelled compound

- pharmaceutical manufacturing of the final product
- quality control of during production stages
- (packing operations)
- distribution and delivery

The different steps are closely connected and they are built each on other

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Main characteristics of medical radioisotopes and most important routes for their production

Classification of the accelerators used for isotope production

Aspects	Classification	Remarks
Field of the application	dedicated	PET, SPECT
	multipurpose	other appl., research
Max. energy	I(<5 MeV)	
	II((<12)	
	III(<20 MeV)	
	V(<40 MeV)	
	V(<100 MeV)	
	VI(<1 GeV	
Energy range	fix	
	variable	
Accelerated particle;	single	p
	double	p.d
	multi	p,d, ^{3}He, ^{4}He
Charge of particle	positive ion	all particles
	negative ion	p,d
Principle of acceleration	electrostatic	
	RFQ	
	linear accelerator	
	cyclotron	
	synchrocyclotron	
	etc.	
Produced intensity	low(10 (<10 μA)	
	middle(<50 μA)	
	high(1 mA)	
Place of installation	hospital	
	production company	
	research institute. etc.	
Supply	local	
	regional	
	word wide	
Technological level	first generation	
	second generation	
	third generation	

Requirements to the main physical parameters of the accelerators

1. Basic equation of isotope production

yield = *function of*: cross section
number of target atoms
beam intensity
irradiation time
energy range
half life of the product

2. Requirements to the accelerator:

energy
particle
intensity

3. Accelerators used for isotope production:

cyclotrons (dominance)
linear accelerators

Technological requirements to the present day accelerators

- low cost accelerator
- easy and low cost shielding
- small, light weight, easily sited
- high reliability operation
- high intensity extracted beam
- low personal dose exposure during the maintenance
- low cost operation
- simple engineering design
- automated controls
- provision of target holding system
- provision of broad range targetry
- efficient installation and commission

- after-sales backup
- availability of spare parts
- confidentiality

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Technological progress in development of cyclotrons

Cyclotron is dominant for accelerator based isotope production.

Positive ion machines:

extraction limits

internal targets

disadvantages: complex target

beam handling not adjustable

beam diagnostic difficult

activation of cyclotron

restricted to metal targets

Negative ion machines

extraction: 100%

external targets

advantages: simple target

easy beam handling

on line diagnostic

unnecessary activation is low

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Common features of dedicated cyclotrons

- negative ion acceleration
- dual beam extraction
- Ion source: external, internal
-
- fix energy, fix frequency
  simple electronics
-
- new magnetic structure:
  deep valley, small hill magnetic field, strong focusing and more simple magnet and coil design
  four sector, four dees
- low power requirements
  energy conversion :15 %.(from 1%)
- quick establishment of the required vacuum
- low activation of cyclotron
- low space requirements
  compact
  vertical plane
- modular shelf shielding
- full computer control

new customised targetry
(Trieste99-Accelerators-Tarkanyi)

New types of small accelerators

Small superconducting cyclotrons

negative ion technology
external ion source
developing phase, prototype
problems of superconducting technology

Linear accelerators

•RFQ linacs

acceleration of fix Z/A to, fix energy)
simultaneously accelerate, focus and bunch
limitation in energy: up to 0.08 c
Proton RFQ, ^{3}He-RFQ
Limited use

• DTL(drift tube linacs)

geometry: 3 MeV/m
goal: similar to compact electron linacs
E=7 MeV, L=4m, P=20 kW
broad application

• Direct voltage accelerators

Coaxial Cascade Accelerator(CCA)
Tandem Cascade Accelerator(TCA)
Nested High Voltage Generator(NHVG)
Pelletrons
advantage: size, weight, shielding
disadvantage: targetry, specific activity

Requirements to the targetry (selector+targets)

Holder and selector

- multitarget handling up to 8 targets
- remote controlled(automation)
- minimal radiation dose
- parallel irradiation possibility
- installation possibility for "independent" targets
- irradiation and transfer possibility for solid targets?

Targets

- complete family of targets
- high production yields
- cheap target material
- high quality product
- low radiation dose
- easy service
- long life

Technological progress on developments of targetry

Holders

- external targets
- target holders on the vacuum chamber or beam line(revolver, elder)
- H^-, parallel irradiation of two targets
- the solid target irradiation is not always concerned (at smaller machines)

Targets

- high intensity
- high pressure
- minimal volume
- special targetry in case of very low energies
- high specific activity
- recovery of enriched isotopes
- duplication
- full line(target+chemistry)

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Comparison of a compact multipurpose and third generation dedicated PET cyclotron

Aspects	MGC 20E	PET Trace
Field of the application	multipurpose (PET,SPECT, Research)	PET,
Max. energy	Ep=18 MeV	Ep=16.5 MeV
Energy range	variable	fix
Accelerated particle;	p, d, ^{3}He, ^{4}He	p. d
Charge of particle	positive ion	negative ion
Intensity (int., μA)	300	75
Intensity(ext., μA)	50	75
Extraction eff.(%)	25-50	100
Beam line	10	no
Simultaneous extract.	no	2
Start up	slow(2 h)	rapid(5 min)
Target changer	2	no
Required power(kW)	150	65
Space	large	small
Technical staff	large	small
Control	manual	fully integrated
Place of installation	research institute.	hospital
Isotope supply	local	local
	regional	regional
Technological level	second generation	third generation
Application	versatile	limited

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Comparison of accelerators used for isotope production and therapy

Basic difference: during therapy the beam is used directly and immediately, when during the isotope production the relation to the patient is more indirect

Isotope production

- There are no upper limit for the parameters of the beam
- The requirements to the accelerator and to the beam are not so strict
  - Energy definition
  - Intensity
  - Energy
  - Energy spread
  - Reliability
- The beam delivery and the irradiation system is relatively simple
- The basic cost is the accelerator

Therapy

- There are modest requirements to performance of the accelerator(energy, intensity)
- The requirements to the concrete beam parameters are very strict
  - Energy definition
  - Intensity
  - Energy
  - Energy spread
  - Reliability
- The beam delivery and the irradiation system is complicated
- The basic cost are the auxiliary irradiation and monitor equipment

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Nuclear data connected to accelerator technology

- **Shielding, radiation safety, waste**
- **Monitoring of beam:** **Shape**
  Energy
  Intensity
- **Accelerator decommissioning**
- **Secondary sources(n)**

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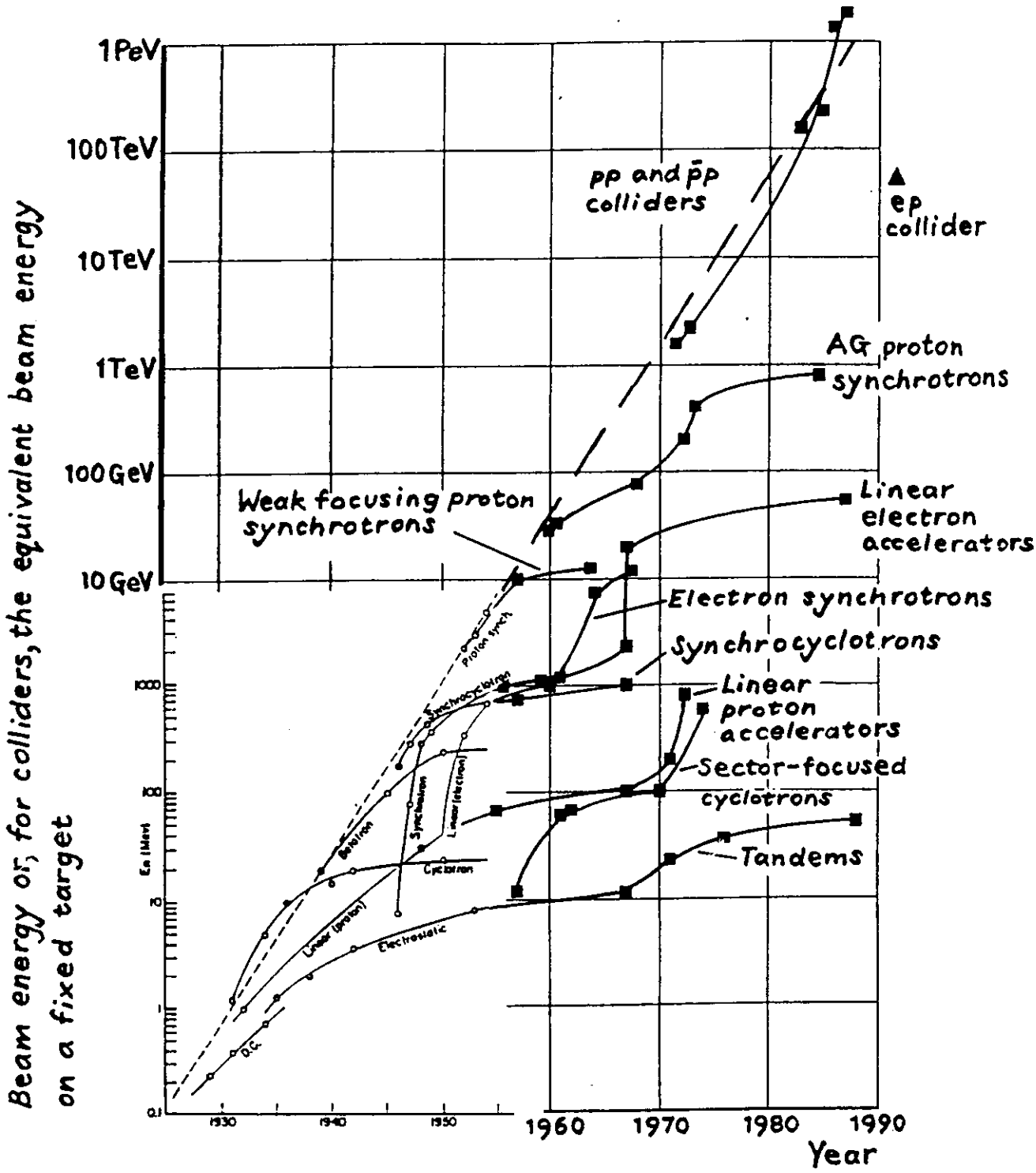
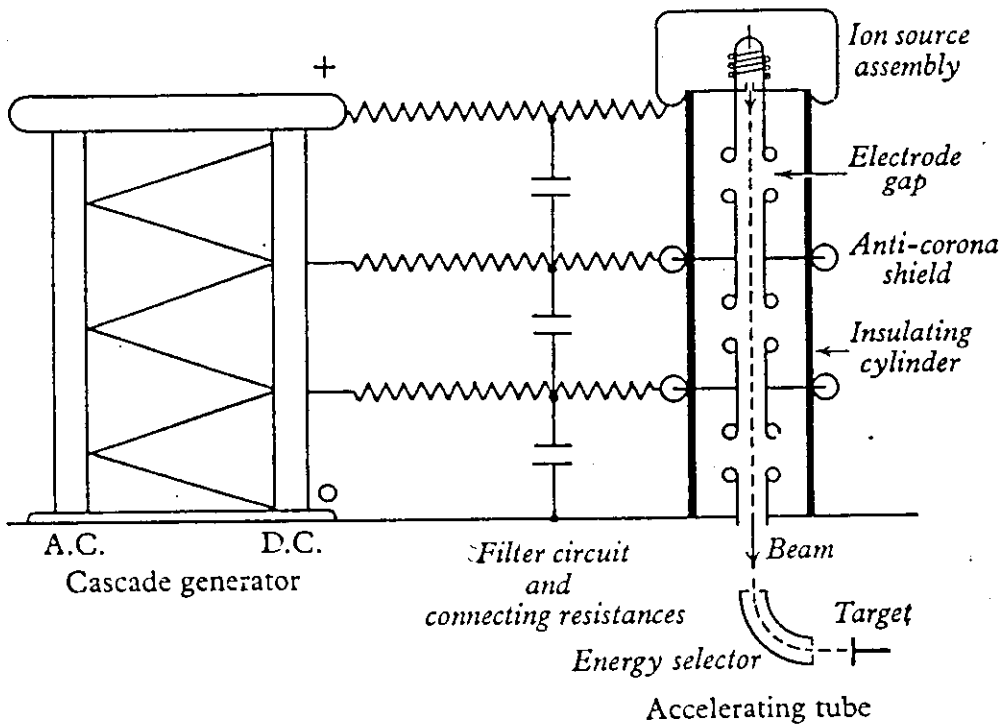
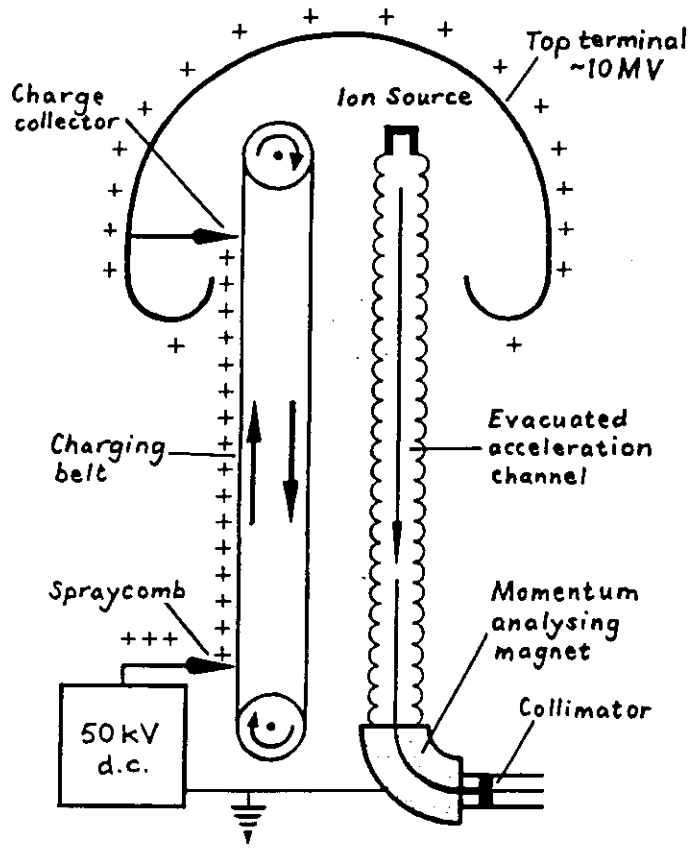


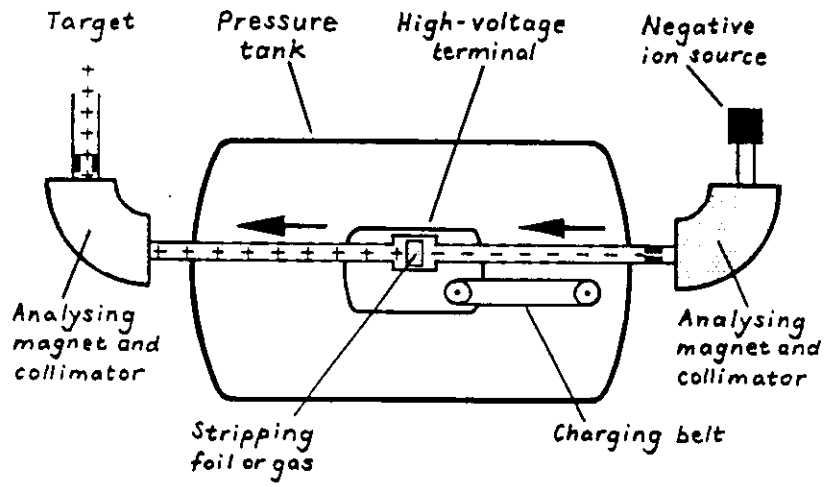
Livingston chart (1989). The insert in Figure 1.1 is a reproduction of the original chart first presented by Livingston in his book *High-energy accelerators* published in 1954 by Interscience Publishers Inc. New York (reprinted by permission of John Wiley & Sons, Inc.). It has since been updated by Livingston himself and many other workers, but the original trend-line has proved to be remarkably accurate.



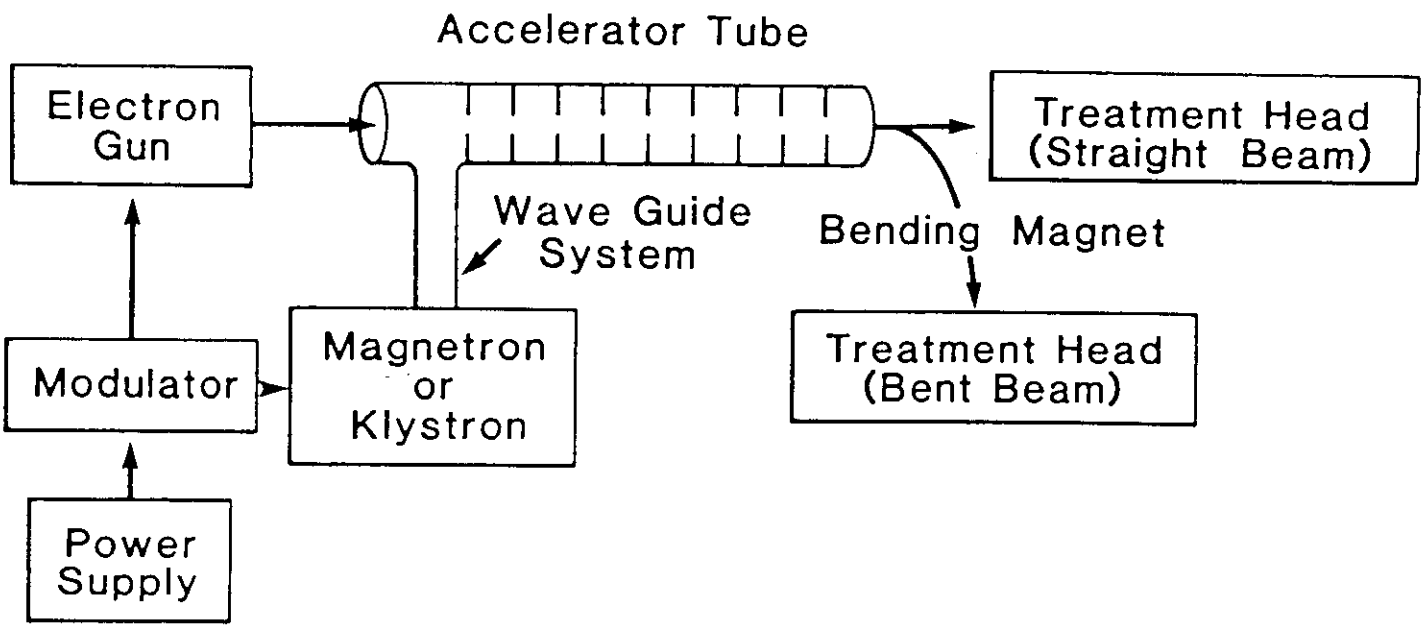
General arrangement of cascade generator and accelerating tube.



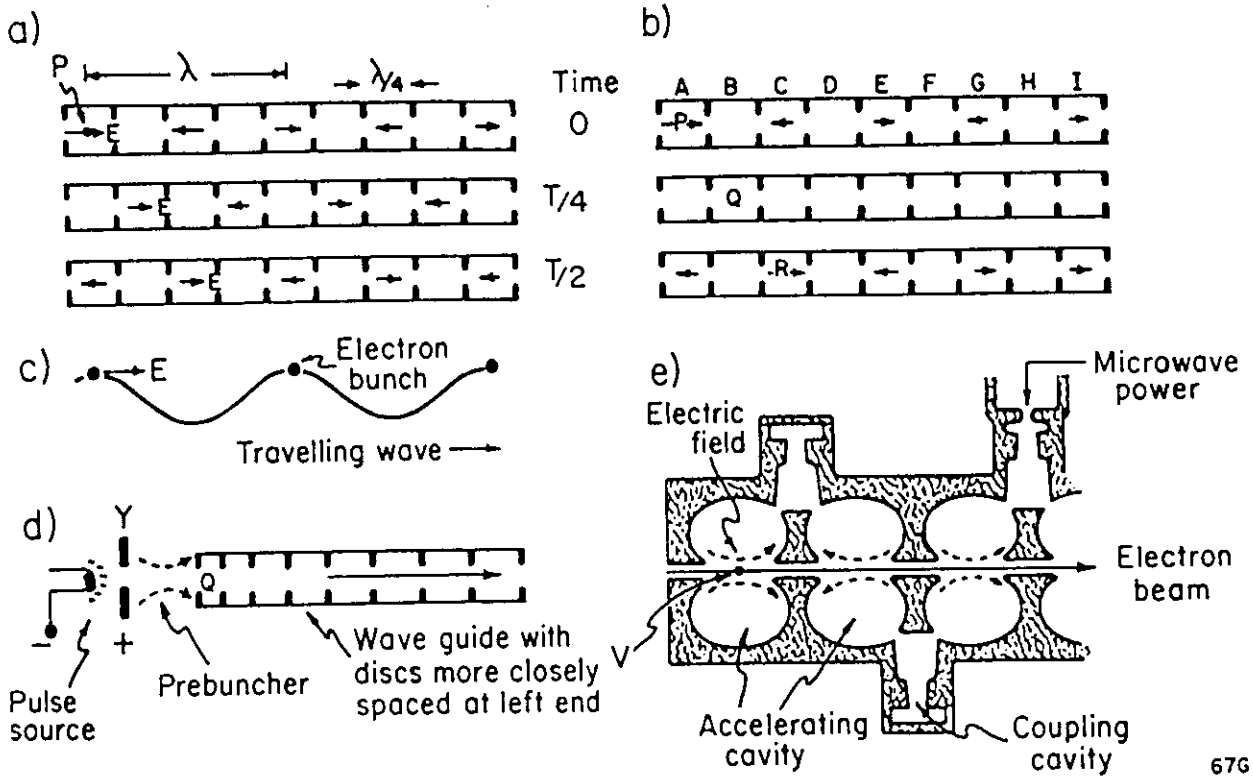
Van de Graaff particle accelerator (shown without pressure vessel and insulating support).



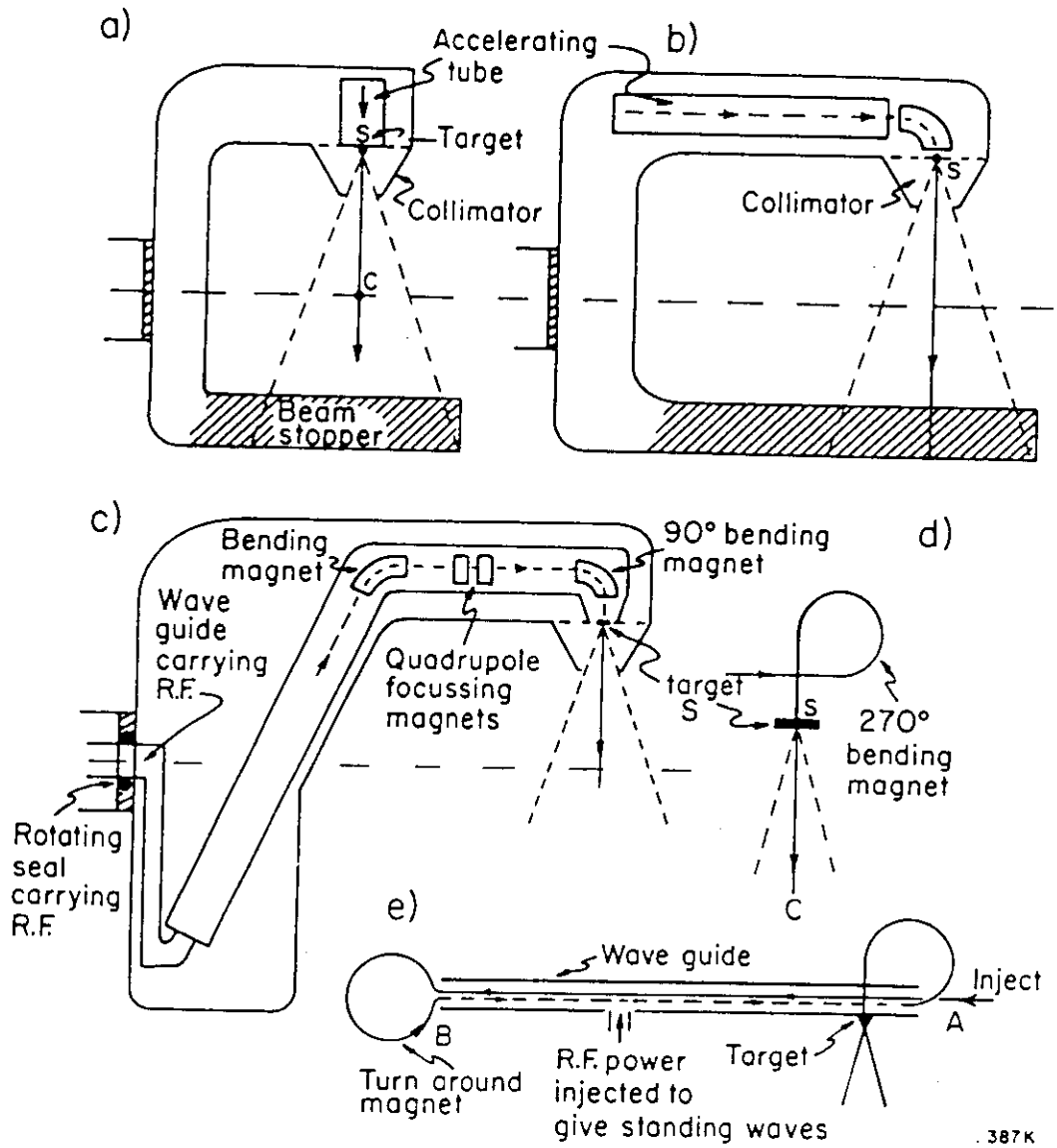
Two-stage tandem accelerator.



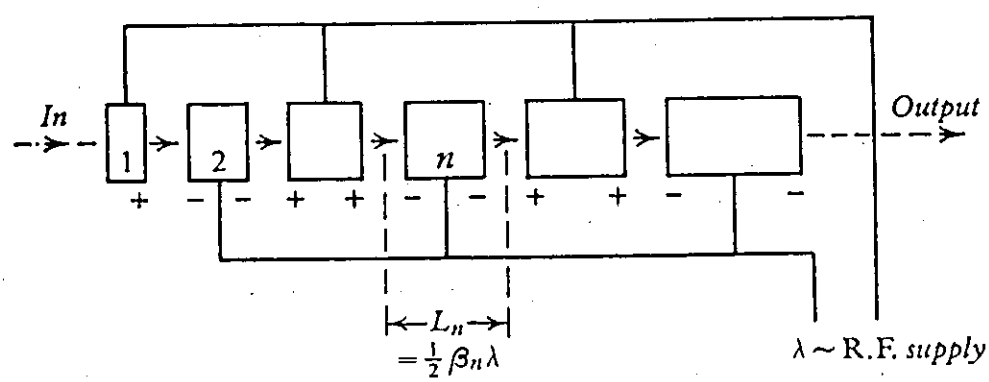
A block diagram of typical medical linear accelerator.



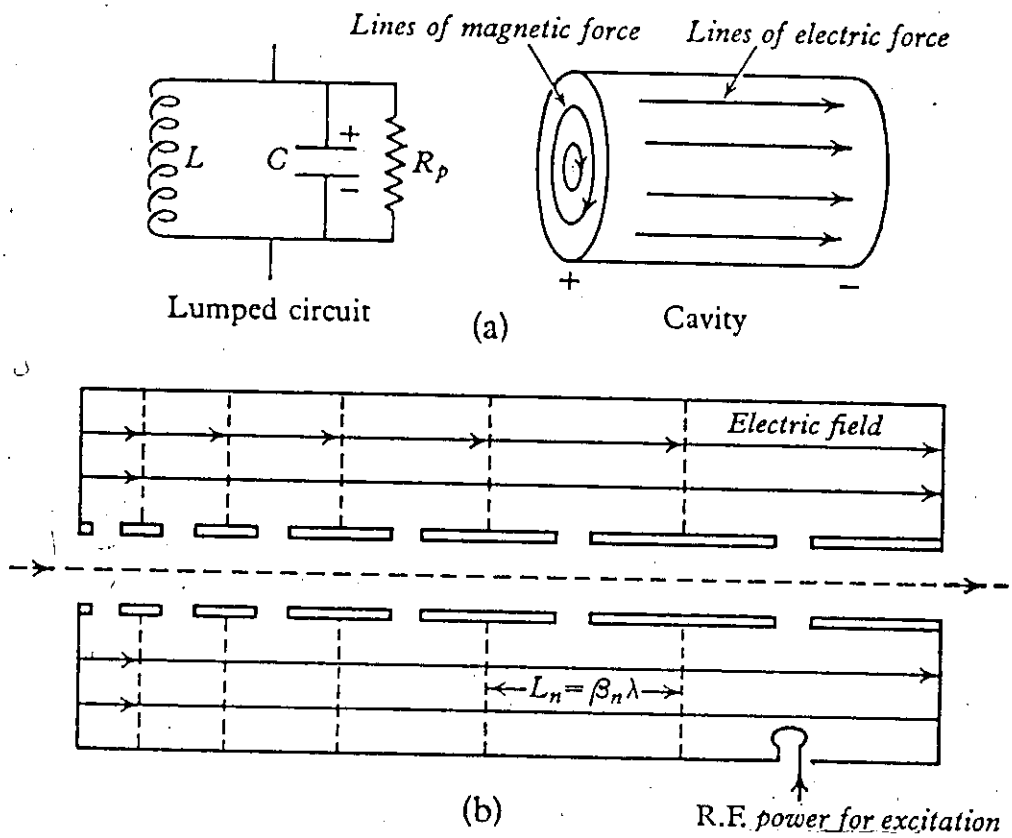
(a) Schematic representation of wave guide with a series of equally spaced discs λ/4 apart. The electric field E at various positions in the wave guide is shown at times of 0, T/4, T/2, etc. when a *traveling* wave is passing down the guide from left to right. (b) Same as a except the electric field configuration is now shown for a *standing* wave. (c) Schematic representation of electron bunch being carried on the crest of a traveling wave. (d) Diagram of buncher showing how electrons are captured into the wave guide. (e) Details of one type of wave guide used to create standing waves.



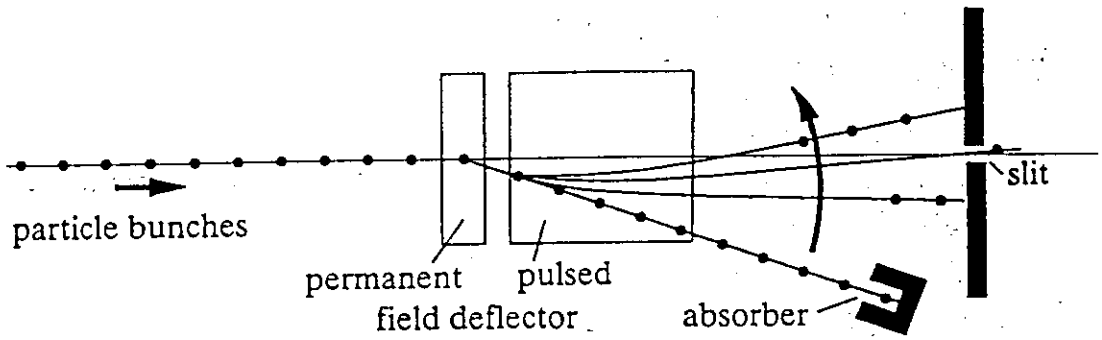
Medical Linacs: Arrangements suitable for (a) 4 to 6 MeV, (b) 8-12 MeV, (c) 30 to 35 MeV. (d) A method of bending the electron beam through 90° by using a 270° bending magnet. (e) The "turn around," or "two pass," linac.



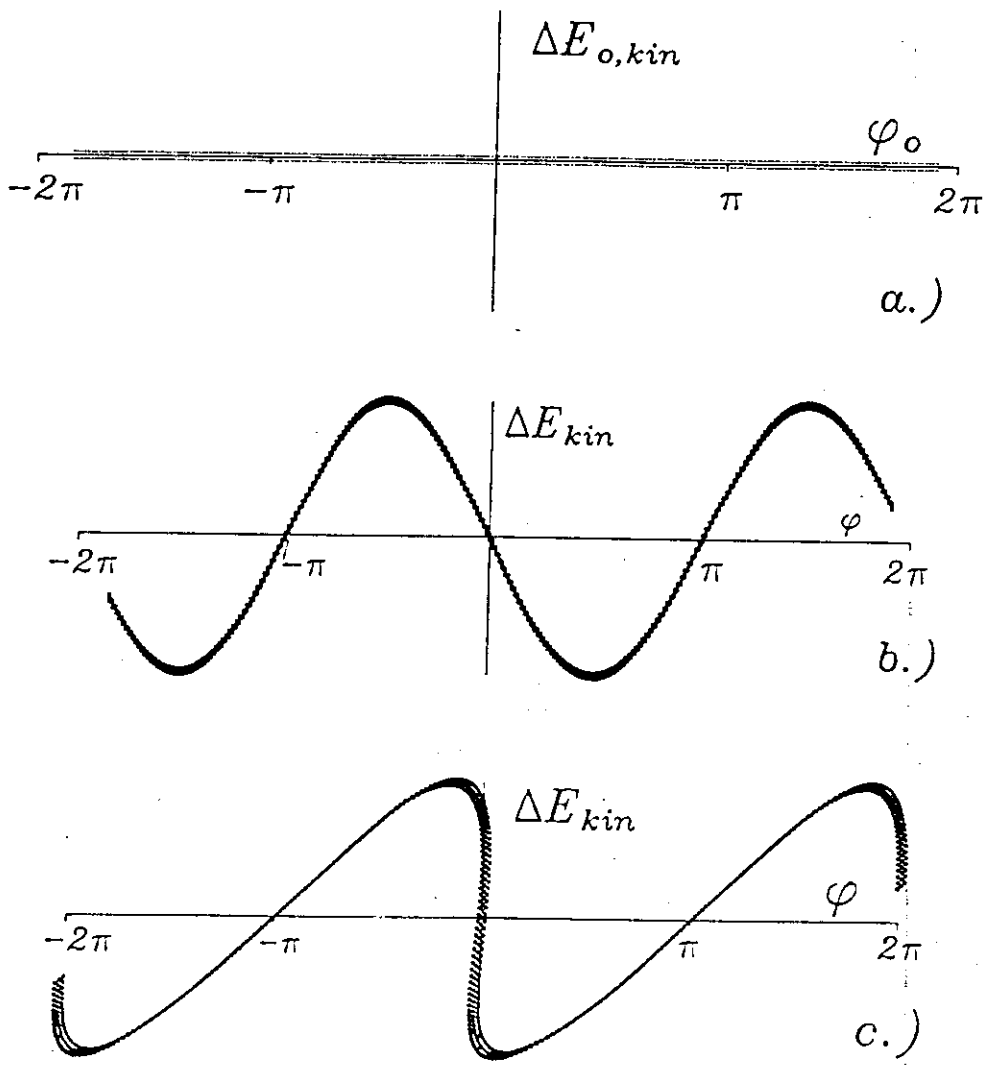
Principle of the Sloan–Lawrence linear accelerator.



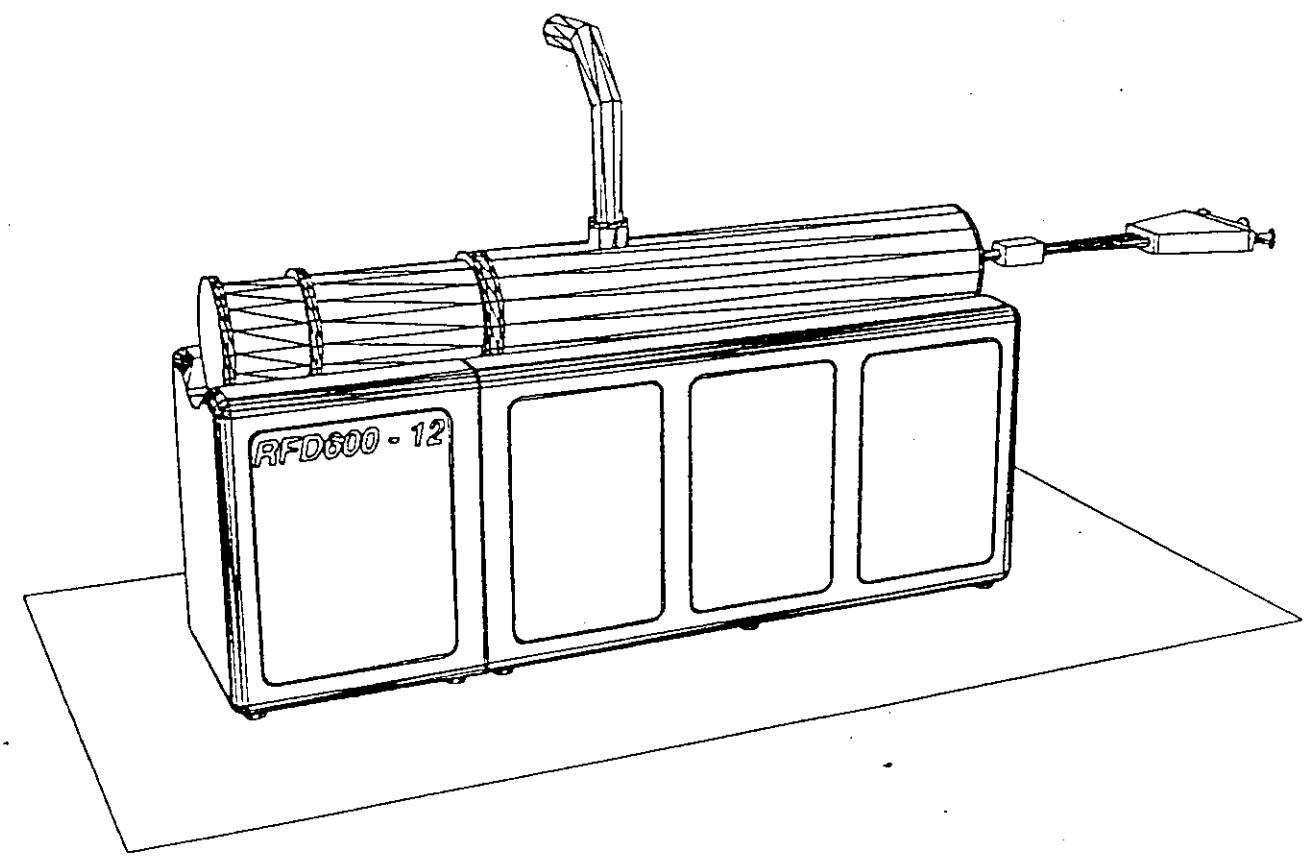
a) Resonant circuits.
b) Alvarez resonant accelerator.



Principal functioning of a chopper system



Phase space diagrams for a continuous beam passing through a prebuncher, a.) before acceleration, b.) right after acceleration, c.) at end of drift space L



12-MeV Proton Linac for PET Isotope Production.

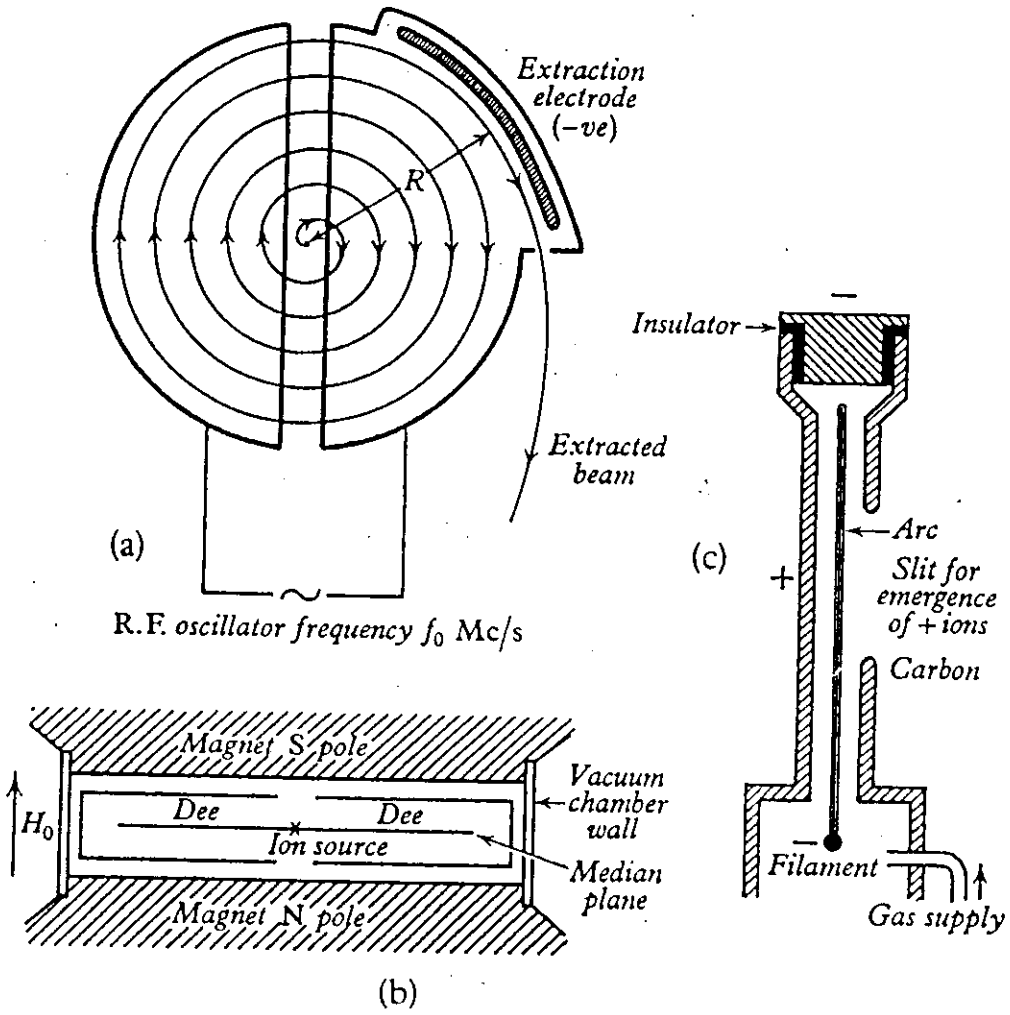
Frequency(ω)	Particle radius(r)	
	r= 0---R_{max}, changing	r=R_{max}=const
	Magnetic field(B)	
	Constant	Varying(raising)
Constant	Cyclotron Microtron	Electron synchrotron
Changing	Synchrocyclotron (ω=raising)	Proton synchrotron (ω=decreasing)
		Betatron

(Trieste99-Accelerators-Tarkanyi)

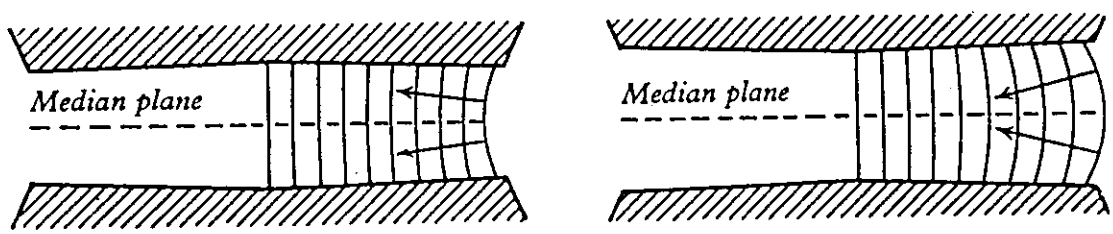
Parameter disposition for different acceleration principles

principle	energy	velocity	orbit	field	frequency	flux
	γ	v	r	B	f_{rf}	
Cyclotron:	1	var.	$\sim v$	const.	const.	cont.[a]
Synchro cyclotron:	var.	var.	$\sim p$	$B(r)$	$\sim \frac{B(r)}{\gamma(t)}$	pulsed
Isochron cyclotron:	var.	var.	$r = f(p)$	$B(r, \varphi)$	const.	cont.[a]
Proton/Ion-synchrotron:	var.	var.	R	$\sim p(t)$	$\sim v(t)$	pulsed
Electron-synchrotron:	var.	const.	R	$\sim p(t)$	const.	pulsed

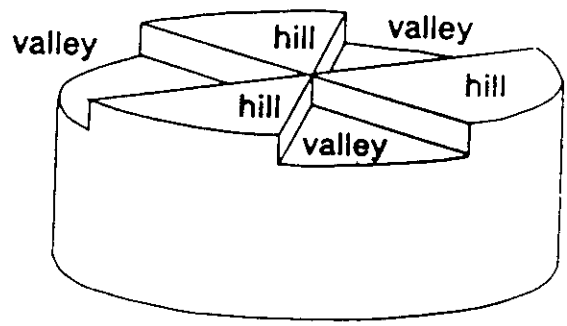
[a] continuous beam, but rf modulated



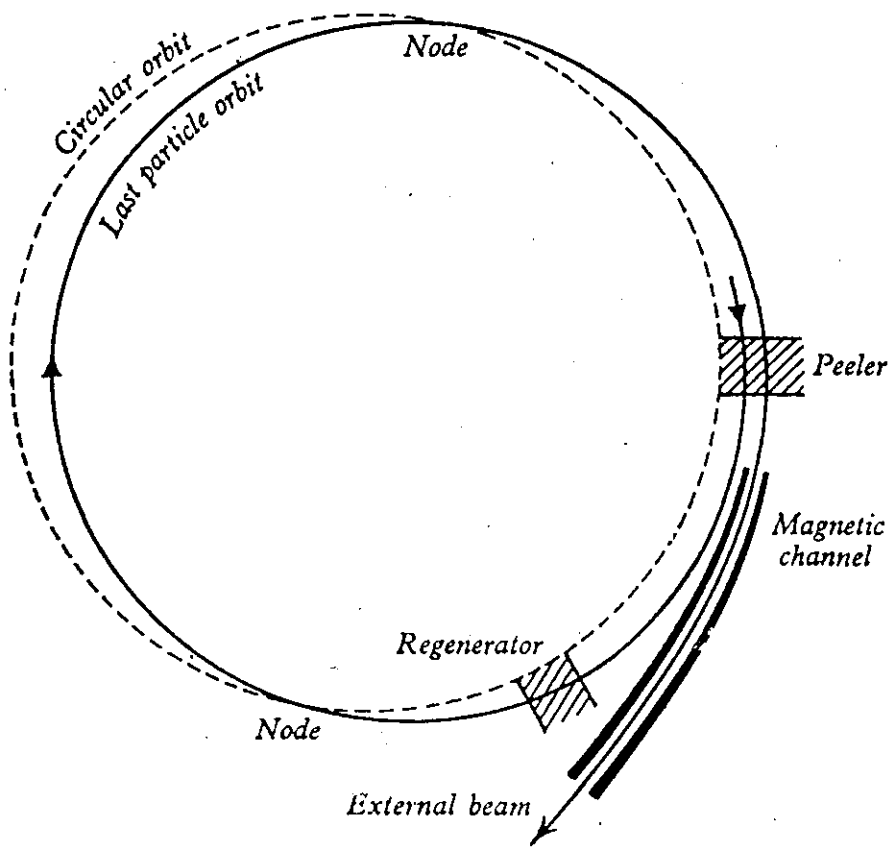
a) Path of ions in the fixed-frequency cyclotron from central ion source to extracted beam.
b) Vertical section showing dees and walls of vacuum chamber in which they are supported.
c) Ion source construction. The arc is constrained to the vertical direction by the main magnetic field.



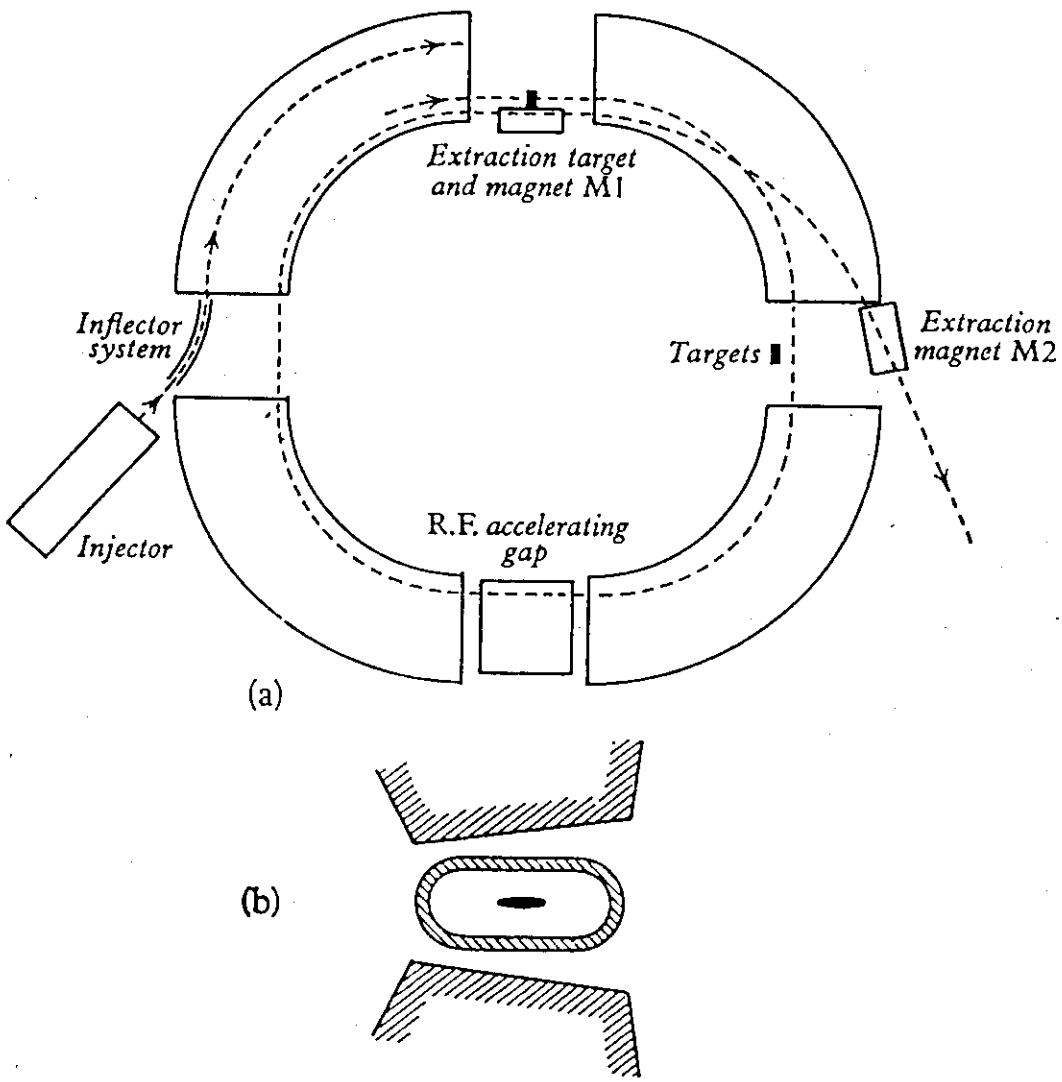
Axial forces in radially varying field in a cyclotron.



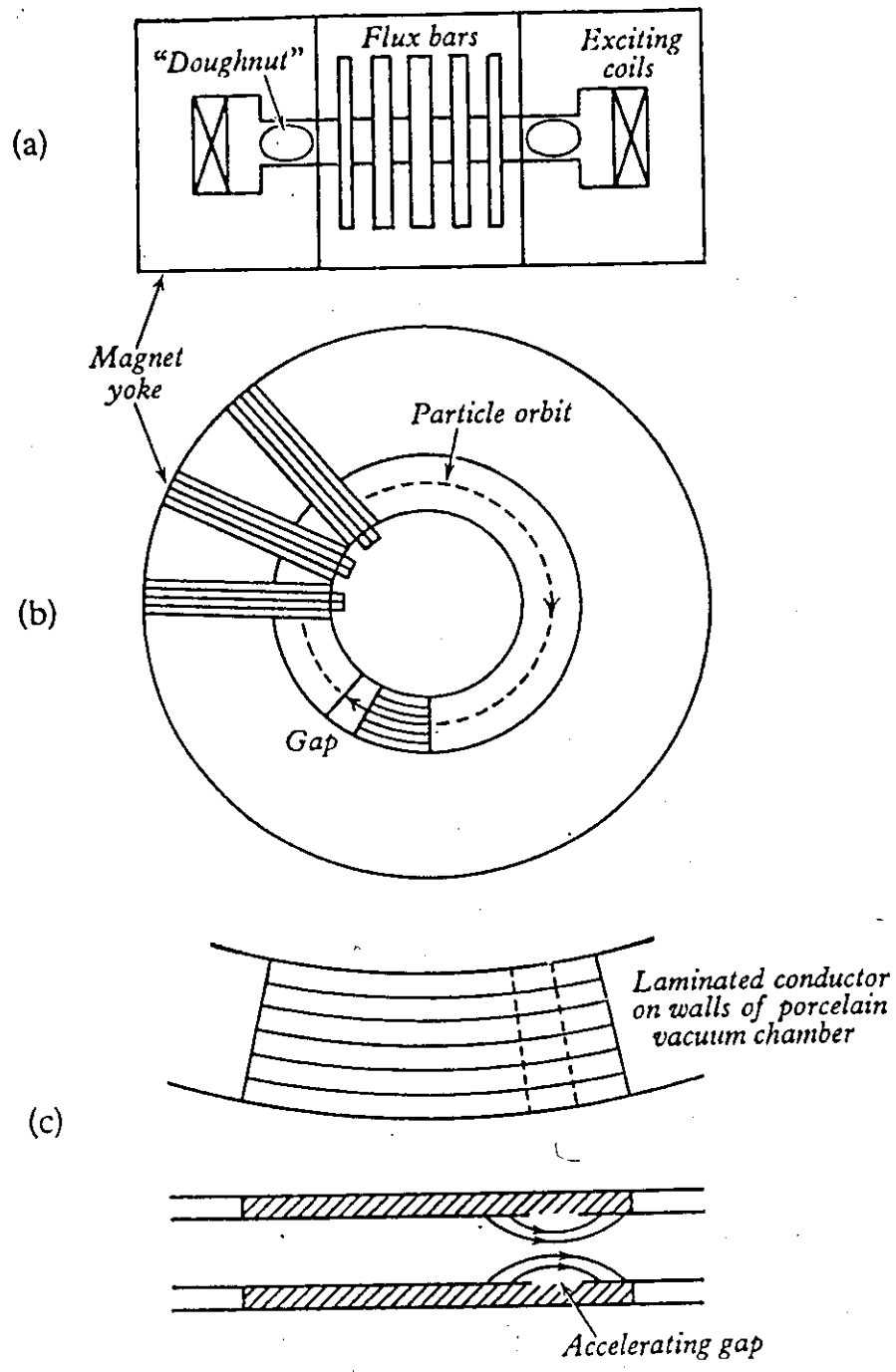
Magnet pole shaping in an isochronous cyclotron.



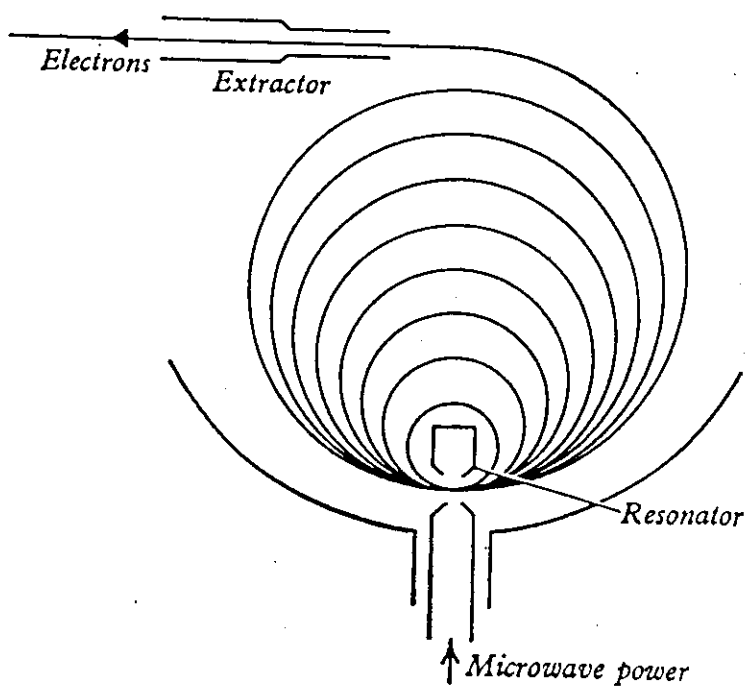
Synchrocyclotron extraction system (Le Couteur, *Proc. roy. Soc.* A, **232**, 236, 1955).



a) Main components of proton synchrotron.
b) Cross-section of synchrotron magnet gap. In the initial stages of acceleration the beam fills the whole cross-section of the vacuum chamber.

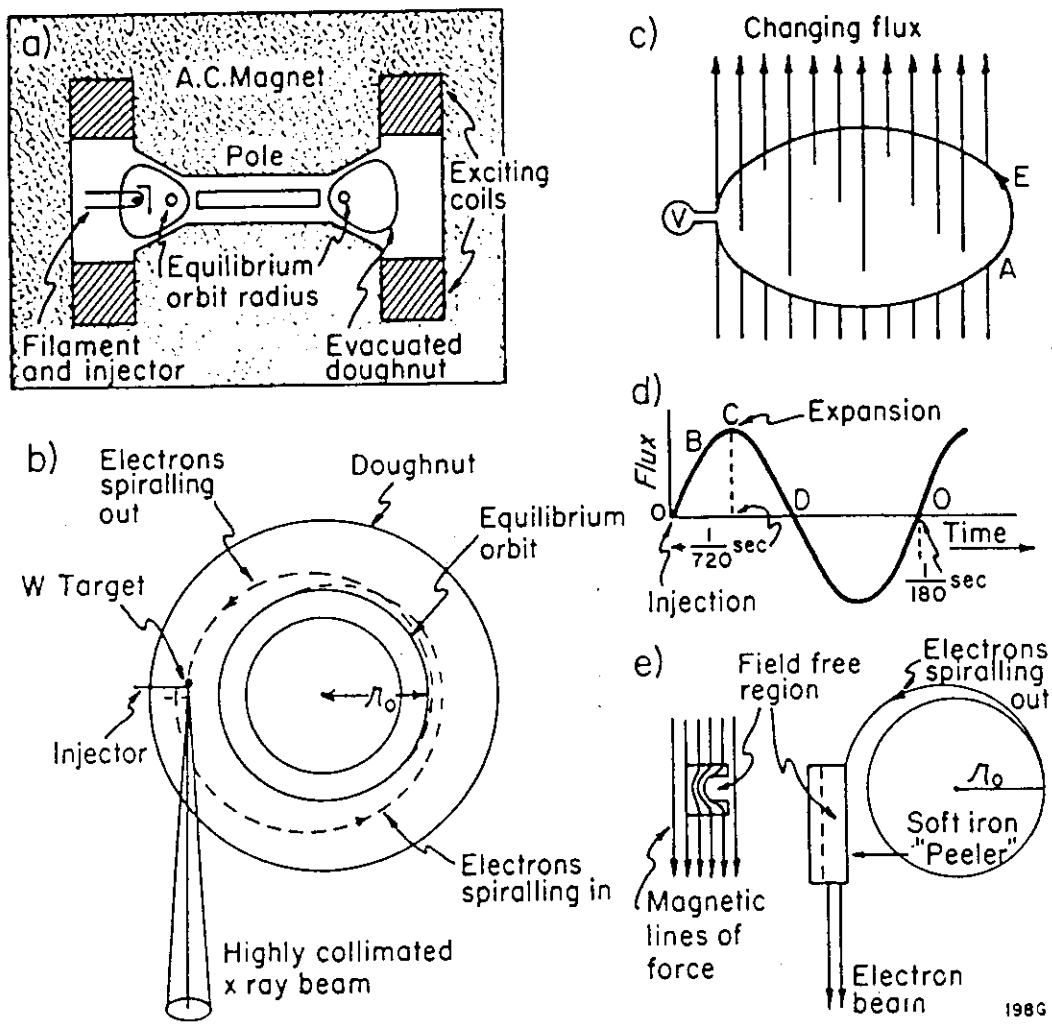


a), b) Layout of electron synchrotron.
c) Synchrotron accelerating cavity (Ref. 8.8).



Successive electron orbits in the microtron (Ref. 8.13).

Betatrons



Diagrams illustrating the construction and operation of the betatron. (a) Cross-sectional diagram showing the AC magnet, the poles, the doughnut, and injector. (b) The paths of the electrons within the doughnut and the method of production of the x rays. (c) How an electric field is produced by a changing magnetic flux. (d) The cycle of operation of the betatron showing the time of injection and expansion. (e) The operation of the electron "peeler" for obtaining an electron beam. The sketch showing the magnetic lines of force is a cross-sectional view of the "peeler" device taken at right angles to the diagram through the center of the "peeler."