HEAVY PARTICLE THERAPY

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HEAVY PARTICLES USED IN A EFFORT TO IMPROVE TUMOR CONTROL , THAT DO NOT RESPOND TO PHOTONS OR ELECTRONS

- BETTER DIFFERNTIAL EFFECT ON TUMOR CELLS Vs NORMAL CELLS
- SUPERIOR LOCALIZATION CAPABILITY, THEREFORE A HIGER DOSE TO THE TUMOR

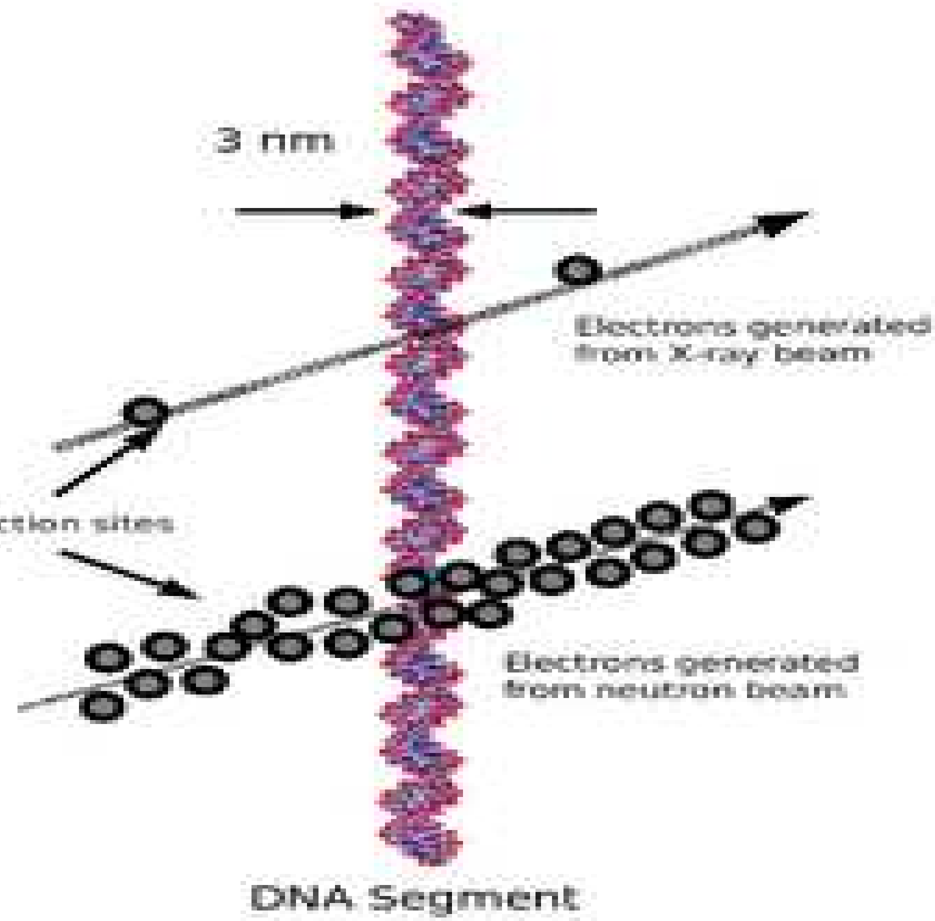
HADRON THERAPY

- NEUTRONS
- NEGETIVE PIONS
- PROTONS
- HEAVY PARTICLES – He 2, C 6, O 8, Ne 10, Ar. 18

} HADRONS

> MASS, RELATIVELY DIFFICULT TO PRODUCE AND CONTROL, LIMITED AVAILABILITY

LET –PARMETER TO DESCRIBE ENERGY LOSS OF THE RADIATION



CONVENTIONAL QUALITY FACTORS (RBE) TO CALCULATE EQUIVALENT DOSES

RADIATION	ENERGY	Q FACTOR --RBE
X-RAYS, GAMMA, ELECTRON , MUONS		1
NEUTRONS	< 10 KeV	5
	10 KeV – 100 KeV	10
	100 KeV --- 2 MeV	20
	2 MeV –20 MeV	10
	> 20 MeV	5
PROTONS	> 2 MeV	2
ALPHA PARTICLES, HEAVY NUCLEI, NUCLEAR FISSION PRODUCTS		20

NEUTRON -- BARYON

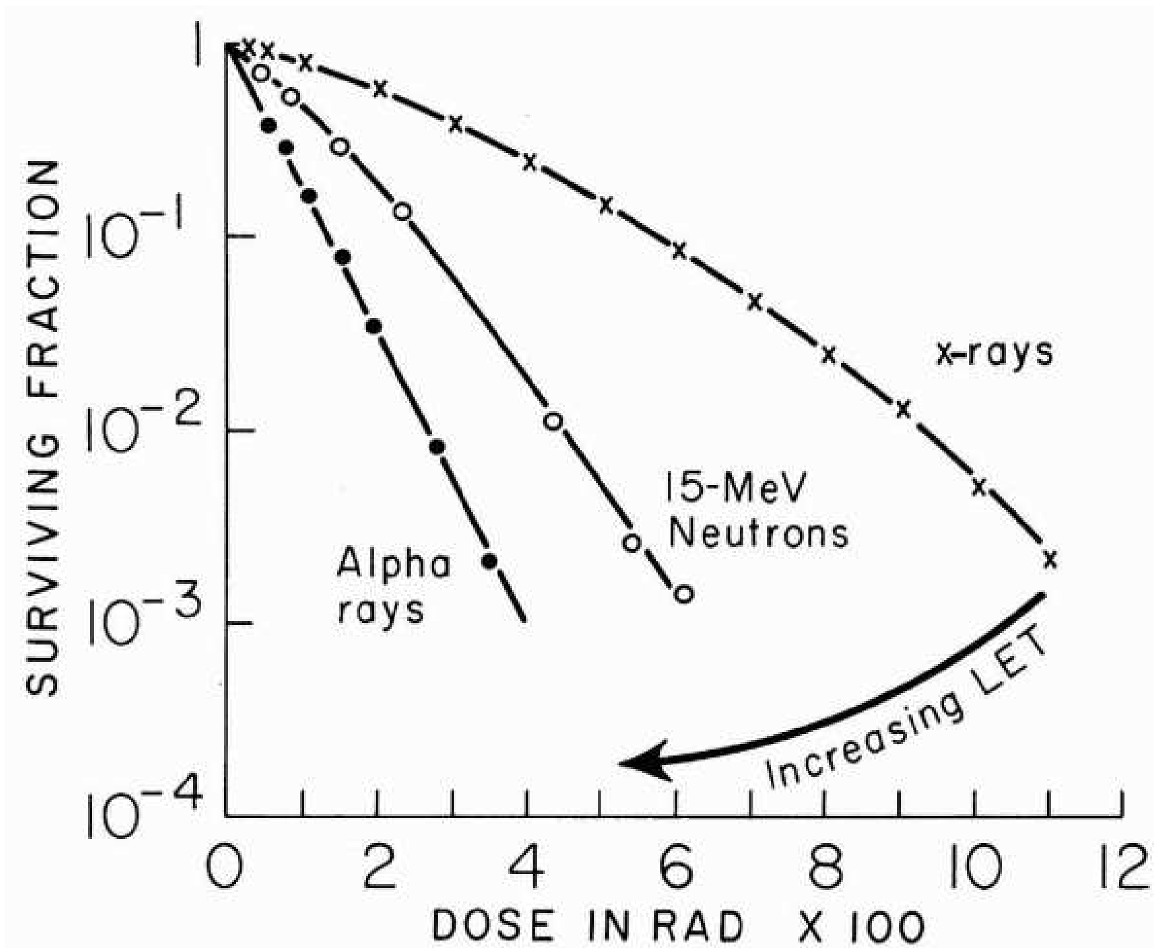
BOTH NEUTRONS AND GAMMA RAYS --- UNCHARGED

1932 CHADWICK DEDUCED ITS EXISTENCE BY OBSERVING RECOIL PROTONS THAT WERE PRODUCED BY FAST NEUTRONS INTERACTING WITH HYDROGEN NUCLEI IN PARAFFIN

- RECOIL PROTONS & RECOIL IONS -- DUE TO NEUTRON COLLISIONS ARE THE PRIMARY ENERGY TRANSFER MECHANISMS TO THE TISSUE – ELASTIC SCATTERING.

- BIOLOGICAL EFFECT DUE TO SECONDARY ELECTRONS PRODUCED

- ENERGY DEPOSITED 30 – 80 keV/ MICRON COMPARED TO 1 KeV/ MICRON WITH COMPTON ELECTRONS


SURVIVING FRACTION
1
10−1
10−2
10−3
10−4
0
2
4
6
8
10
12
DOSE IN RAD X 100
x-rays
15-MeV
Neutrons
Alpha
rays
Increasing LET

NEUTRON GENERATORS

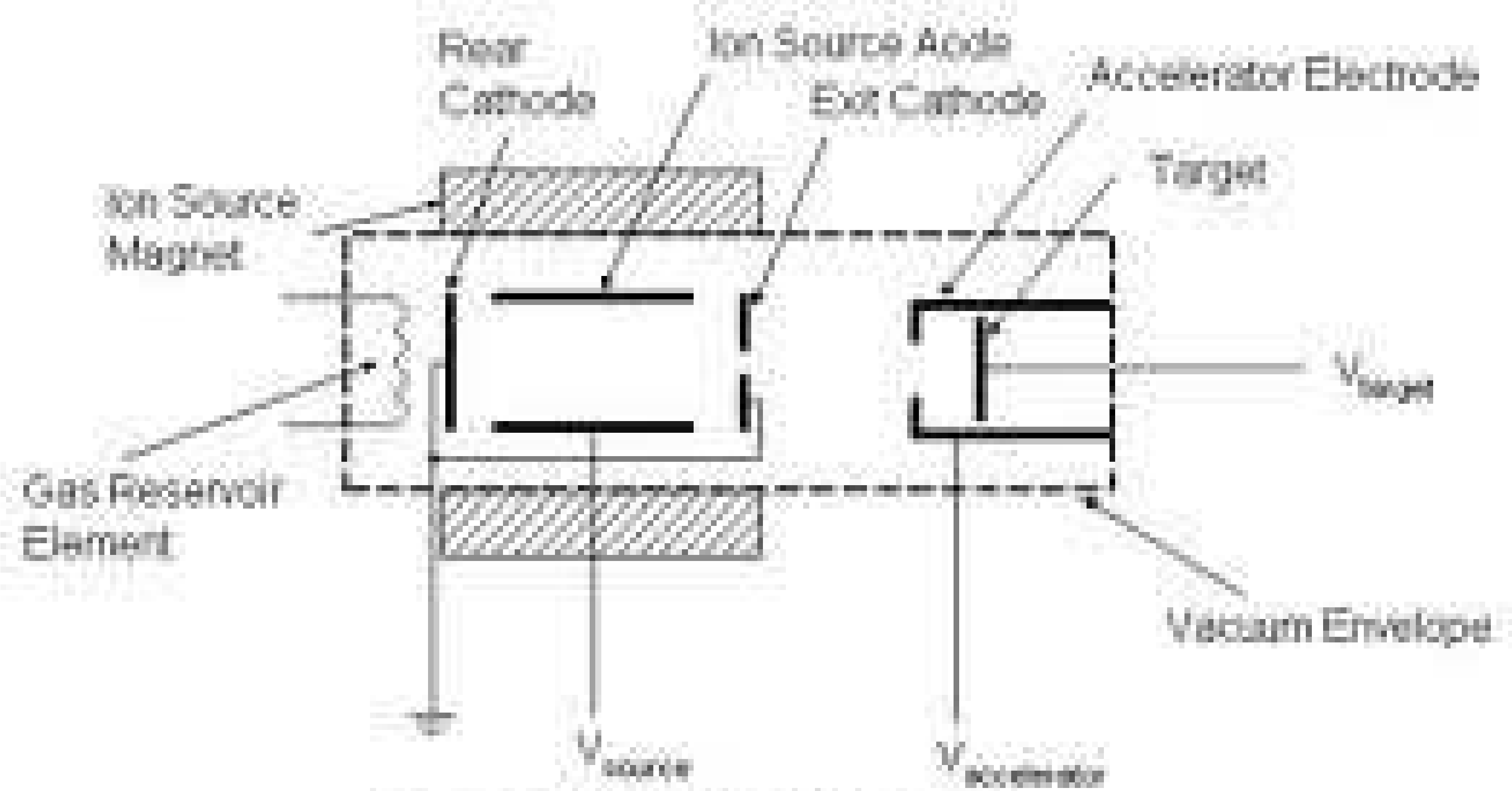
- **14.1 MeV Neutrons (DT)**

For a 14 MeV neutron generator (deuterium-tritium): APPROX 250 KeV

$_1D^2 + {_1T^3} \dashrightarrow {_2He^4}$ (3.5 MeV) + $_0n^1$ (14.1 MeV)

- D→D NEUTRON GENERATOR , 2.5 MeV
- T→ T NEUTRON GENERATOR, 0 – 9 MeV

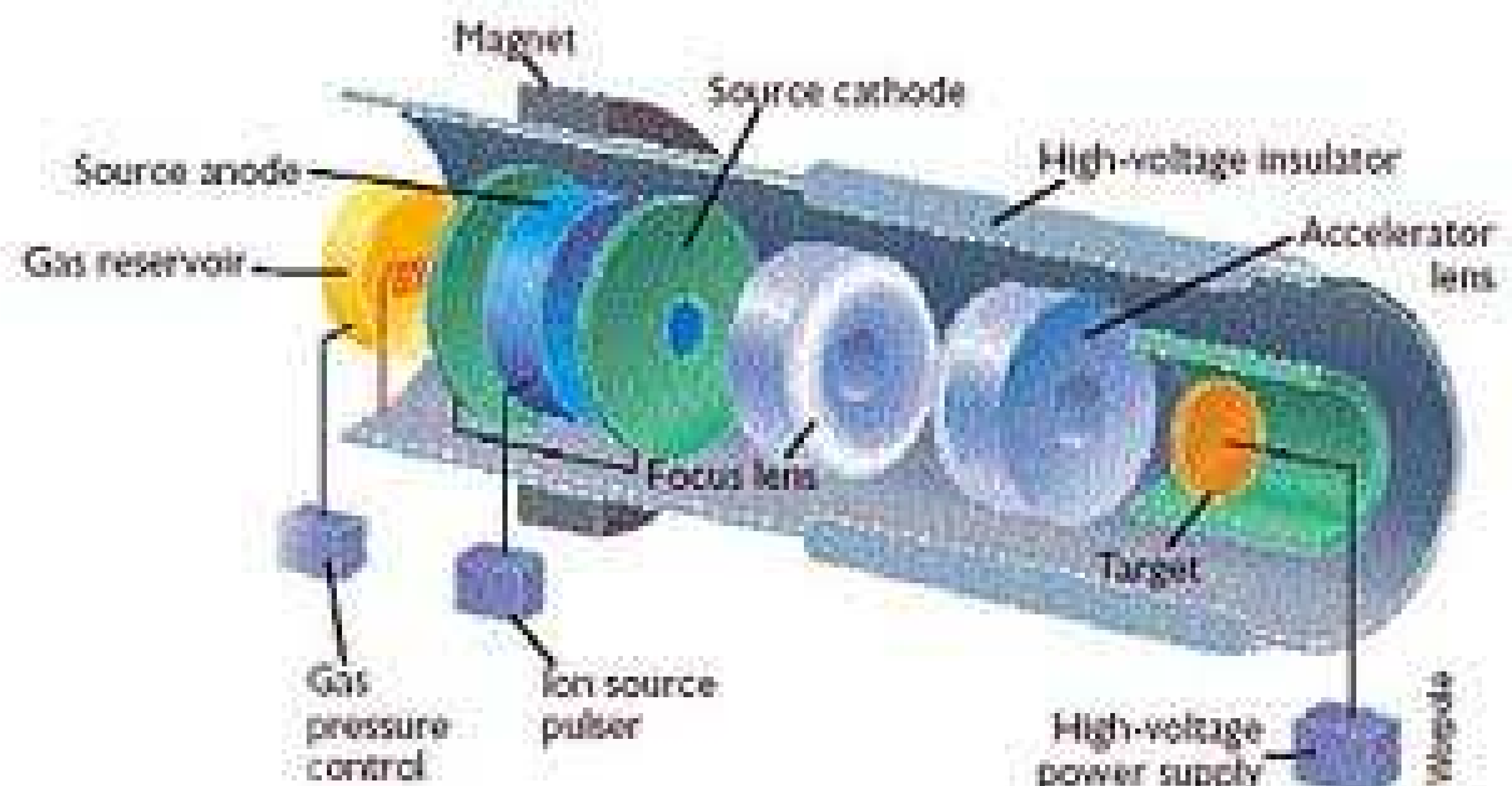
D – T GENERATOR



NEUTRON TUBE SCHEMATIC

ICRO 2012, BHATINDA

D – T GENERATOR



D – T GENERATORS

- 10 – 15 cgy/MIN
- TRITIUM CONSUMPTION
- HEAT DISSIPATION
- USUAL SSD 75 CM→ PRECLUDES ADJUSTABLE COLLIMATORS
- ISOTROPIC EMISSION OF NEUTRONS→ EXTN. SHEILDING
- PENETRATION </= CO 60. D50 = 9.5CM Vs 11.5

NEUTRON GENERATORS

- CYCLOTRONS (PARTICLE ACCELARATORS)

→ 16 MeV DEUTRONS →Be = 6MeV NEUTRON

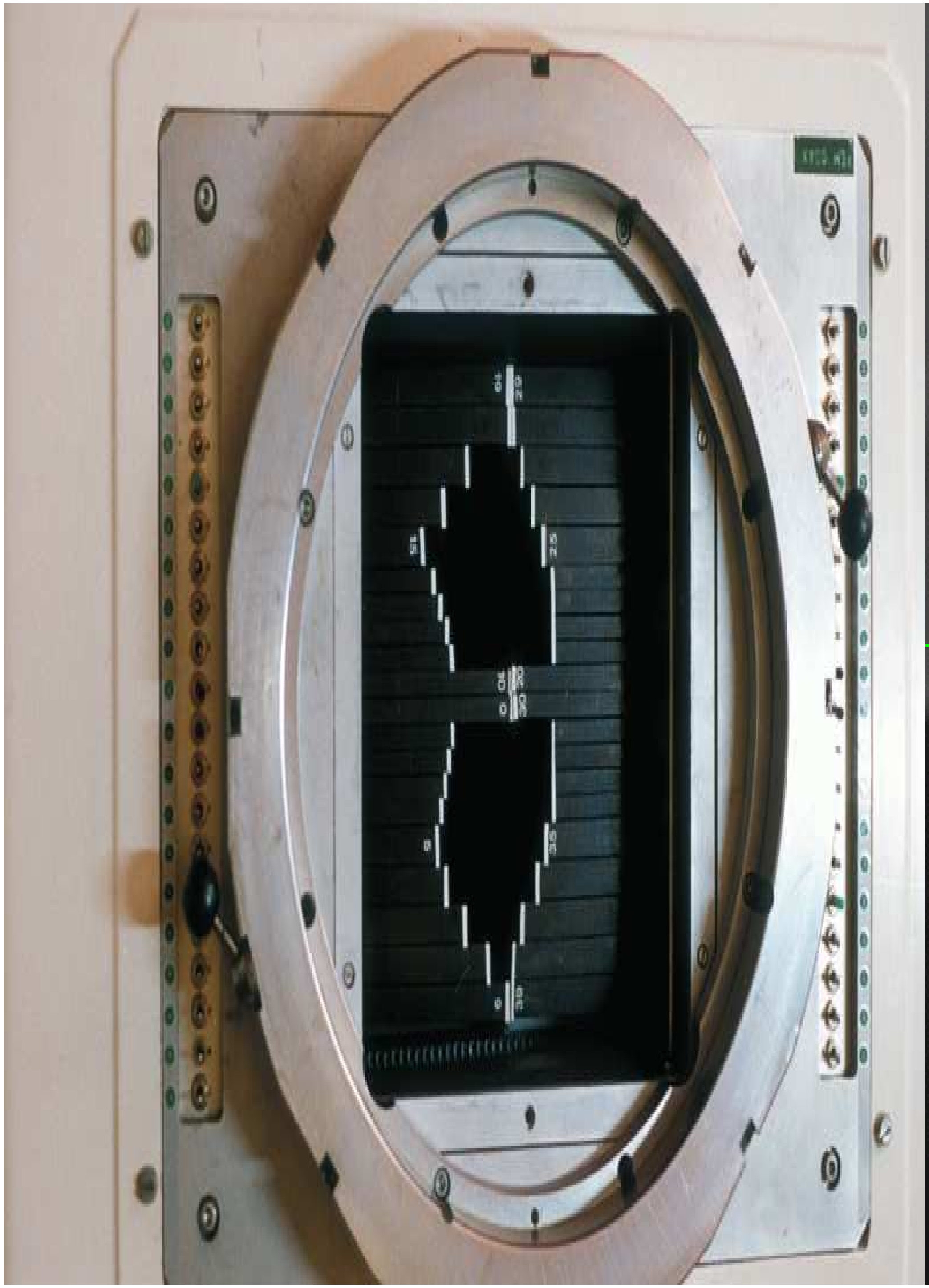
POOR DEPTH DOSE & FIXED BEAM GEOMETRY

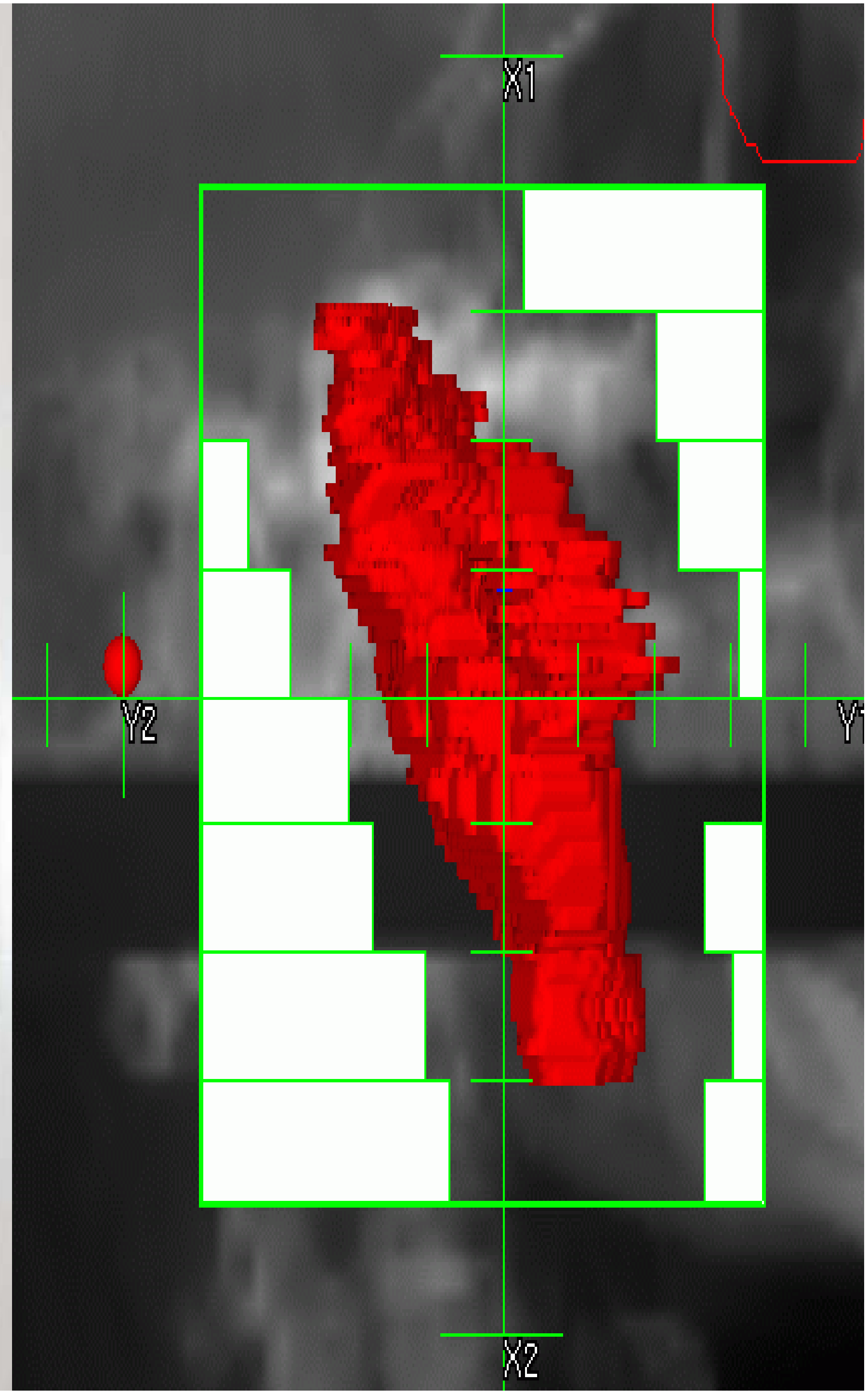
- LARGER CYCLOTORNS → 22 – 50 MeV DEUTRONS ***OR*** 67 MeV PROTONS → Be

ADEQUATE DOSE RATES AND GOOD DEPTH DOSES

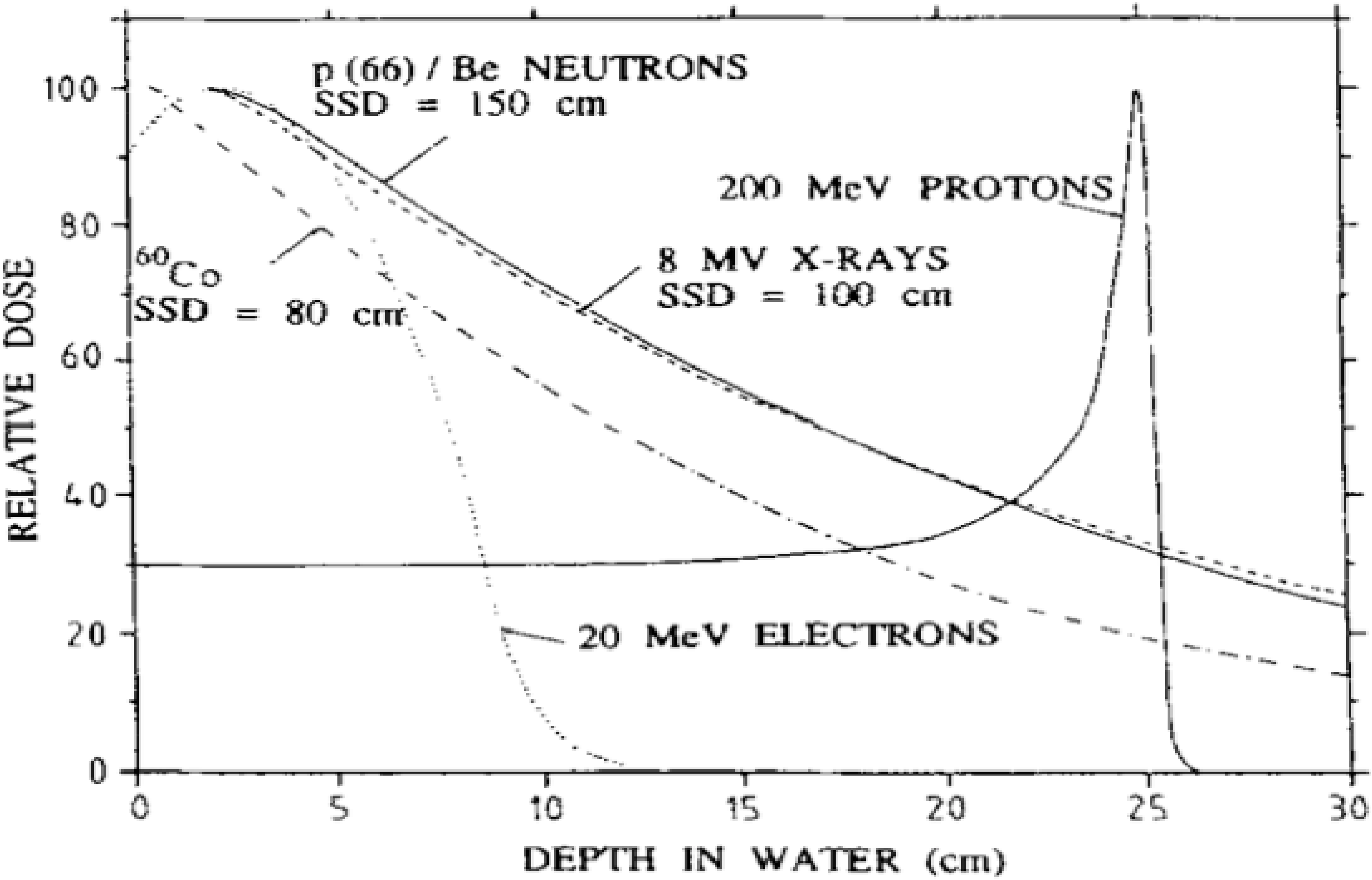
FIXED HORIZONTAL BEAMS & IN PHYSICS INSTILLATIONS → INTEREST WANED BY MID 80'S

P+ $\rightarrow$ Be NEUTRONS




X1
Y2
X2

DD % CURVES COMPARISON



CLINICAL APPLICATIONS

- **SALIVARY GLAND TUMORS** (EXECPT SCC)→ REDUCED VARIATION IN SENSITIVITY THROUGH OUT THE CELL CYCLE WITH SLOWLY CYCLING CELLS
- ADENOID CYSTIC CA.→ HIGHEST RBE (8.O) WITH # NEUTRON THERAPY. RBE > THAN FOR NORMAL TISSUE
- TREATING ADENOID CYSTIC CA. WITH 20 NEUTRON Gy = 160 Gy (PHOTONS) & =66 Gy IN EFFECT TO NORMAL TISSUE.

  THERAPEUTIC GAIN = 2.5

RESULTS

- NCI/ MRC TRIAL ---- LOW LET PHOTONS + ELECTRONS Vs NEUTRONS

- ADVANCED SALIVARY GLAND Tm. , > 7CM, UNRESECTABLE

- 10 YEAR LOCOREGIONAL TUMOR CONTROL 56 % WITH NEUTRONS Vs 17 % LOW LET RADIATION (P = .009). 10 Yr SURVIVAL NO DIFFERENCE DUE TO DEVELOPMENT OF DISTANT METASTASIS IN BOTH GROUPS

- **SCCHN CA.**---- RESULTS EQIVOCAL, NO OVERALL DIFFERENCES OBSERVED IN EITHER LOCOREGIONAL TUMOR CONTROL OR SURVIVAL.
- CERVICAL ADENOPATHY PRESENT –

	LOCAL CONROL	LOCAL CONTROL
RANDOMIZED STUDY	NEUTRONS	PHOTONS / ELECTRONS
MRC	22 / 38 (58 %)	20 / 41 (49 %)
RTOG	49 / 109 (45 %)	23 / 87 (26 %)
NCI / MRC	35/57 (61%)	33 / 67 (49 %)

- **NSCLC** – COMBINATIONS OF NEUTRONS + PHOTONS → INCREASED TUMOR STERILIZATION AT AUTOPSY.
- UNIV. OF WASHINGTON – 70 % LCR
- M.D.A. C.C. – 91 % LCR WITH PANCOAST TM.→ IMPROVEMENT OF SURVIVAL RATES
- NO SURVIVAL BENEFIT WITH IN LOCALLY ADVANCED , INOPERABLE NSCLC.
- MAY SHOW BENEFIT ONLY IN THE GROUP OF PATIENTS WITH GOOD PROGNOSTIC INDICATORS AND SUPERIOR SULCUS TUMORS

- **PROSTATE CANCER** – STASTICALLY SIGNIFICANT ADVANTAGES IN TERMS OF LRC, OS & DFS
- RTOG – 178 PTS. 5 YEAR SURVIVAL 89 % FOR NEUTRONS & 68 % FOR PHOTONS (P < 0.01)

  PSA ELEVATED AT 5 YRS IN 17 % FOR PTS TREATED WITH NEUTRONS Vs 45 % FOR THOSE TREATED WITH PHOTONS

- **SARCOMAS –**

	LOCAL CONTROL	LOCAL CONTROL
SARCOMA	NEUTRONS	PHOTONS / ELECTRONS
SOFT TISSUE SARCOMA	158/ 297 (53 %)	49 / 128 (38 %)
OSTEOGENIC SARCOMA	40 / 73 (55 %)	15 / 73 (21 %)
CHONDROSARCOMA	25/ 51 (49 %)	10/ 30 (33 %)

Proton Therapy

- 55,000 patients have been treated with proton therapy World Wide
- In the United State there are five facilities offering this treatment
- Approximately 20,000 patients have been treated between two of this facilities
  – The Harvard cyclotron laboratory at Massachusetts General Hospital
  – The Proton Treatment Center at Loma Linda University Medical Center (LLUMC)
- The other three new centers providing this service in the US are
  – M.D. Anderson Proton Therapy Center in Houston
  – University of Florida's Shands Medical Center in Jacksonville
  – University of Pennsylvania's proton facility in Philadelphia

PROTON BEAM GENERATORS

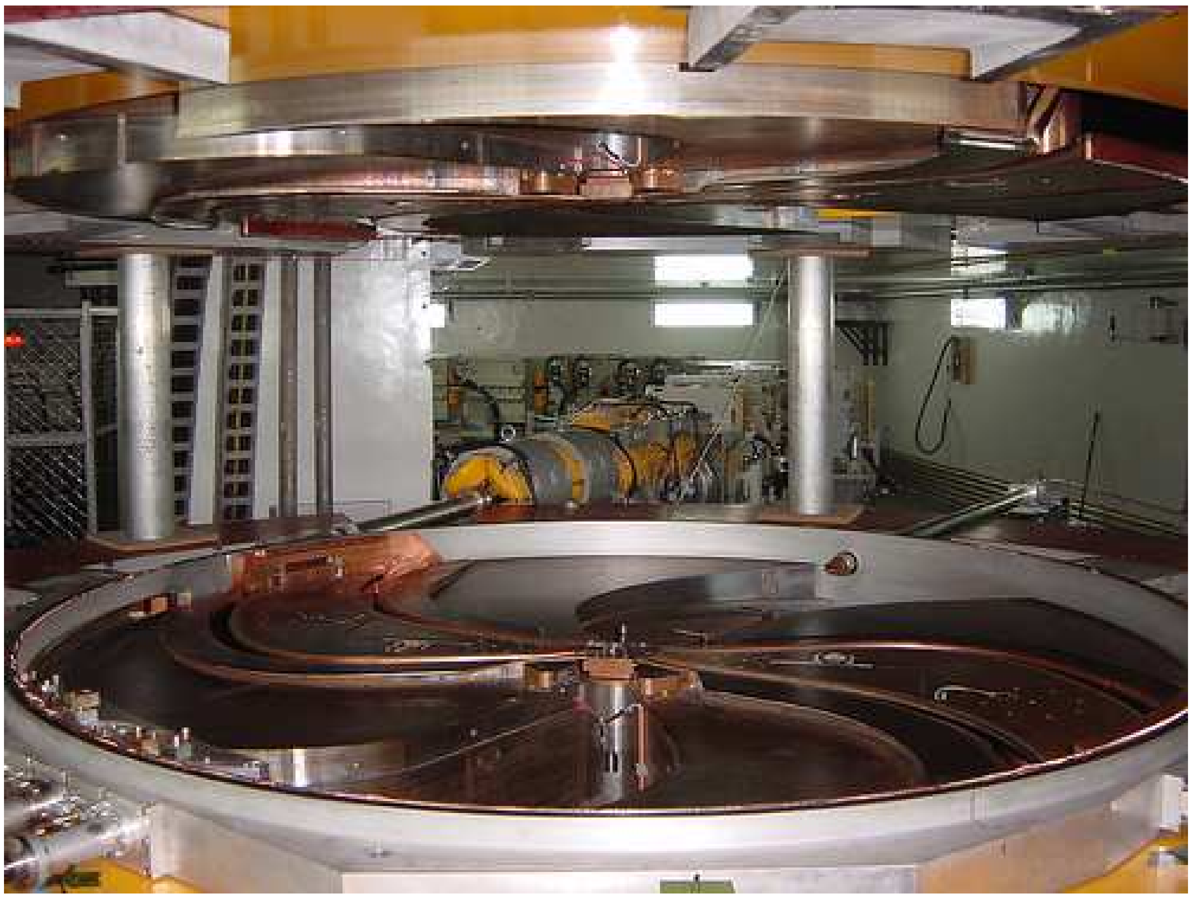
ION SOURCE → PROTONS →

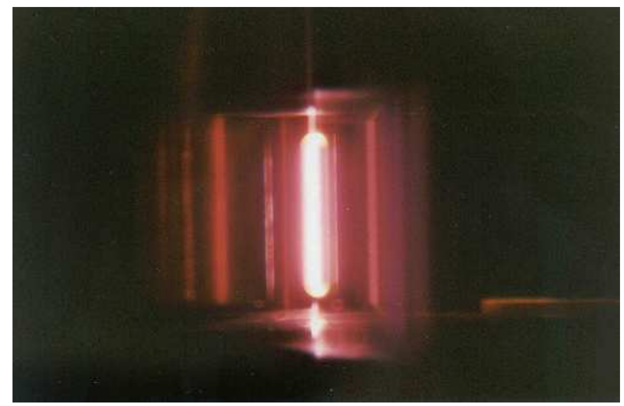
VACUM LINEAR ACCELARATOR TO, 7 MeV IN MICRO SECONDS →

ENTER THE SYCHOTRON WHERE ACCELARATED TO ENERGIES 70 MILLION – 250 MeV → BEAM TRANSPORT

PROTON BEAM MACHINES

235MeV proton cyclotron used for proton cancer therapy at Boshan, China





Hydrogen plasma ion source inside of the accelerator

Protons vs Photons

- Irradiate smaller volume of normal tissues
- Photon beam decreases exponentially with depth in the irradiated tissues
- Protons have a finite range
- Protons deposit most of their radiation energy in what is known as Braggs peak

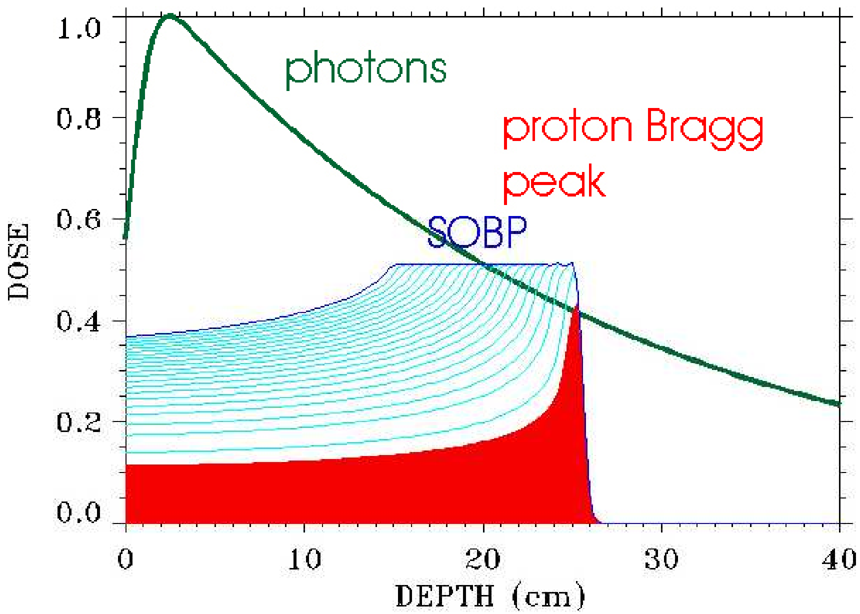


Image courtesy of Dr Annie Chan, Dept of Radiation Oncology, MGH, Boston, MA

Bragg's Peak

- Described by William Bragg over 100 years ago
- Depth is dependent on the energy of the proton beam
- This energy can be control very precisely

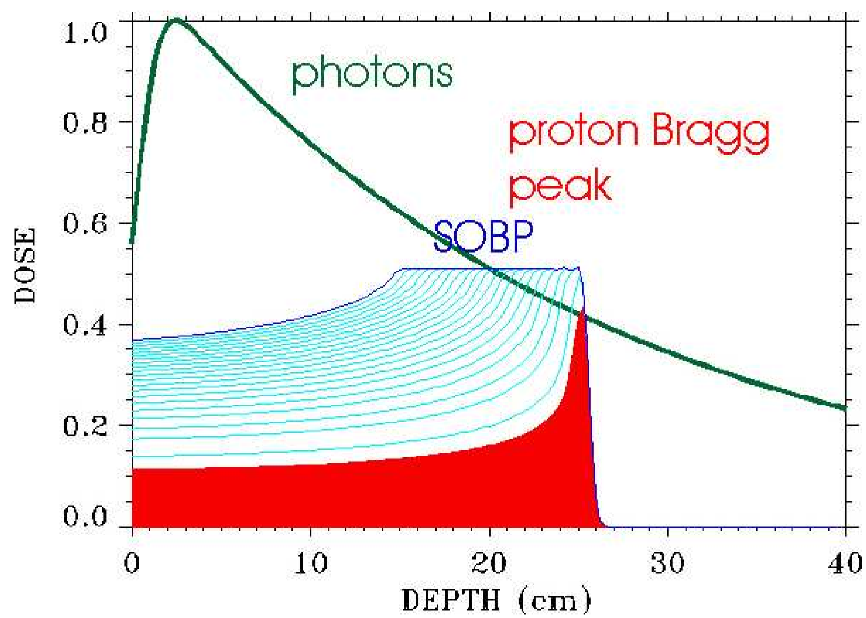


Image courtesy of Dr Annie Chan, Dept of Radiation Oncology, MGH, Boston, MA

Proton Therapy

- Spread-out Bragg peaks (SOBP)
  - The dose peak may be ‘spread out’ to achieve a uniform dose
- Spot scanning method
  - Recently introduced
  - Small pencil beams of a certain energy deposit their peaks to obtain ‘dose-sculpting’ of the target

Dose Equivalent

- Relative biological effectiveness (RBE)
  - **Ratio of the photon dose to the particle dose required to produce the same biological effect**
- An RBE value of 1.1 is generally accepted for clinical use with proton beams
- Gray equivalents (GyE) or cobalt Gray equivalents (CGE) often used with protons
  - **Gray multiplied by the relative biological effectiveness (RBE) factor specific for the beam used**

Carbon ions

- The RBE of carbon ions has a estimated value of 3
- Carbon ion therapy attempts to capture the ‘best of both worlds,’
  - Presence of the proton’s Bragg peak
  - Advantage of their high RBE to increase the tumor control probability

IMPT

- Intensity modulated proton therapy (IMPT)
  - Radiation portals which adds more accuracy to target zone
  - Also, in contrast to the two-dimensionality of IMRT, IMPT is able to modulate the Bragg peak allowing three-dimensional optimization.

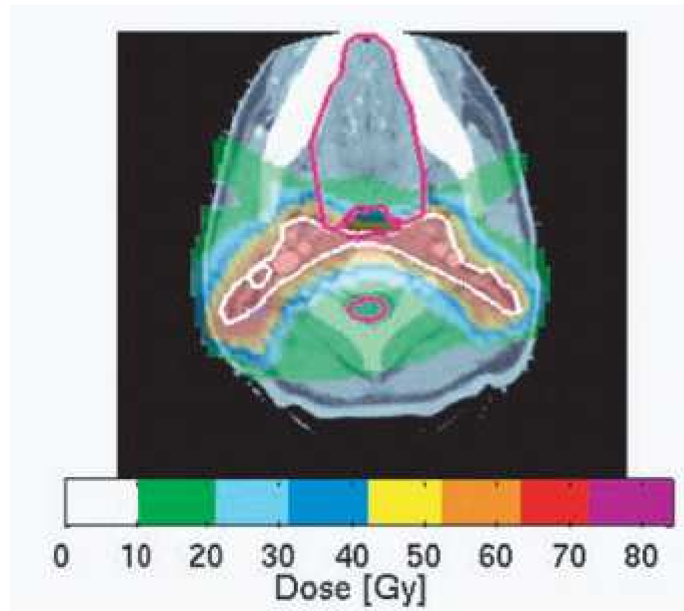
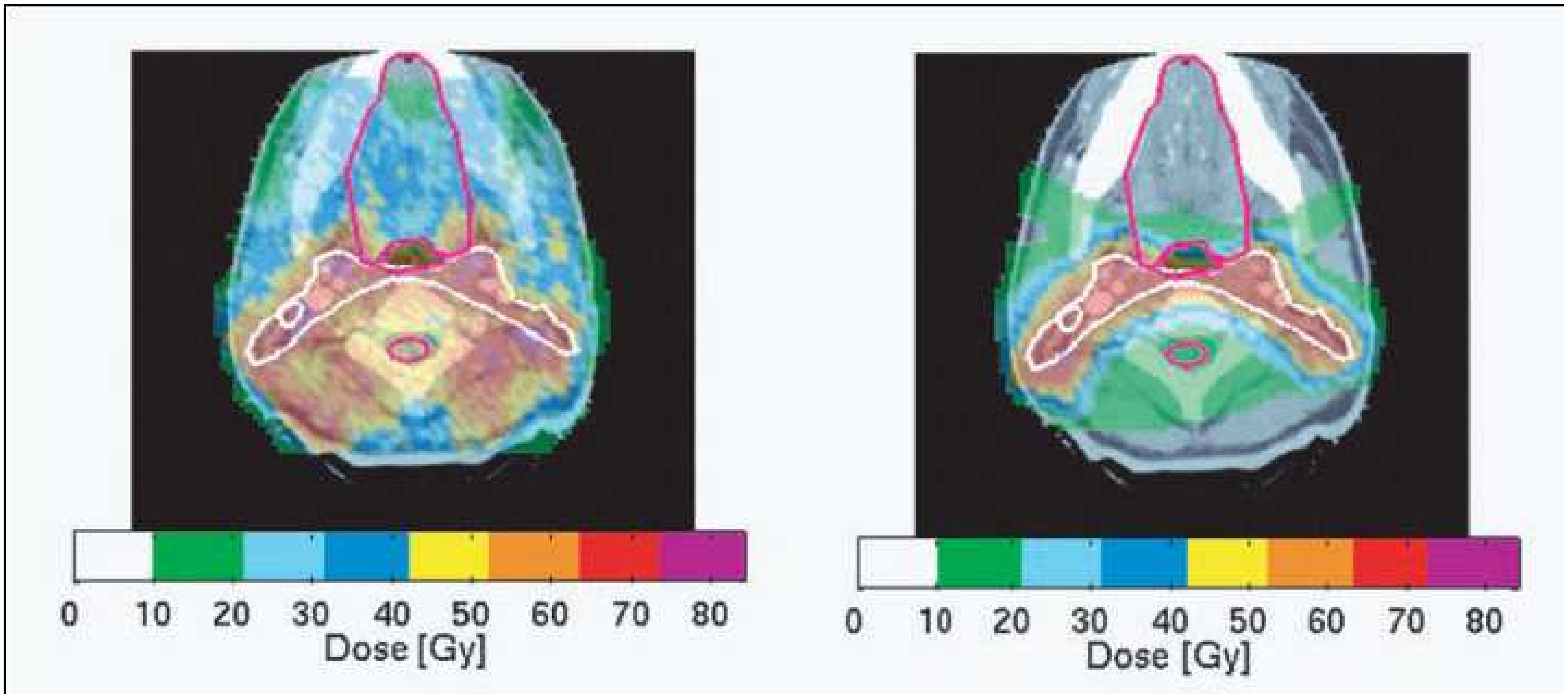


Image from CHAN A.. Proton Radiation Therapy for Head and Neck Cancer. Journal of Surgical Oncology 2008;97:697–700

IMRT IMPT



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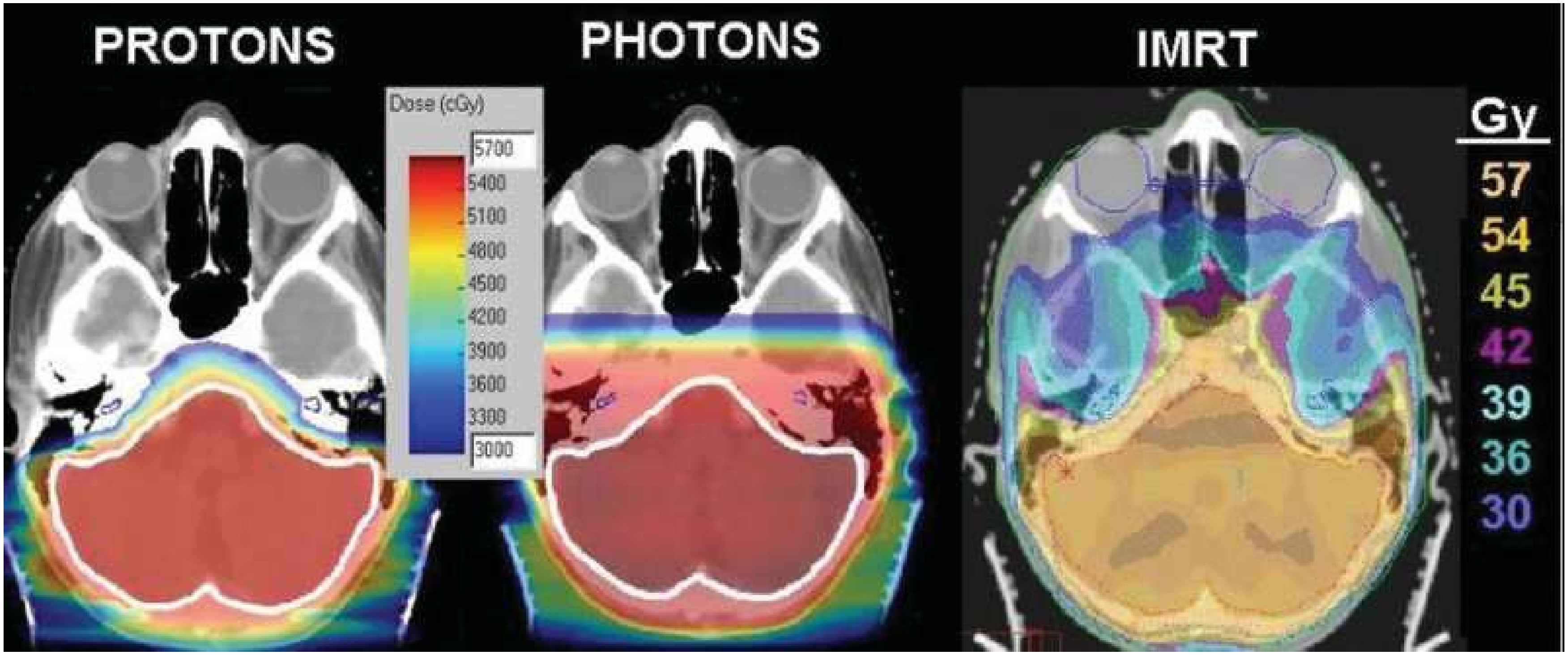
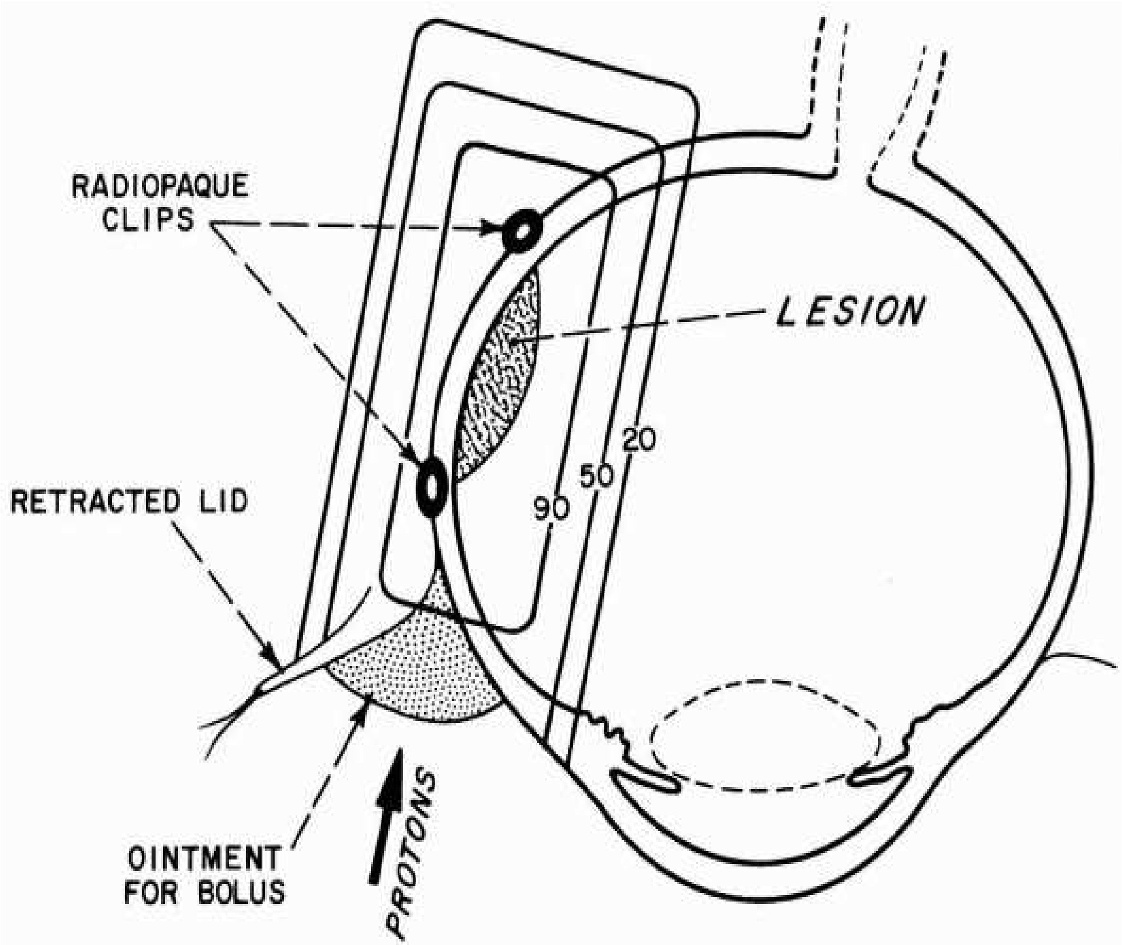


- The dose to 90% of the cochlea was reduced from 101% with standard photons, to 33% with IMRT, and to 2% with protons

Image from Greco C. Current Status of Radiotherapy With Proton and Light Ion Beams. American CANCER society April 1, 2007 / Volume 109 / Number 7

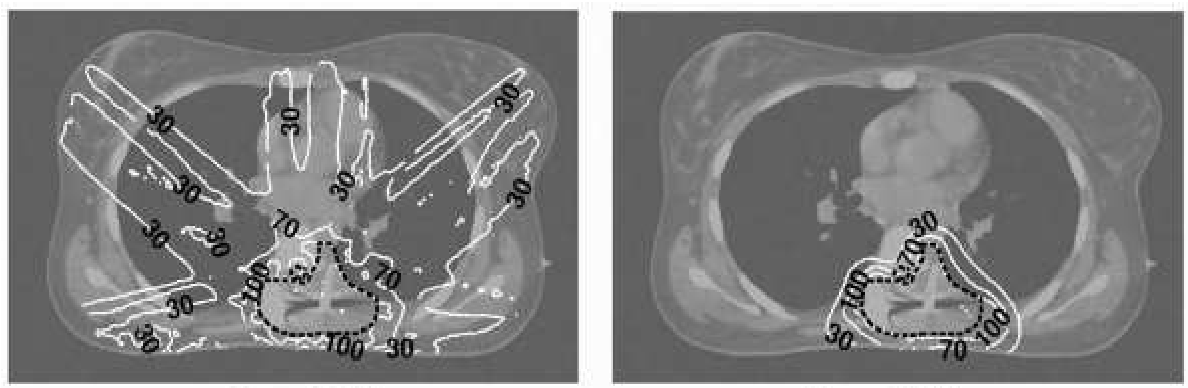
CLINICAL APPICATIONS OF PROTONS AND HEAVY IONS -UVEAL MELANOMA



EQIVALENT OF 70 GY / 5 # / 8-9 DAYS

5 YrS	PROTONS	HELIUM IONS
LOCAL CONTROL	96 %	97 %
EYE RETAIN	89 %	83 %
MET. FREE SURVIVAL	80 %	76 %

SARCOMAS ADJACENT TO CNS TISSUES



Photon IMRT Proton IMRT

CHORDOMAS OR CHONDROSARCOMA
POST OP PHOTON RADIATION LRC = 35 – 40%
HAVARD CYCLOTRON – 68.5 PHOTON Gy EQIV. @ 1.8 PHOTON Gy
5 Yr LCR = 91 % FOR CHONDROSARCOMAS AND 65 % FOR CHORDOMAS

PROSTATE CA.

- INTIAL LOMA LINDA EXPERIENCE – 1255 PTS. , 1991 OCT. – DEC 1997.
- BIOCHEMICAL RELAPSE AND TOXICITY
- 30 CGE BOOST + 45 Gy PHOTONS – 4 FIELD 3 D CONFORMAL TECHNIQUE
- DFS @ 10 Yrs – 73 % AND 90 % WHEN INITIAL PSA <= 4 .
- LONG TERM OUTCOMES COMPARABLE TO OTHER MODALITIES INTENDED FOR CURE

SUMMARY OF CLINICAL INDICATIONS FOR PARTICLE THERAPY

NEUTRONS

- SALIVARY GLAND , ADVANCED
- PROSTATE CANCER T2 – T4, N0 – 2, M0
- UNRESECTABLE SOFT TISSUE, BONE, CARTILAGE SARCOMAS
- SCCHN PRESENTING WITH LARGE NECK NODES

PROTONS

- UVEAL MELANOMAS
- CHORDOMAS OR CHONDROSARCOMA ADJACENT TO CNS TISSUE

THANK YOU