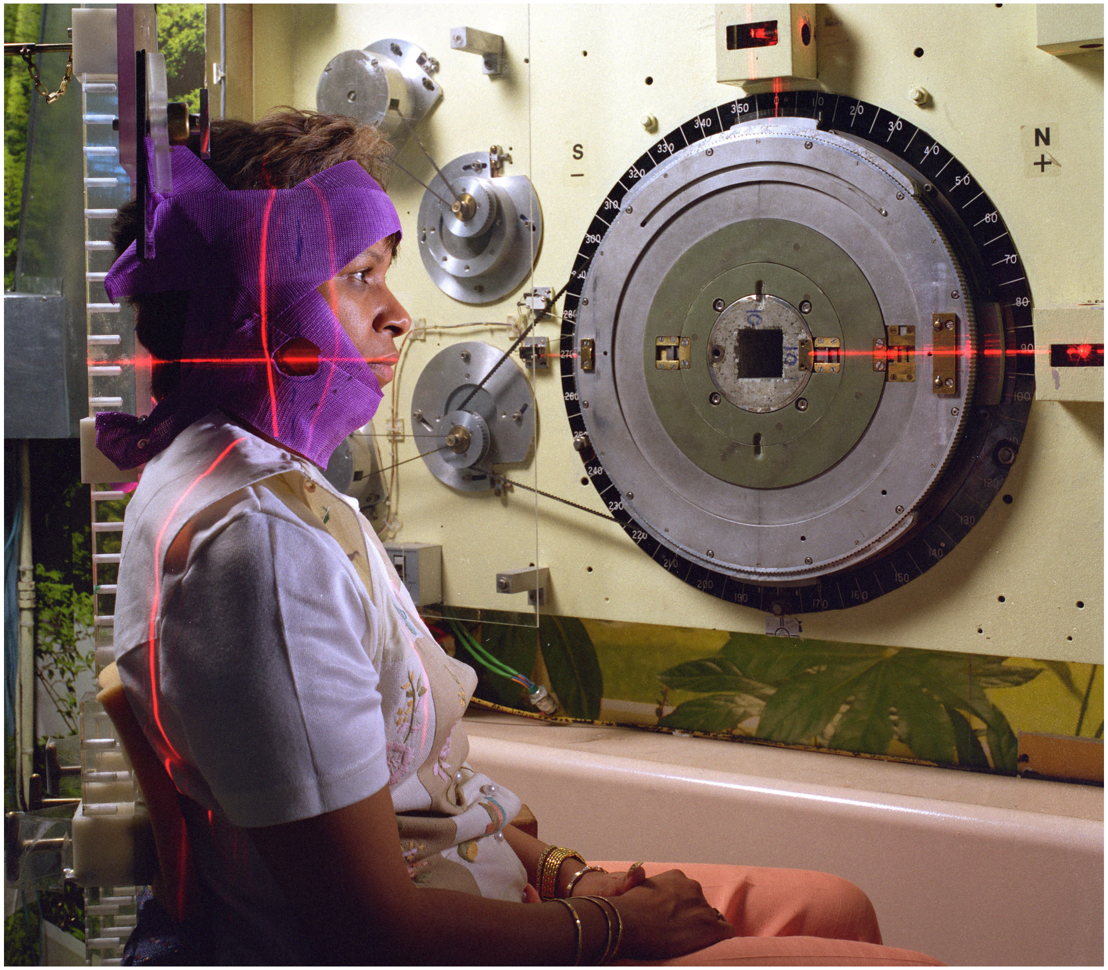
HADRON THERAPY FOR CANCER TREATMENT



Seminar presented by Arlene Lennox at Fermilab on Nov 21, 2003

CANCER STAGES

LOCAL TUMOR

REGIONAL METASTASIS

SYSTEMIC DISEASE

CANCER TREATMENT

SURGERY

RADIATION THERAPY

CHEMOTHERAPY/IMMUNOTHERAPY

Photon radiation therapy is easily available

Gantry rotates around patient.

Therapy accelerators are manufactured by several vendors.

Hadron therapy is radiation therapy using strongly interacting particles

- Neutrons
- Protons
- Pions
- Ions (alphas, C, Ne)

Reference: Petti and Lennox, Hadronic Radiotherapy,
Ann. Rev. Nuclear & Particle Science, 1994. 44:154-197.

Proton and neutron therapy address deficiencies in photon therapy

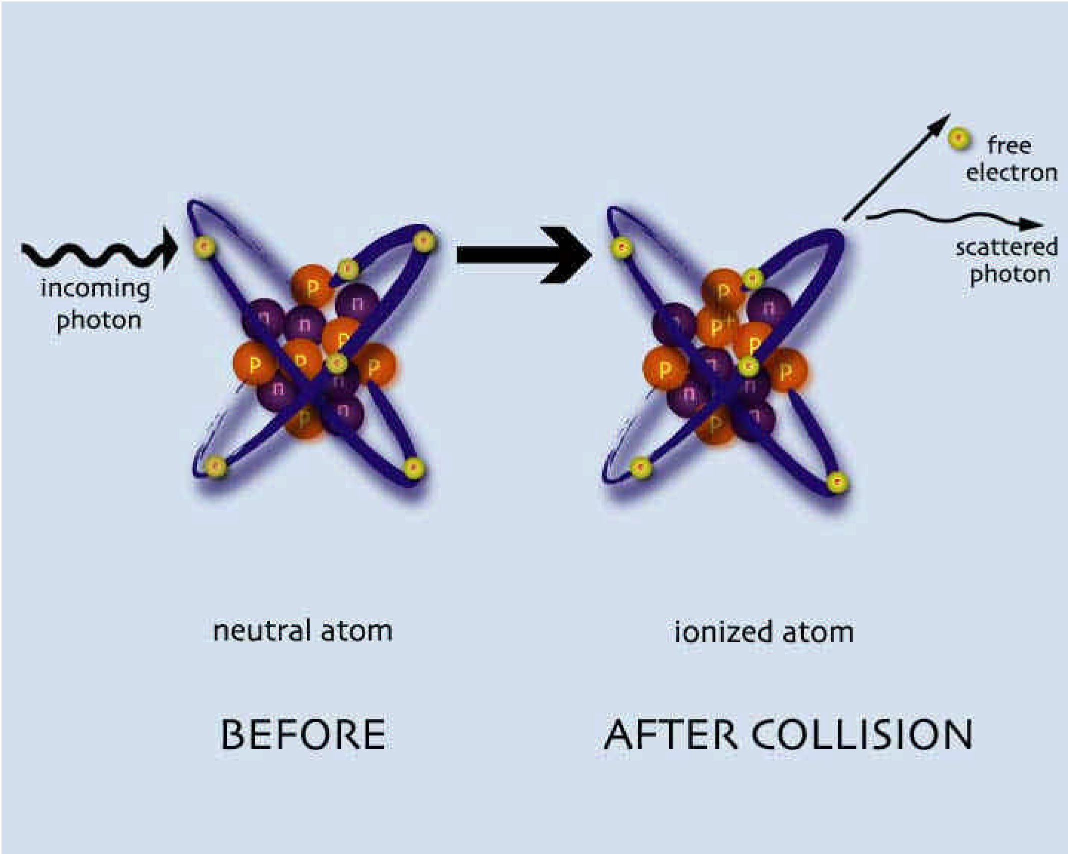
- *Protons: better dose distributions*
- *Neutrons: better tumor killing*

  - *Clinical Results*

  - *Current Challenges*

  - *Proposed Solution*

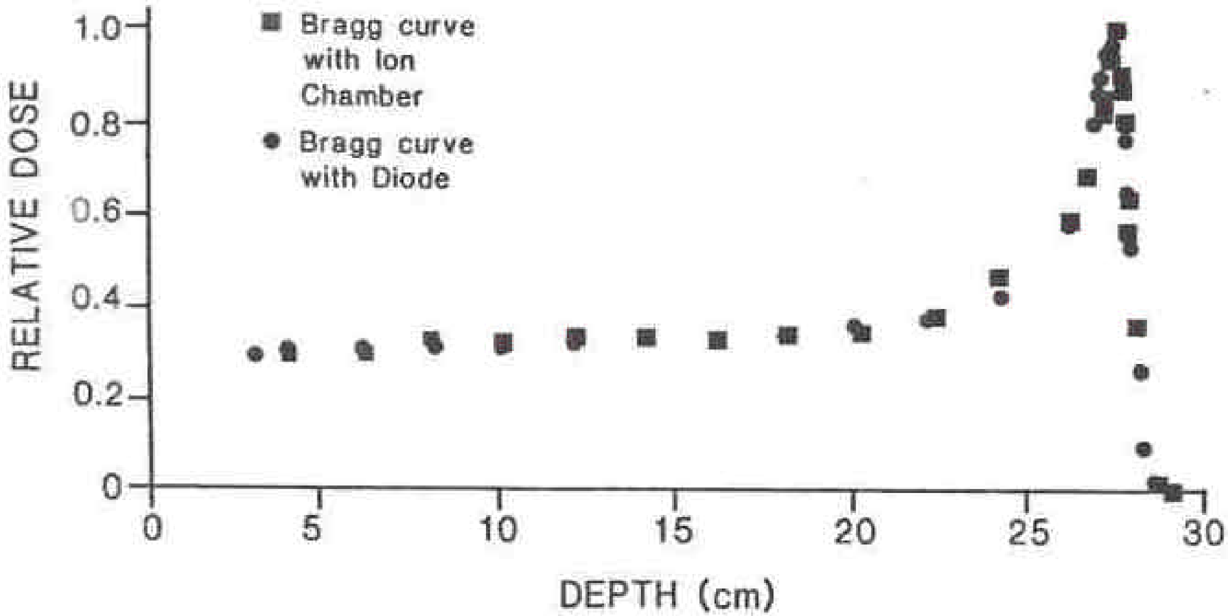
Low Linear Energy Transfer (LET)



- **Protons and photons**
  - **are low LET radiation.**
  - **have similar biological effectiveness.**

235 MeV Proton Bragg Curve

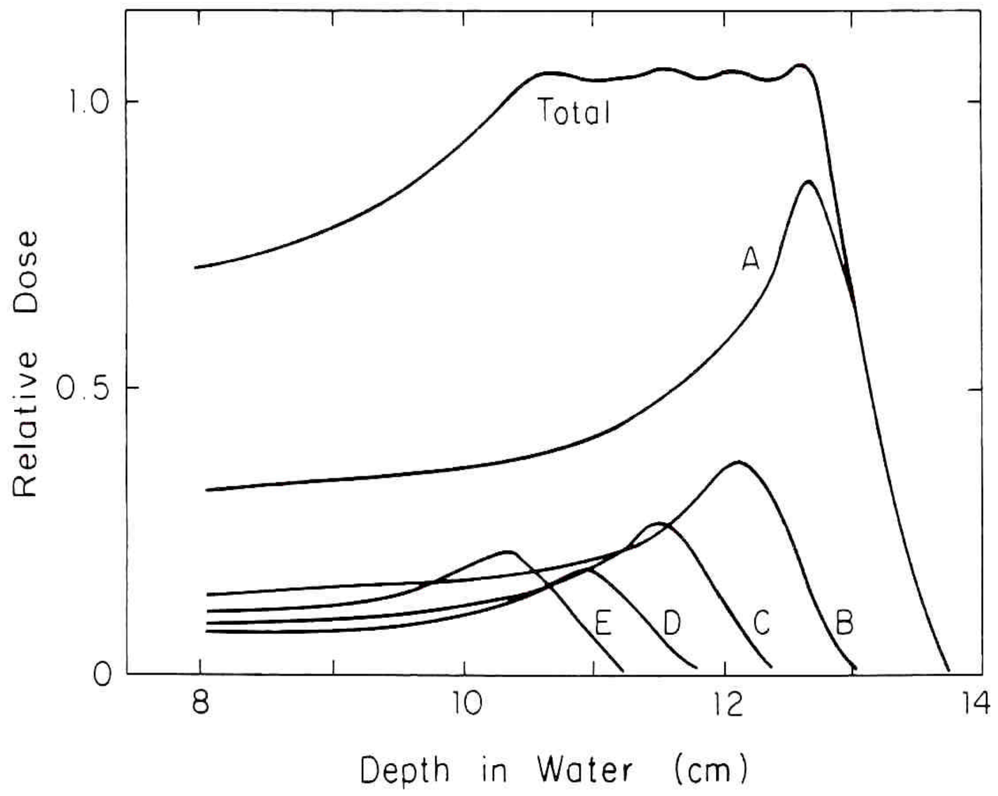
Loma Linda University Medical Center



- Suitable for 1.5 cm diameter tumor.
- Skin dose ~30% of maximum dose.

Coutrakon *et al,* Med. Phys.1991. 18:1093-1099.

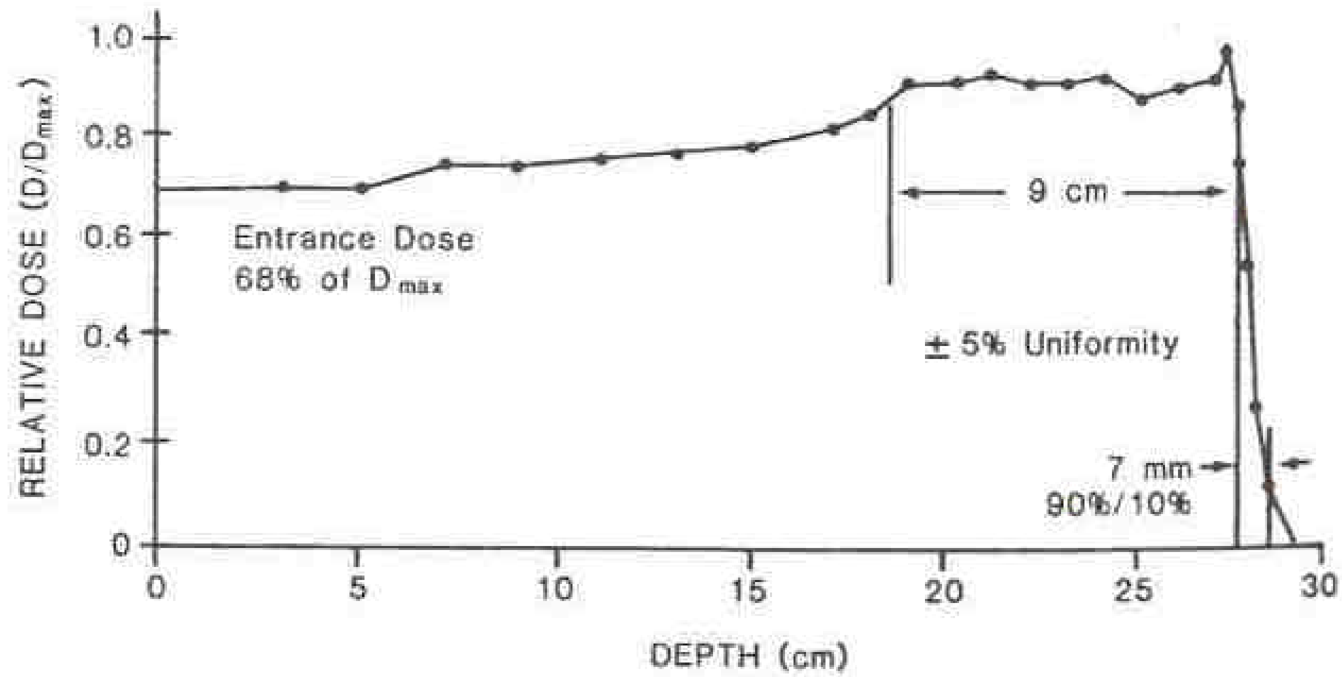
Spread-Out Bragg Peak



Koehler et al, Radiology 104:191-95 (1972)

235 MeV Spread Out Bragg Peak

Loma Linda University Medical Center

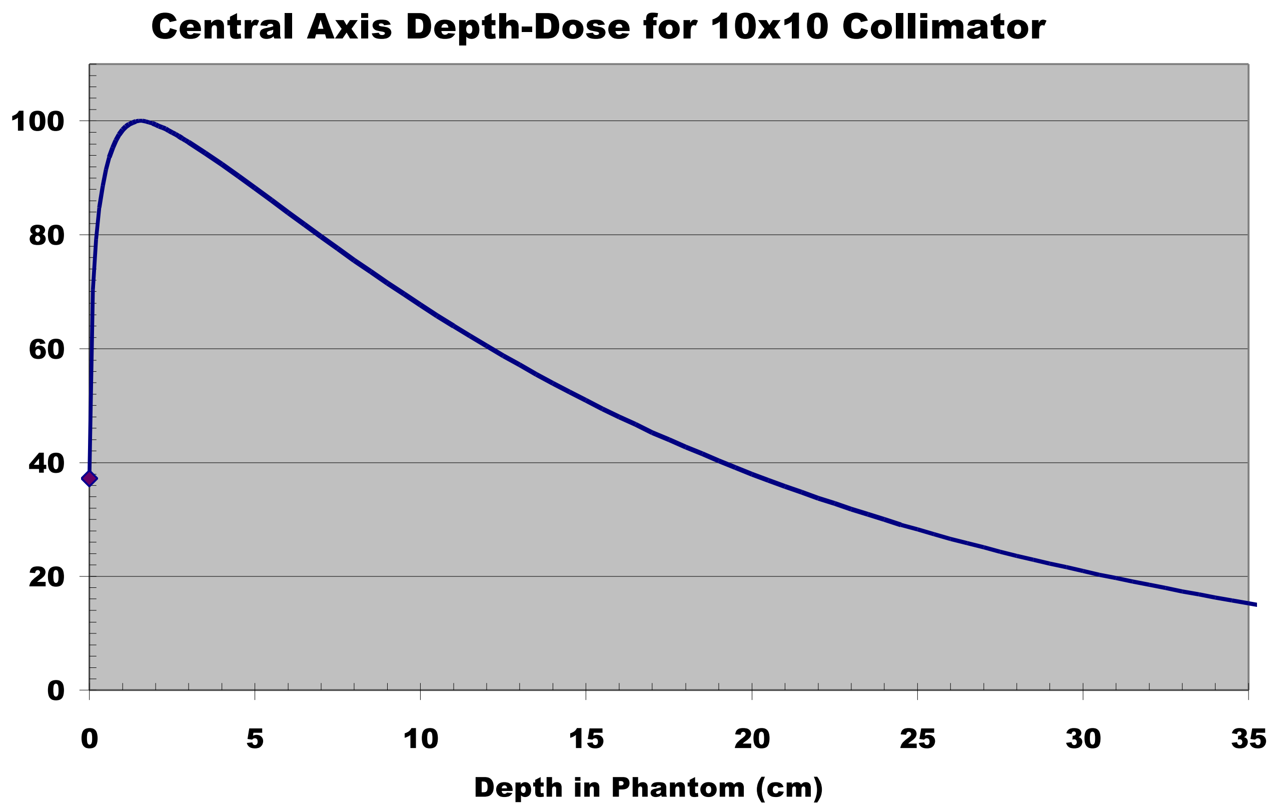


- Suitable for 9 cm diameter tumor.
- Skin dose 68% of maximum dose.

Coutrakon *et al,* Med. Phys.1991. 18:1093-1099.

p(66) Be(49) Neutron Therapy Beam

(same as 8 MV photon beam)

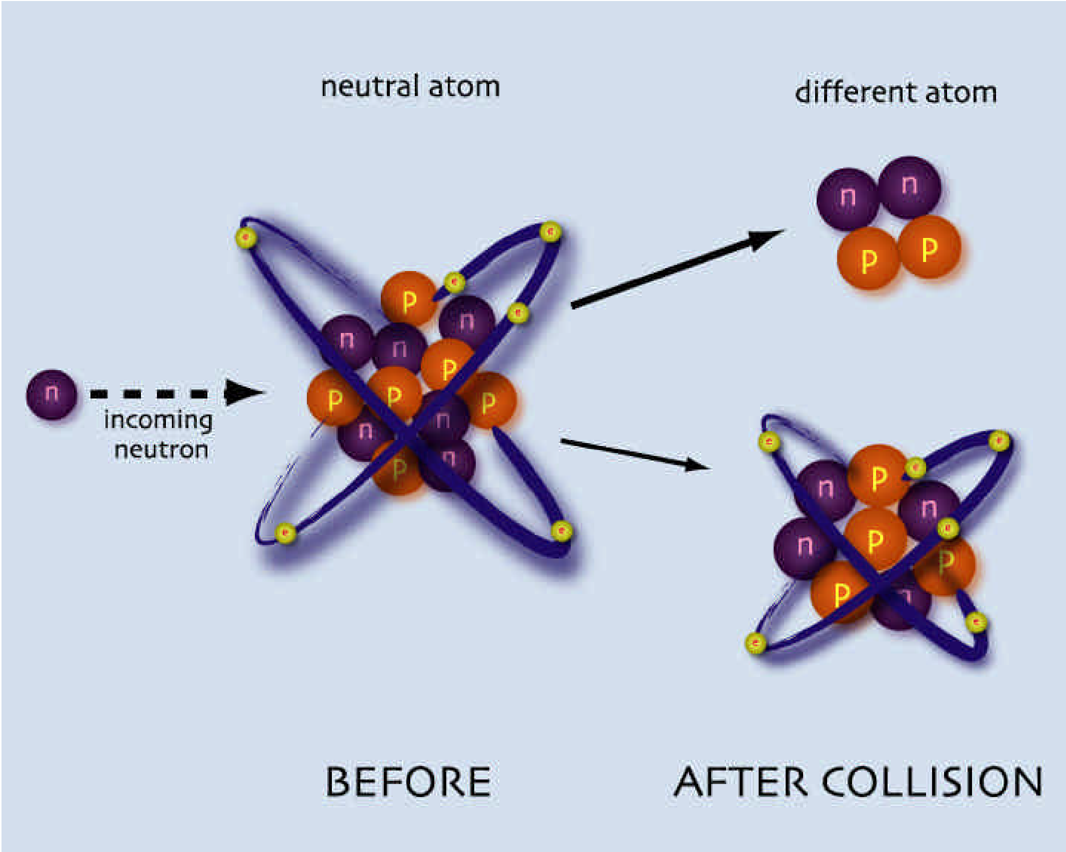


Results of Proton Clinical Trials

Reference: Petti and Lennox, Hadronic Radiotherapy, *Ann. Rev. Nuclear & Particle Science,* 1994. 44:154-197.

- ***Tumors where protons are superior to photons are:***
  - **Skull-base chordoma and chondrosarcoma**
  - **Arteriovenous malformations**
  - **Uveal melanoma (pages 174-177)**
- ***Tumors where more research is needed are:***
  - **Skull-base meningioma, craniopharyngioma, pituitary adenoma**
  - **Lung**
  - **Esophageal**
  - **Liver**
  - **Uterine cervix**
  - **Prostate (pages 174, 178)**
  - **Wet macular degeneration**

High Linear Energy Transfer (LET)

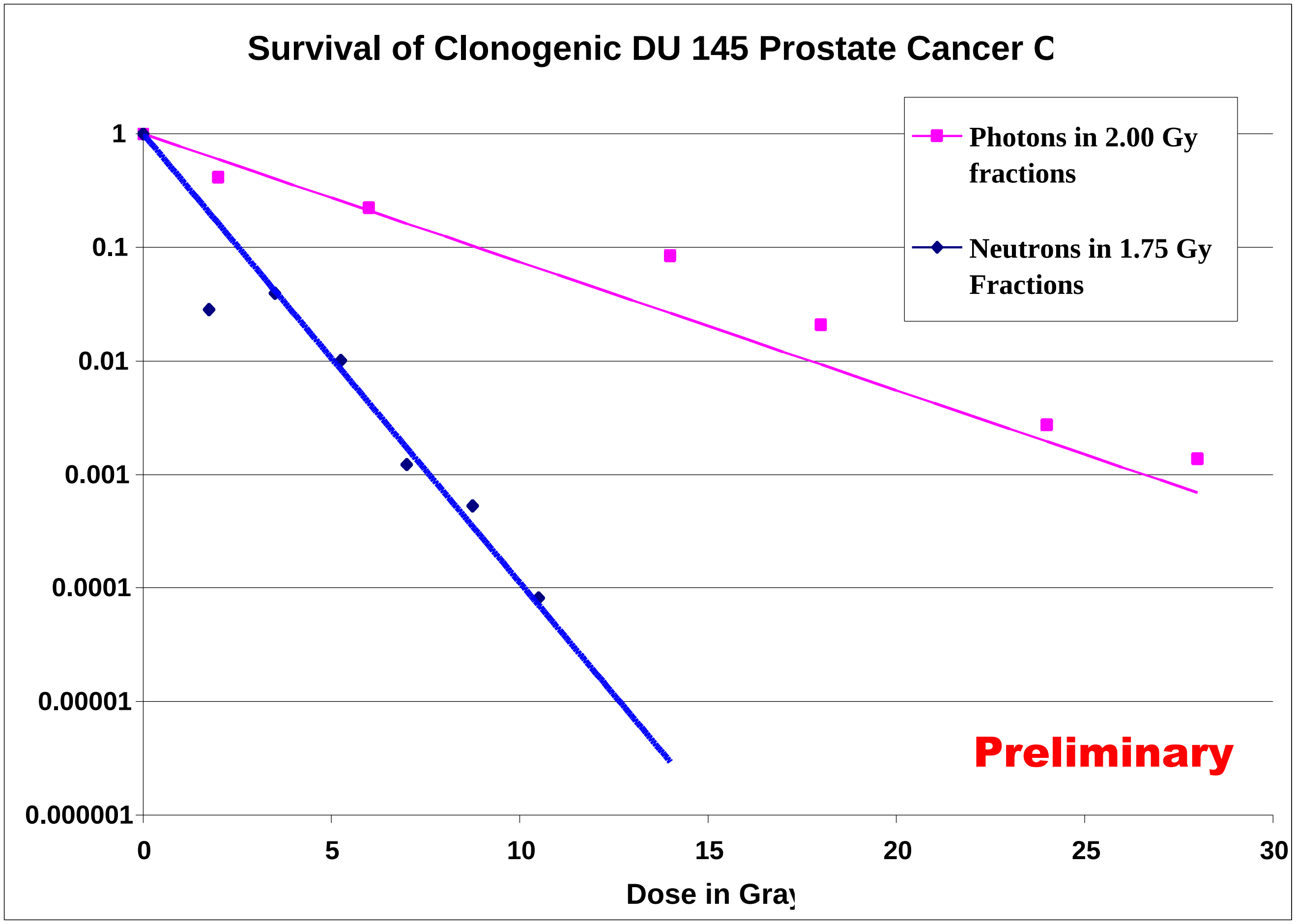


- **Neutrons and ions**
  - **are high LET radiation**
  - **have high biological effectiveness (RBE)**

Survival of prostate cancer cells after one exposure to photon or neutron radiation

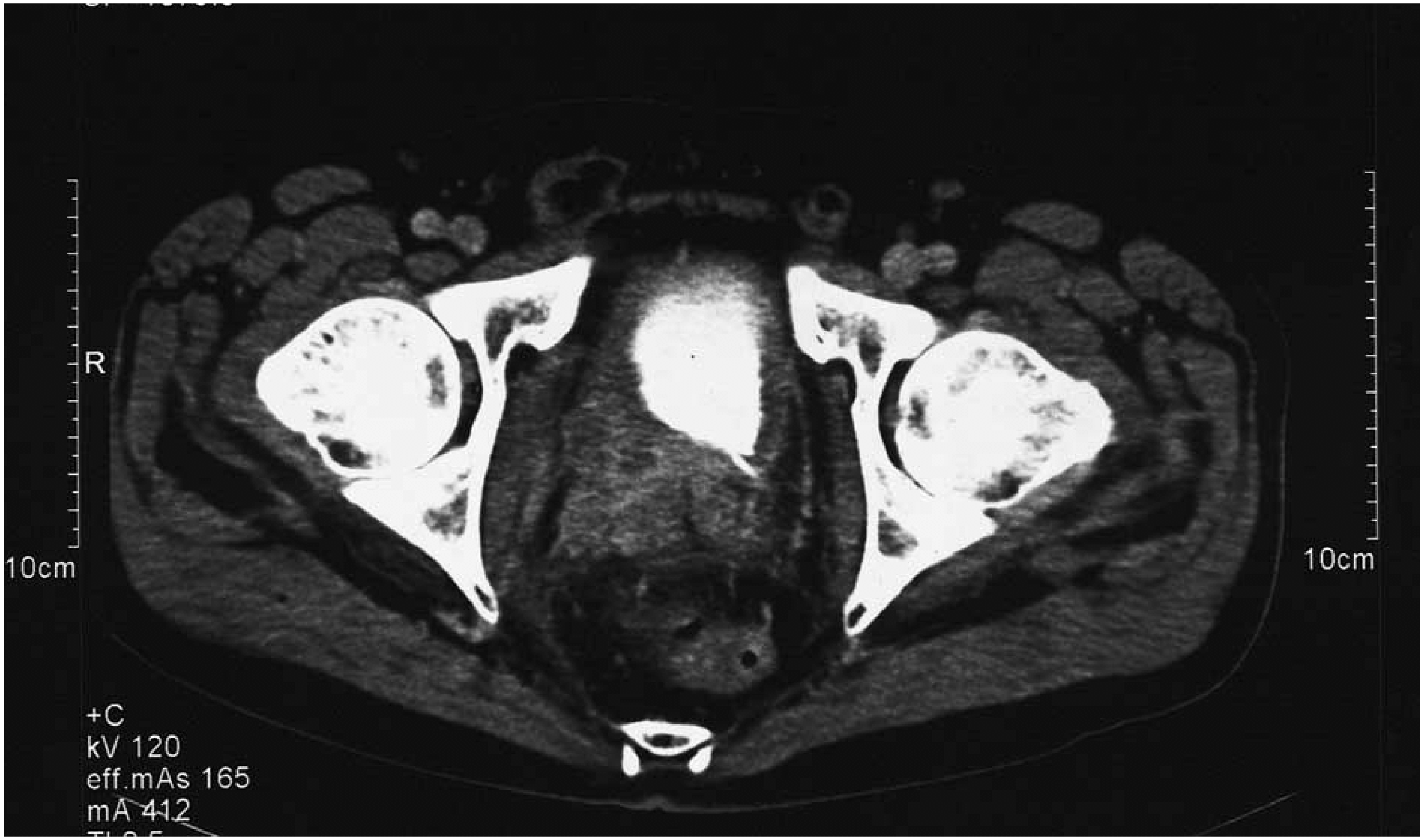
- **Radioresistant** tumors are better controlled by neutrons.

Fermilab 66 MeV neutrons exhibit RBE = 4 for Prostate Cancer



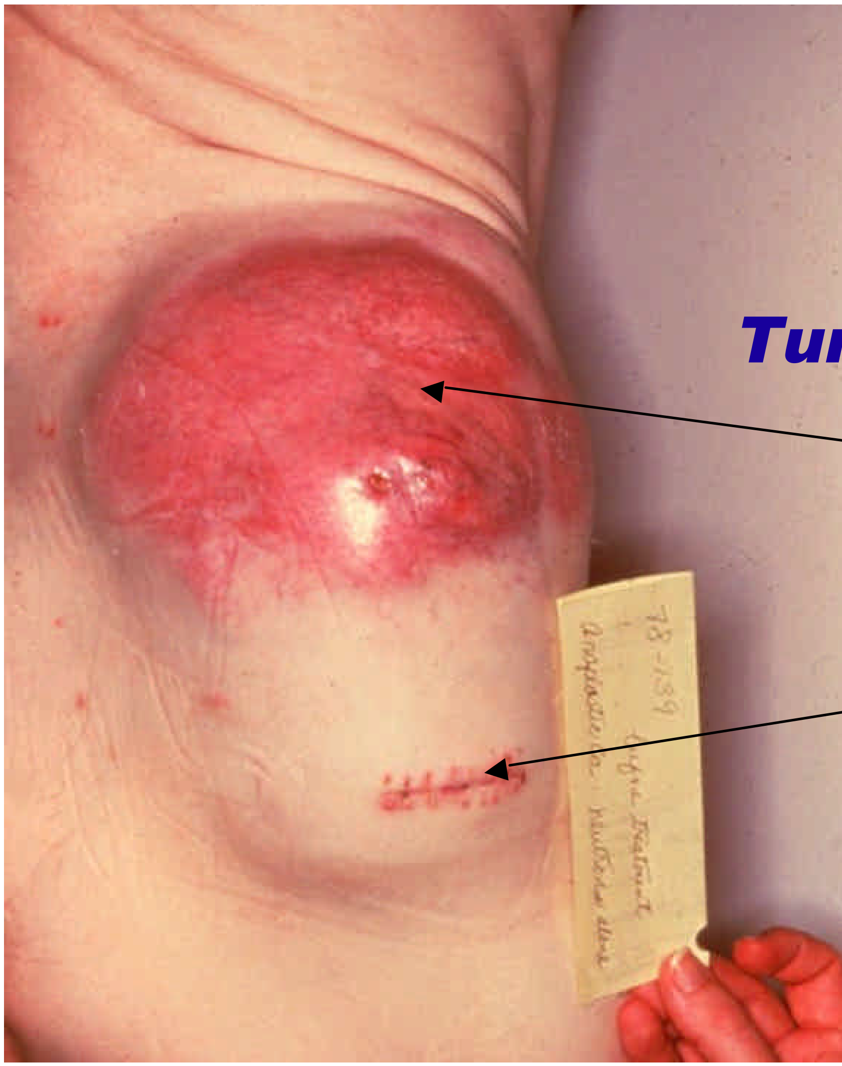
Blazek, Urbon, Lennox, Kroc, Pientak (in press)

Before Neutron Therapy



After 7 treatments 12.25 Gy of neutrons

Inoperable Soft-tissue Sarcoma



Tumor compromises the skin

Biopsy scar

End of Neutron Treatment

Skin reddening in Caucasions

Treatment mark

Two-month follow-up

Fibrosis

Inoperable neck tumor before neutron therapy

Squamous cell carcinoma from snuff chewing

Two years after Neutron Therapy

Results of Neutron Clinical Trials

Reference: Nuclear data for neutron therapy: Status and future needs - IAEA TECDOC 992 (1997) - page 23

- ***Tumors where fast neutrons are superior to photons are:***
  - **Salivary glands -** *locally extended, well differentiated*
  - **Paranasal sinuses -** *adenocarcinoma, mucoepidermoid, squamous, adenoid cystic*
  - **Head and Neck -** *locally extended, metastatic*
  - ***Soft tissue, osteo, and chondrosarcomas***
  - ***Locally advanced prostate***
  - ***Melanomas*** *Inoperable/recurrent*

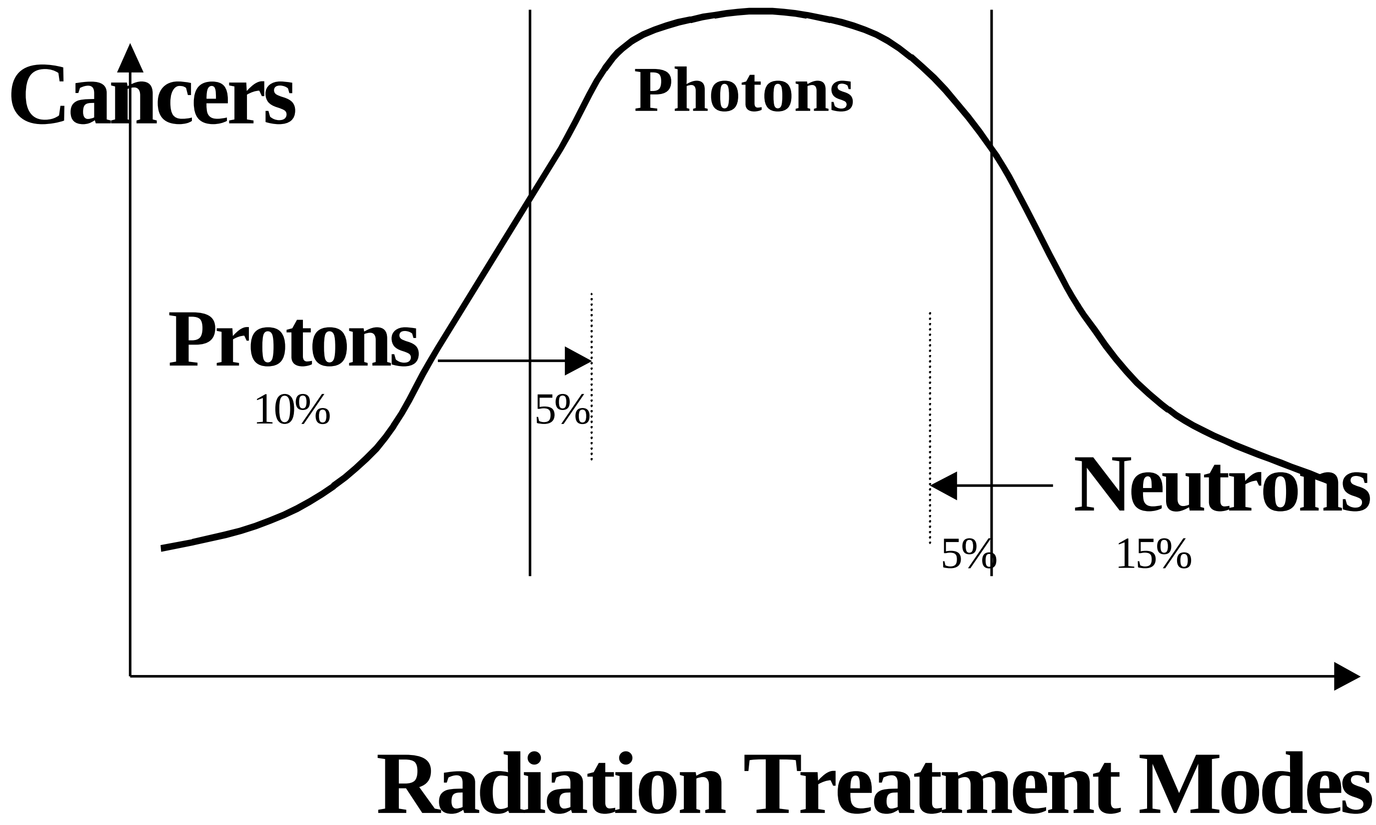
Results of Neutron Clinical Trials

Reference: Nuclear data for neutron therapy: Status and future needs - IAEA TECDOC 992 (1997).

- ***Tumors for which more research is needed***
  - **Inoperable Pancreatic**
  - **Bladder**
  - **Esophagus**
  - **Recurrent or inoperable rectal**
  - **Locally advanced uterine cervix**
  - **Neutron boost for brain tumors (pp13-22)**

"The proportion of patients suitable for neutrons ranges from 10-20%, but this is probably a lower limit…with high energy modern cyclotrons neutron therapy will be useful for a larger proportion of patients. " (page 24)

Hadron Therapy is an Important Option for Radiation Therapy Patients.



The Challenge(s)

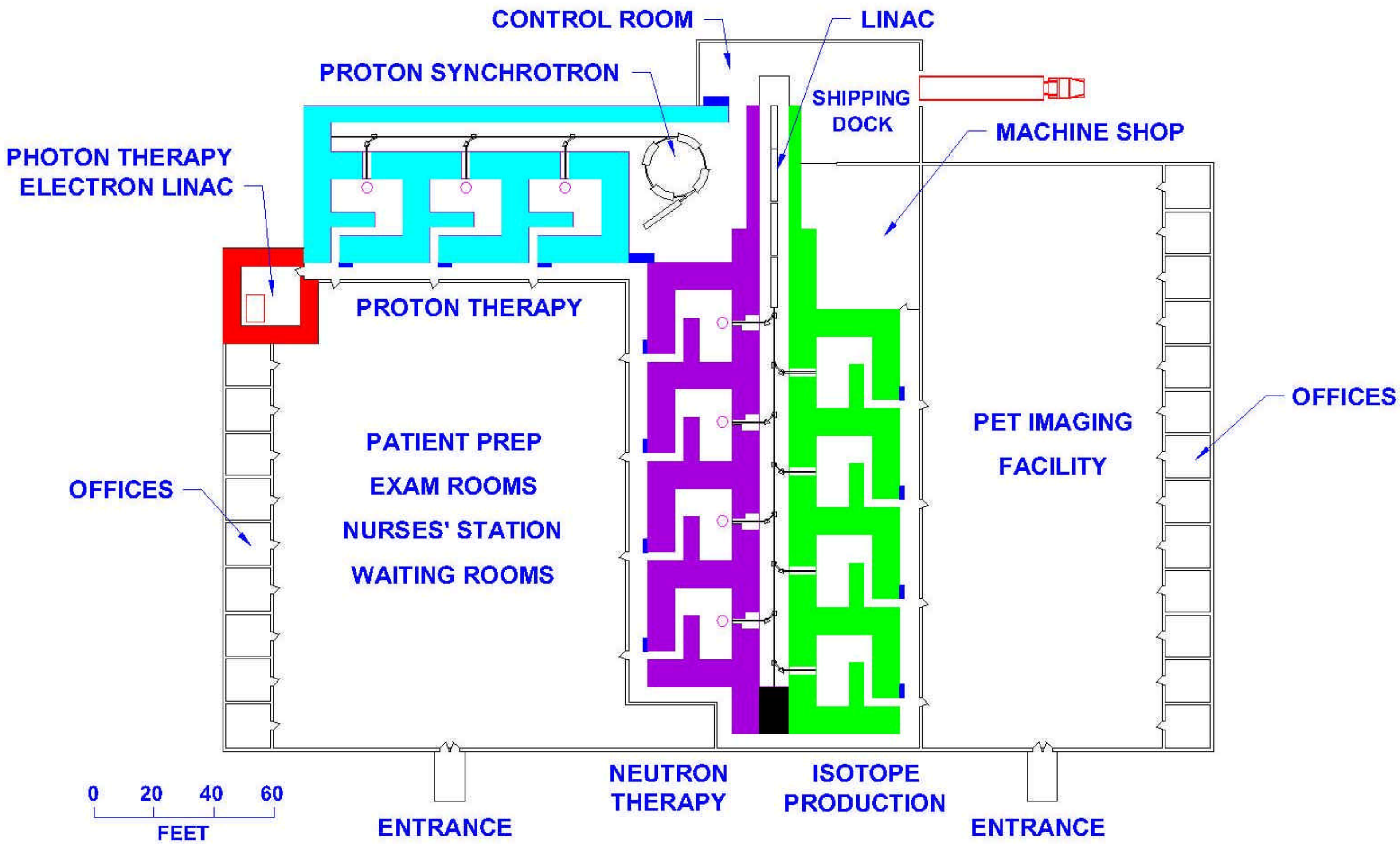
- ***Difficulty establishing uncontestable advantage of hadron therapy over competing therapies***
  - Inadequate statistics at individual clinics
  - Lack of uniformity in treatment techniques
  - Lack of money to support clinical trials
- ***Number of hadron facilities is small***
- ***Neutron facilities have pronounced differences in beam characteristics at different facilities***
  - Different energy spectra
  - Different collimation techniques
- ***Lack of standardization keeps costs high***
  - Each hadron clinic has one-of-a-kind accelerator
  - Need more standardized engineering
- ***Hospitals and physicians are reluctant to refer patients away from their facilities***

The Proposed Solution

- ***A clinic that provides both hadron and conventional therapy***
  - Salaried, research-oriented physicians
  - International collaborations
  - Strong educational outreach program
- ***Near high-tech institution(s)***
- ***Multidisciplinary research***
  - Accelerator development
  - Beam delivery techniques
  - Imaging techniques
  - Radiation sensitizers
  - Detector development
  - Electromedicine

Hadron Therapy Facility

First Floor - Plan View



Institute for Hadron Therapy

A Multidisciplinary Program

- ***Physicians treat up to 1500 patients per year***
- ***Specialists work to make hadron therapy more cost effective and accessible***
  - Accelerator, mechanical, electrical engineers
  - Accelerator and medical physicists
  - Software and controls specialists
- ***Radiobiologists study biological effectiveness***
- ***Pharmaceutical specialists develop radiosensitizers***
- ***Isotope specialists track changes in tumors***
- ***Basic scientists have access to research isotopes***