Low and High-LET in clinical radiation oncology

DGBNCT talks around the campfire

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June 8, 2023

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Cancer Care with Radiotherapy – Facts & Analysis

- 19,3 million new cancer cases worldwide in 2020, expected 24,6 million in 2030
- About 50 % of all cancer patients receive radiation in the frame of their disease
- About 70% of patients have loco-regional disease at initial diagnosis, of these 60% are cured
- About 60% of patients who die have uncontrolled local tumor disease
  - (a challenge for radiation therapy)

Sources: DeVita et al.: Cancer - Principles and Practice of Oncology 12th edition, 2023
NIH: Statistics and Graphs, 2023
Deutsche Krebsgesellschaft: Onko Internetportal

Cancer Care with Radiotherapy – Facts & Analysis

- Radiotherapy (RT) Market USD 6.1bn in 2022, **USD 7.3B projected by 2026,** CAGR 4.2%
- Global cancer burden on the rise – **24.6M new cancer cases per year by 2030**
- Conventional Photon Therapy well established. Strong innovation pipeline
- Proton Therapy has not fulfilled the promise on effectiveness
- Unsatisfactory clinical results for some challenging indications

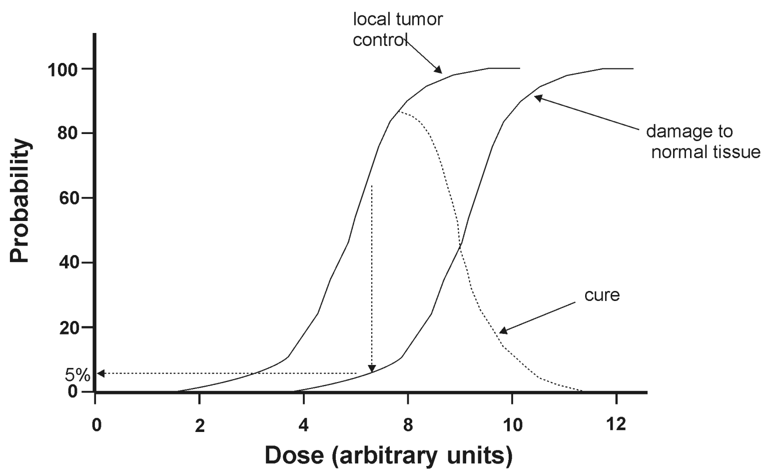
Sources: Radiotherapy - Global Forecasts 2021 to 2026, Markets and Markets
Expanding global access to radiotherapy. Lancet Oncol. Vol 16, Sept. 2015

The basic biological principle of radiotherapy

Radiotherapy exploits the different ability of tumor and normal tissue to repair radiation-induced DNA damage.

The probability of curing a tumor and of inducing severe damage in the normal tissue

After: H. Holthusen, Strahlentherapie 57:254-269, 1936.



How to improve radiotherapy?

Improving the physical selectivity

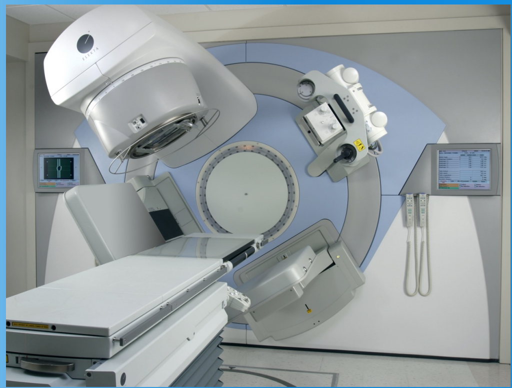
High dose to the tumor, low dose to the surrounding tissues: precision

Technology, physics, geometry, imaging

Improving the differential effect

Increased effects on cancer cells, reduced effects on normal tissues: effectiveness

Radiobiology, combined treatments, **LET**



Radiation used for treatments

Beams with low LET

- Photons
- Electrons
- Protons

Beams with high LET

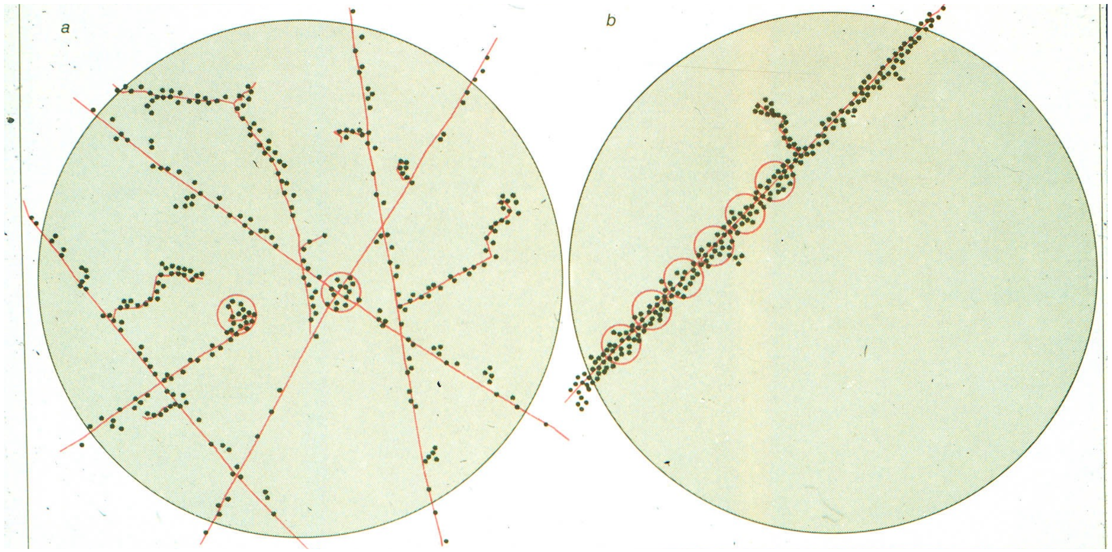
- Fast neutrons
- Carbon ions
- BNCT

Hadrons used in radiotherapy

Why are they used?

- Protons: precision
- Helium ions higher precision at depth
- Fast neutrons: high LET
- Carbon ions: precision and high LET
- BNCT: cellular targeting and high LET

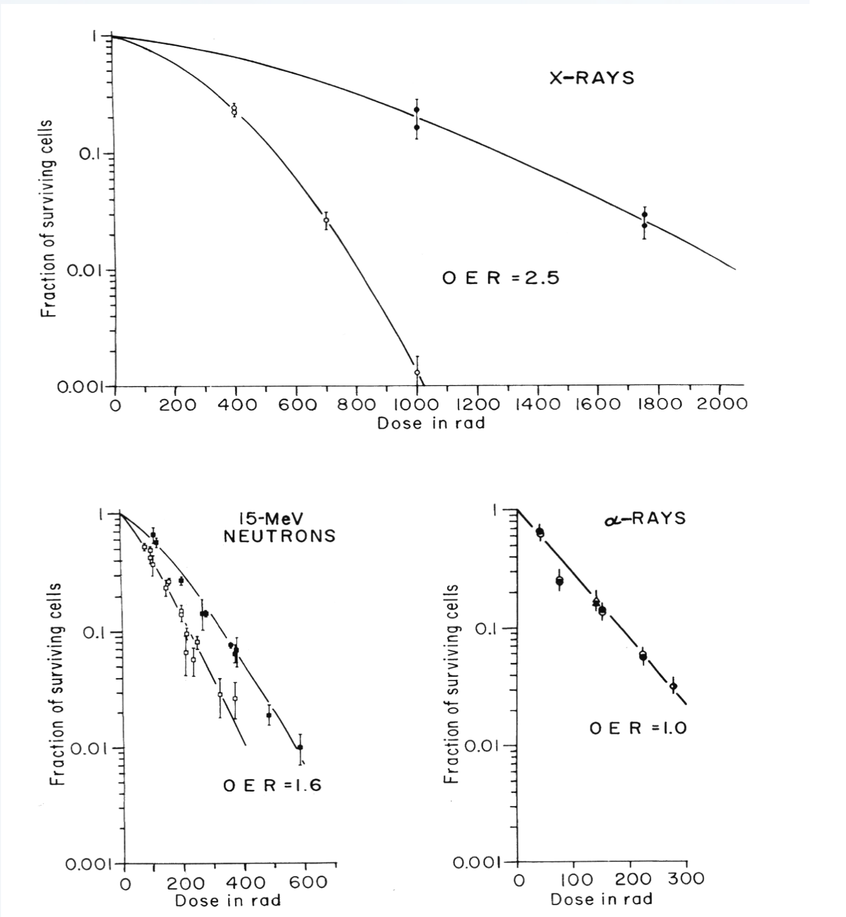
Linear Energy Transfer LET



LET is the amount of energy that an ionizing particle transfers to the material traversed per unit distance. It describes the action of radiation into matter.

Effects of radiation with high LET

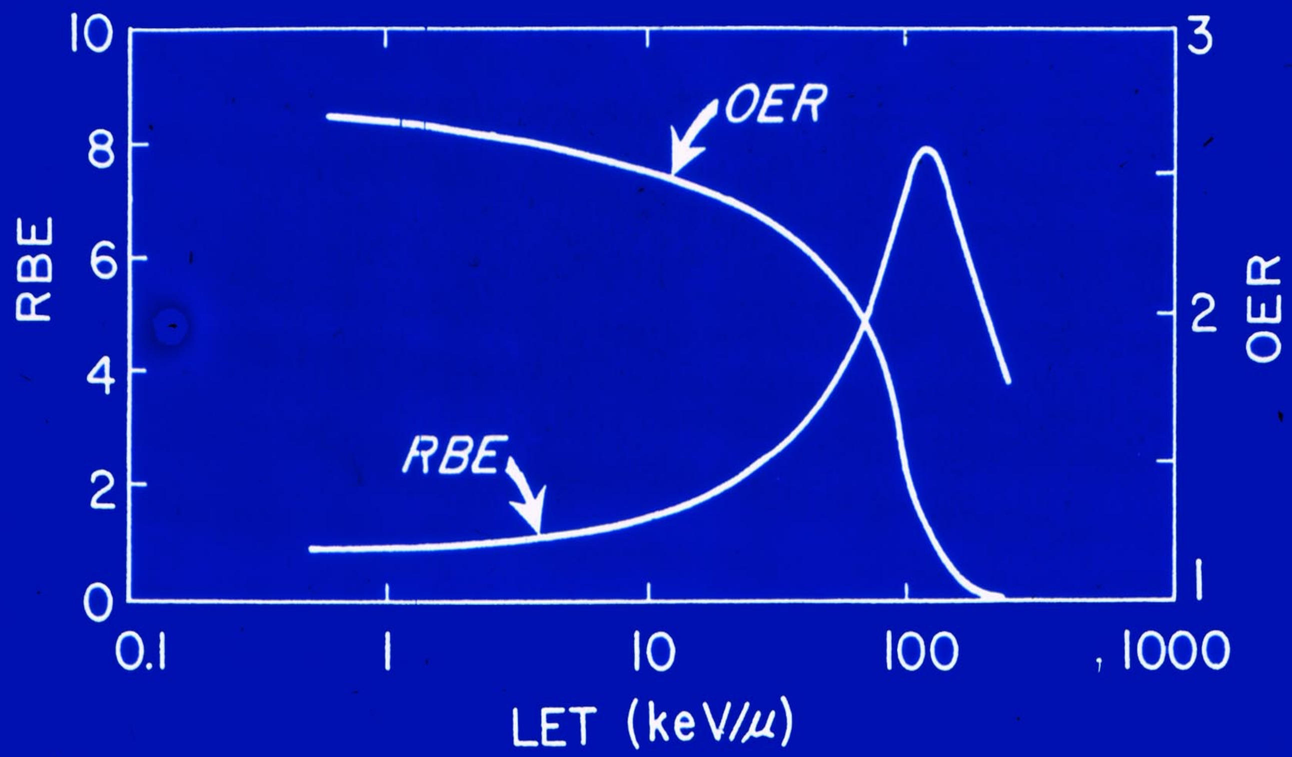
- High ionization density
- Double strand breaks
- Increased biological effectiveness
- Reduced repair capacity
- Reduction of the oxygen effect



Oxygen effect

OER = oxygen enhancement ratio

Variation of the OER and the RBE as a function of the LET of the radiation involved.



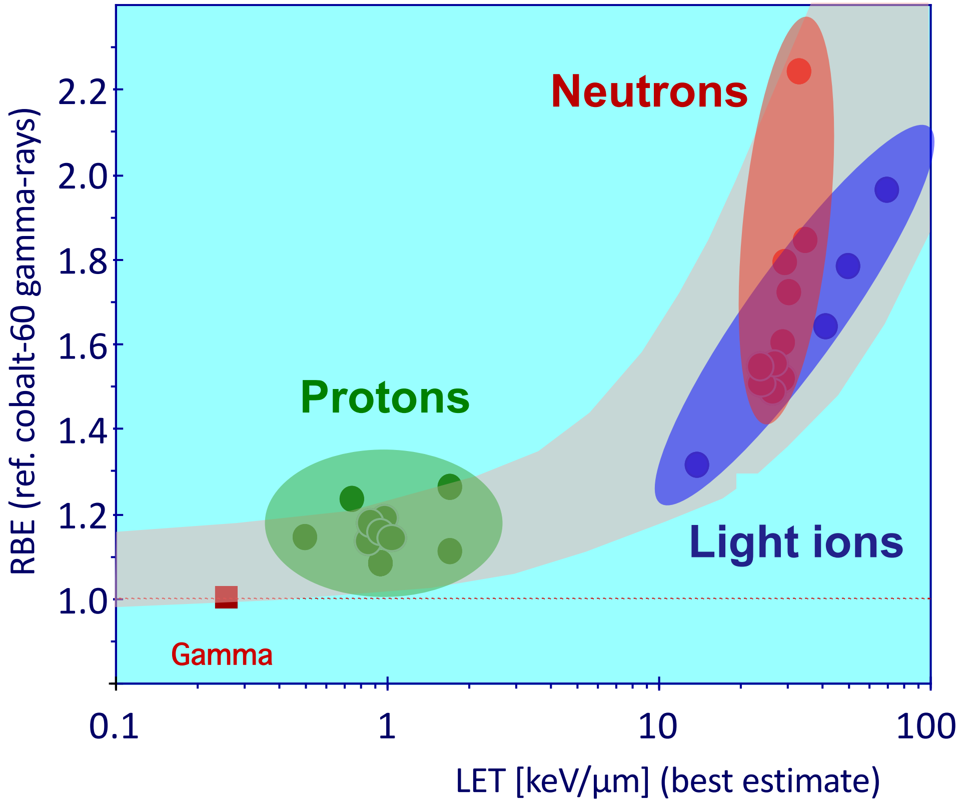
(Redrawn from Barendsen GW 1972)

Radiation Quality

RBEs of fast neutrons and light ions are in the same range

Protons have a low RBE

(except in the fall-off region of the Bragg peak)

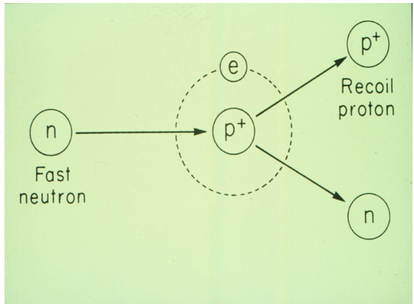


Courtesy J. Guelette

The interactions of neutrons with materials

Fast Neutrons:

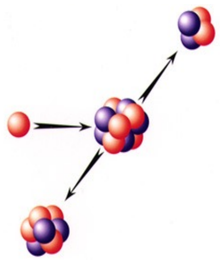
inelastic scattering –
production of recoil protons



Fast neutron therapy

Thermal neutrons

nuclear reactions



Neutron Capture Therapy (BNCT)

Increased late side effects

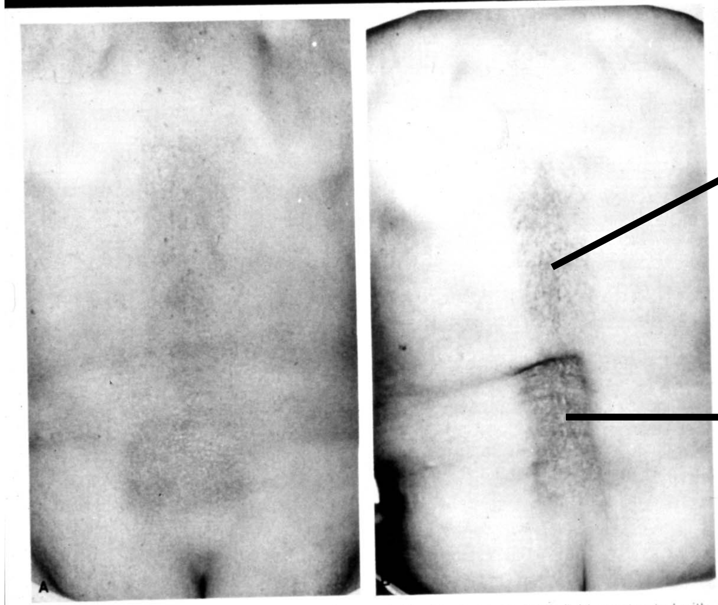
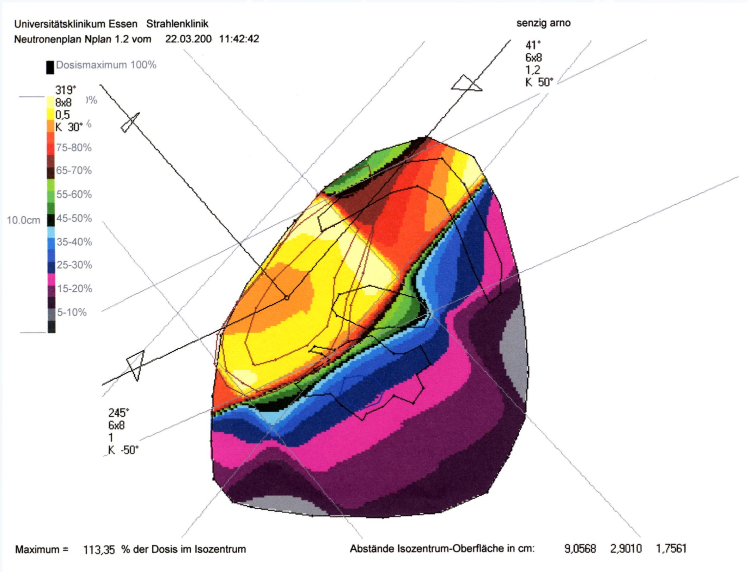


Figure 13-7. A patient treated for ankylosing spondylitis. The top half of the field was treated with x-rays, the bottom half with neutrons. Doses were matched in a 20-fraction regimen so that the early responses to x-rays and neutrons at the end of treatment were equivalent **(A)**. Two years later **(B)**, the neutron-treated area shows a much more severe late response than the area treated with x-rays. This demonstrates clearly that the neutron relative biological effectiveness (RBE) is greater for late- than for early-responding tissues, at least in multifraction regimens. (Courtesy of Prof. William Duncan, Edinburgh University)

W. Duncan, Edinburgh

Ankylosing spondylitis

In contrast to charged particles, the benefit of fast neutrons lies not in their precision, but in their <u>special biological effect</u>



Loko-regionale Kontrolle bei adenoidzystischen Karzinomen

Konventionelle Strahlentherapie

➡ **26% (79/299 Patienten)**

Bestrahlung mit schnellen Neutronen

➡ **67 % (208/309 Patienten)**

(Griffin et al. 1992)

Fast neutron therapy

Adenoid Cystic Carcinoma

3 years

18 years

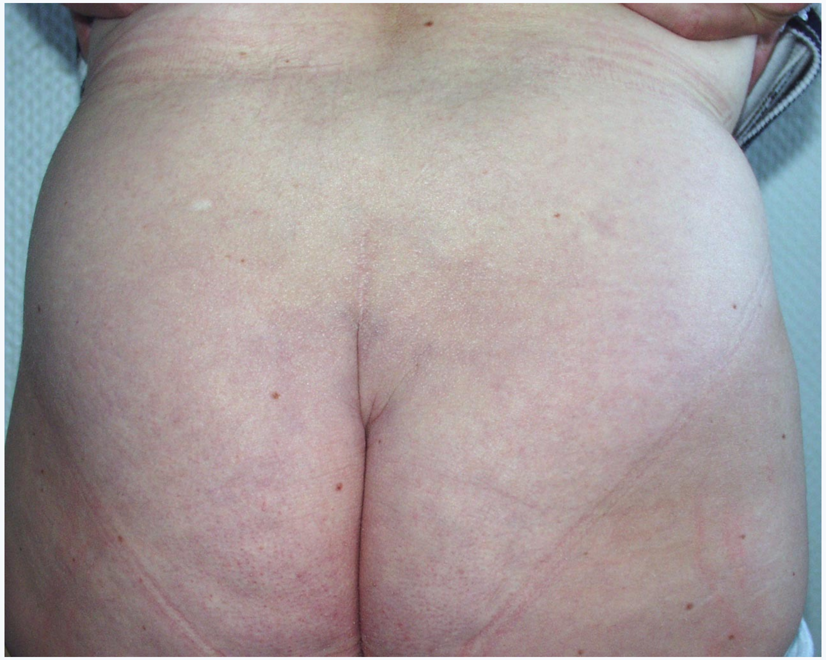
Fibrosis and skin damages

12 years after single field irradiation of a chondro-sarcoma

Fast neutron therapy

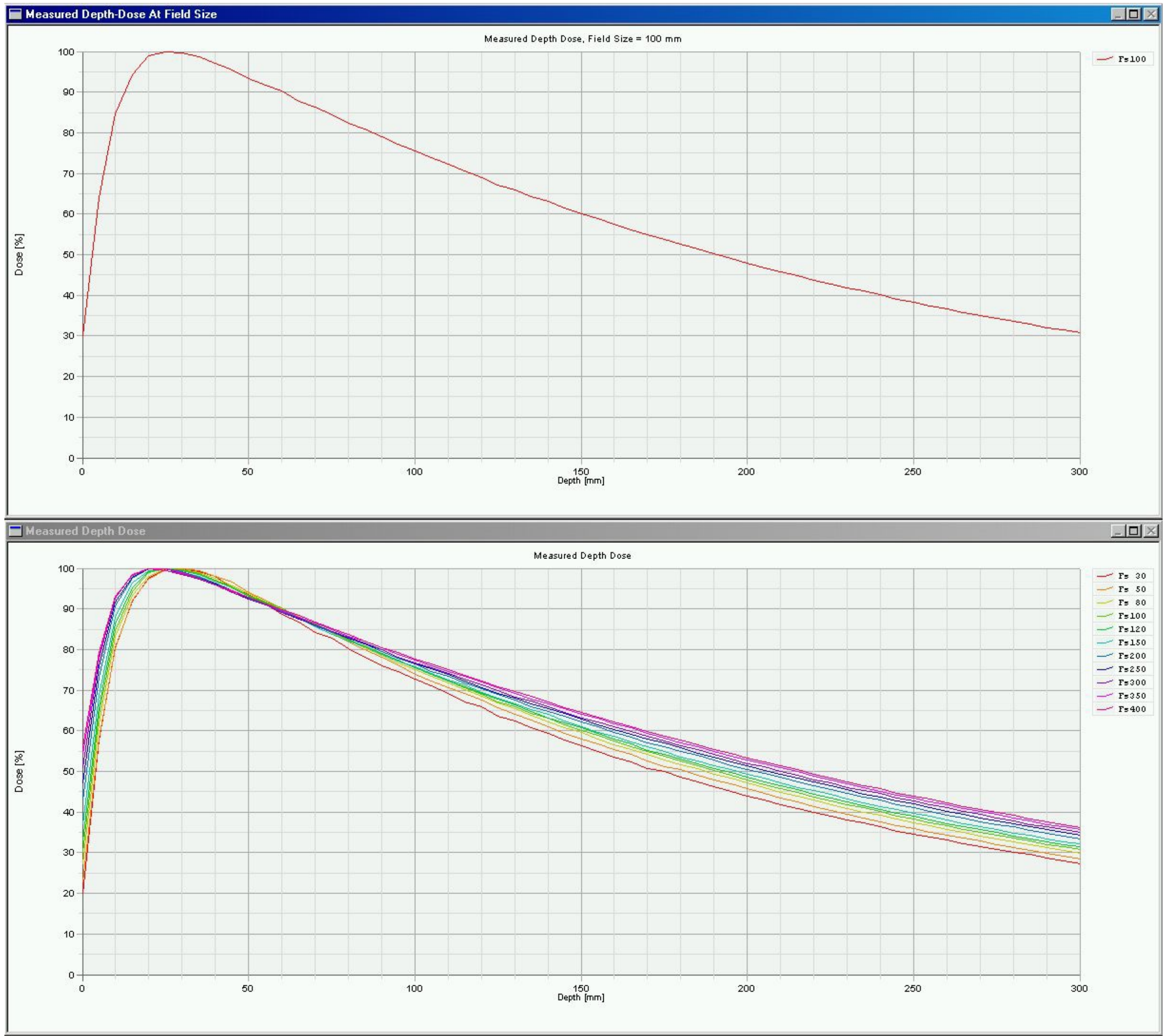
We learned how to handle neutrons

Today’s patients do not show such side effects

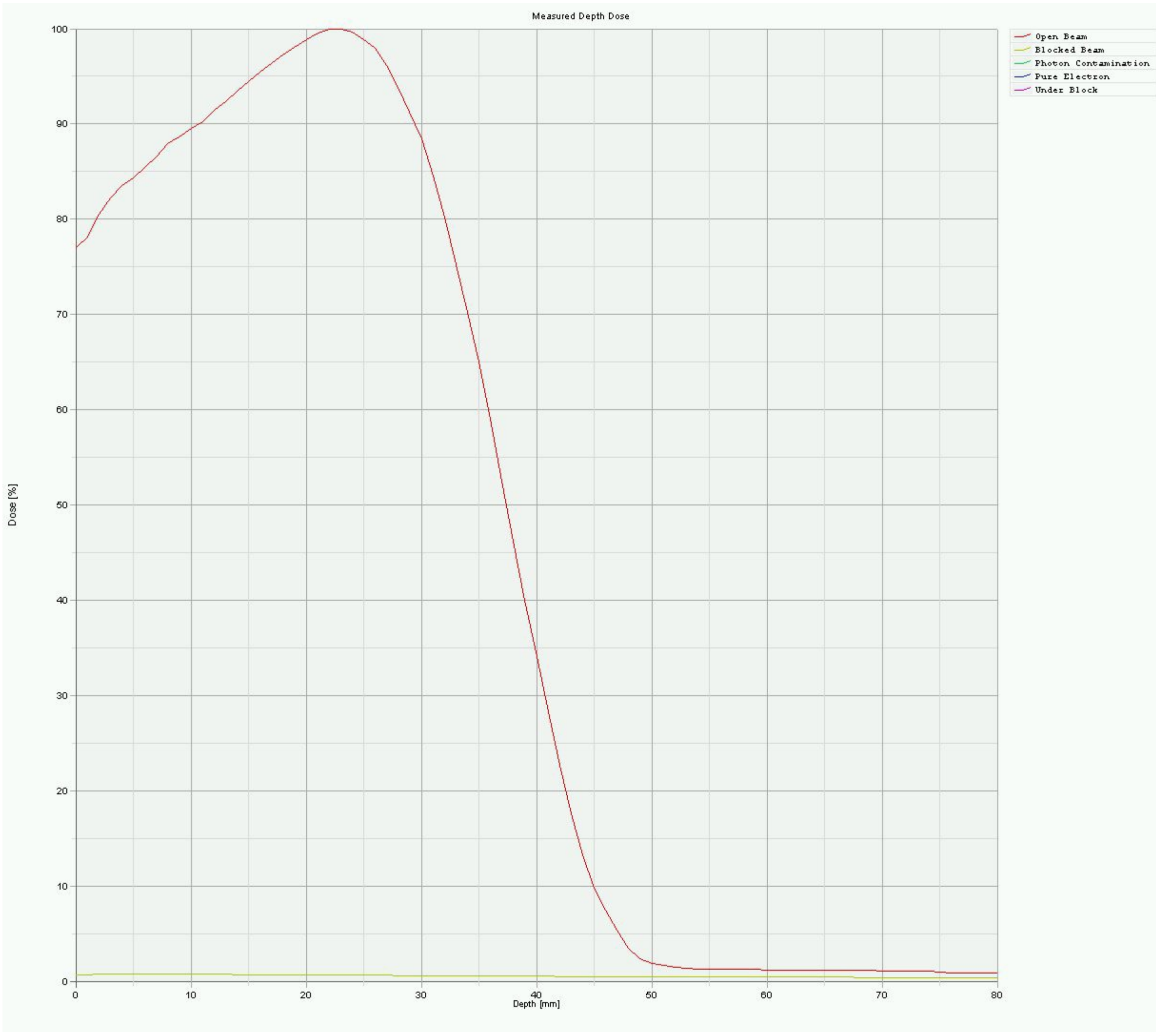


15 years foolow up after treatment of a giant cell tumor invading the entire pelvis and resulting parplegia of the lower

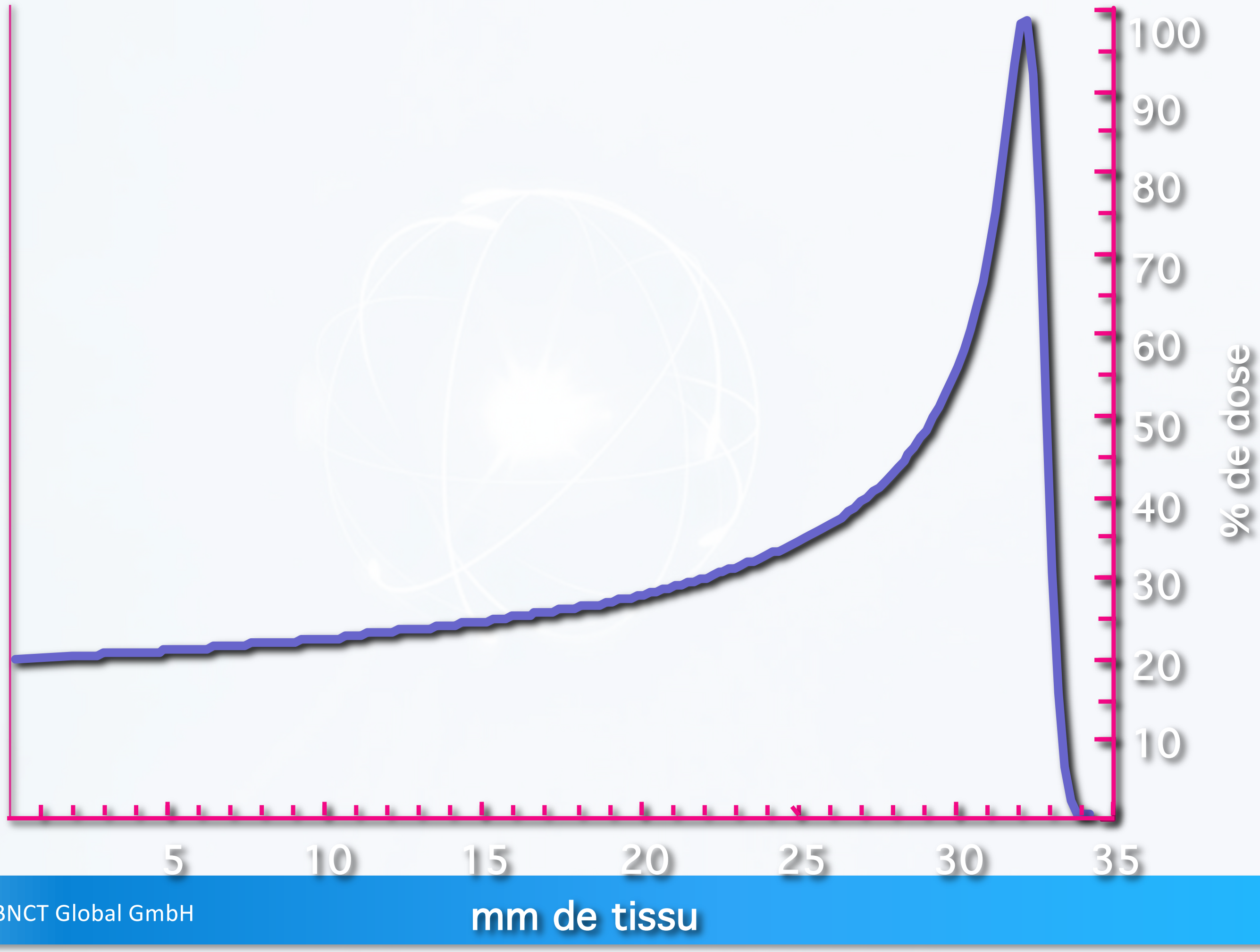
Depth dose distribution (15MV photons)

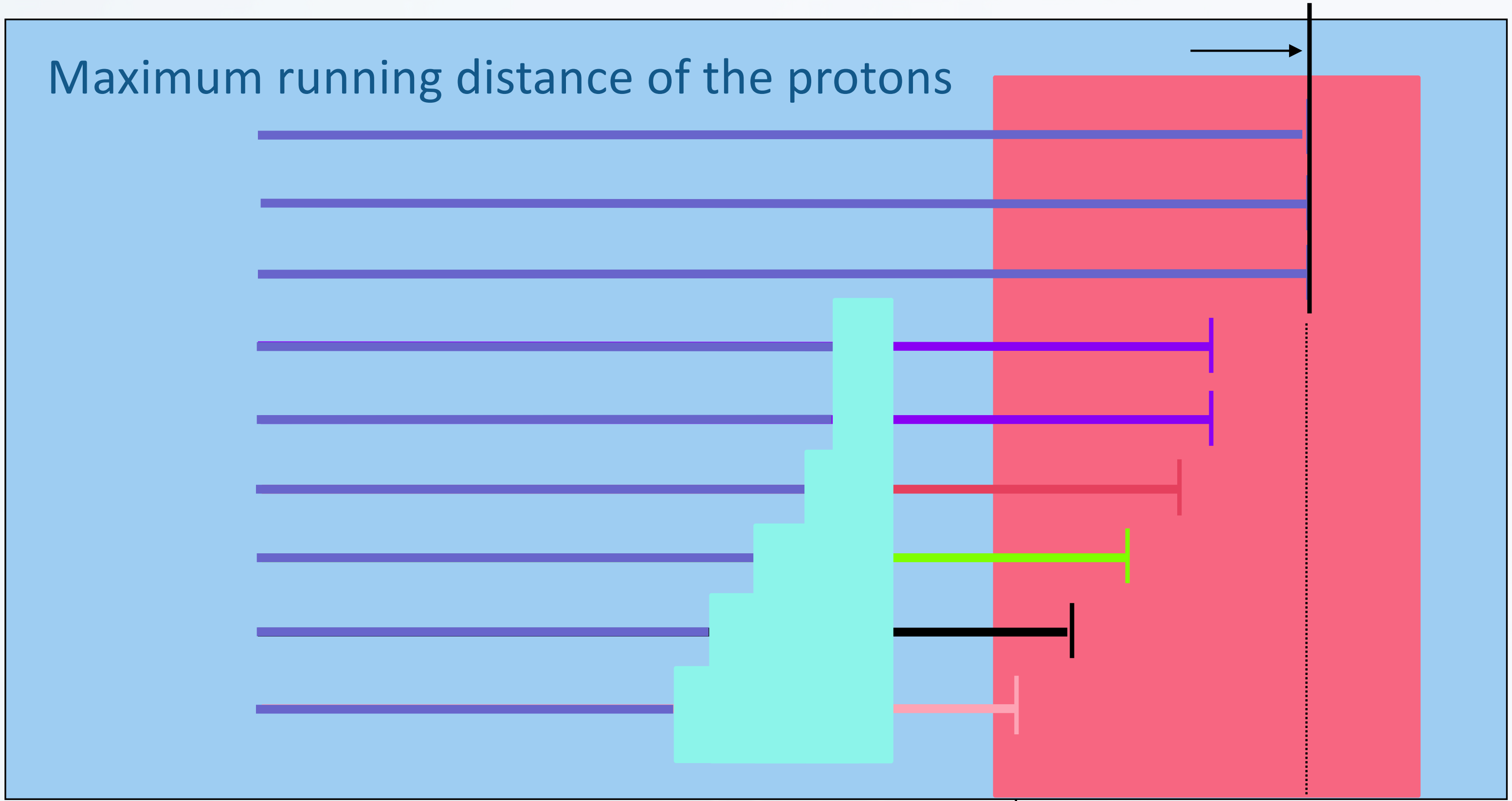


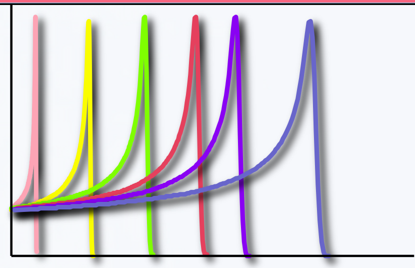
Depth dose distribution - 9MeV electrons



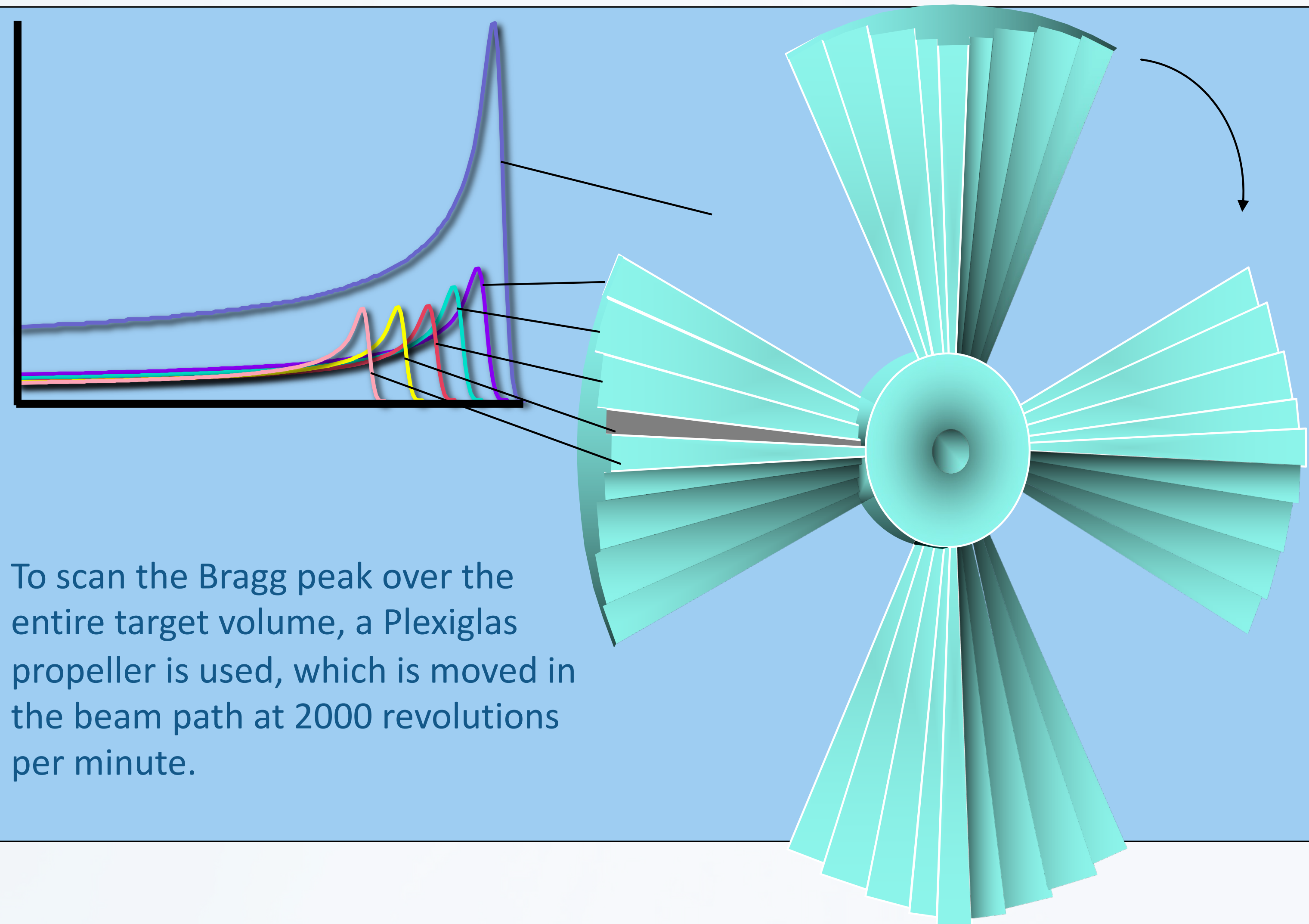
"Bragg-Peak"



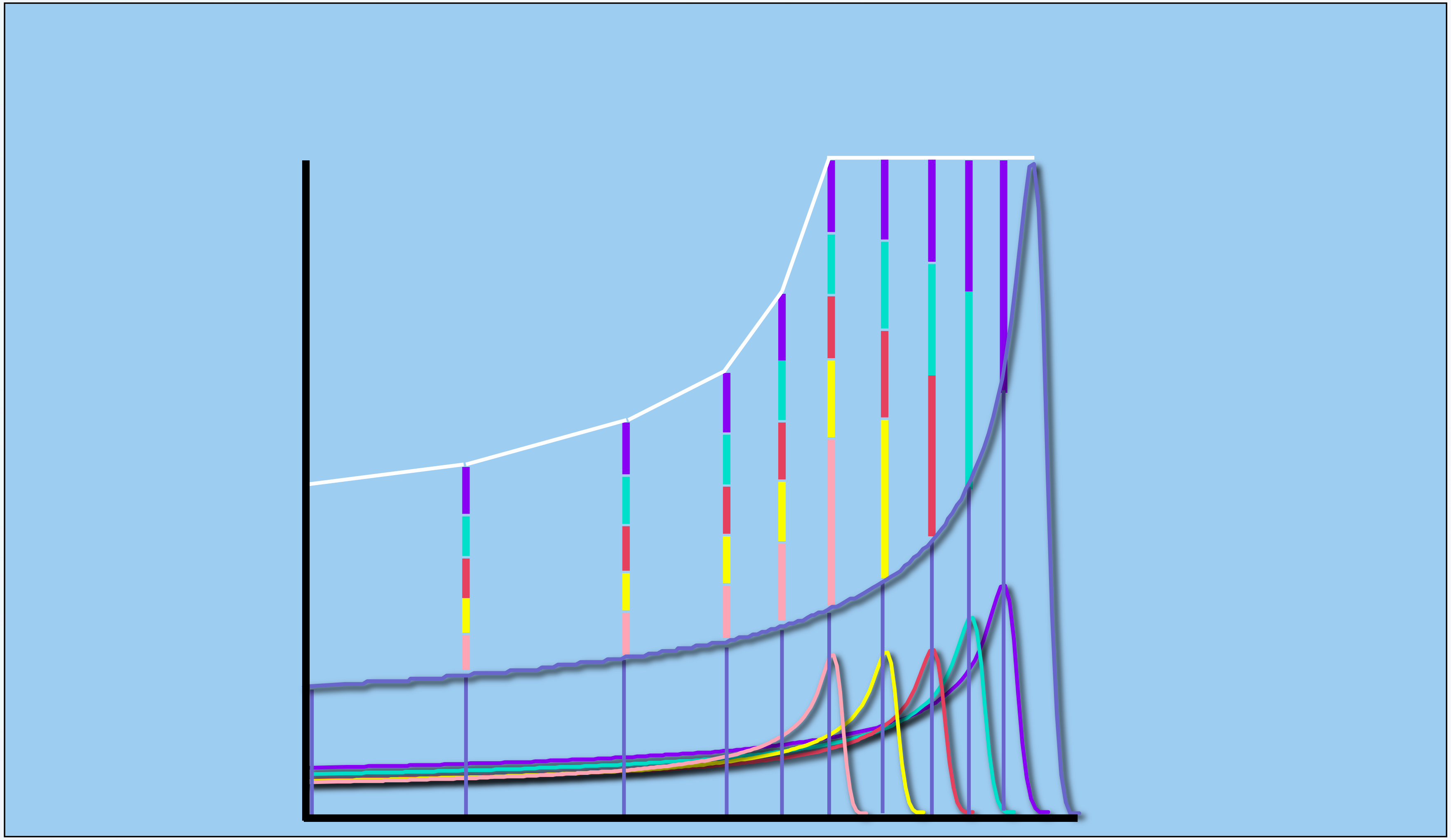




Additional material in the beam path shortens the running distance

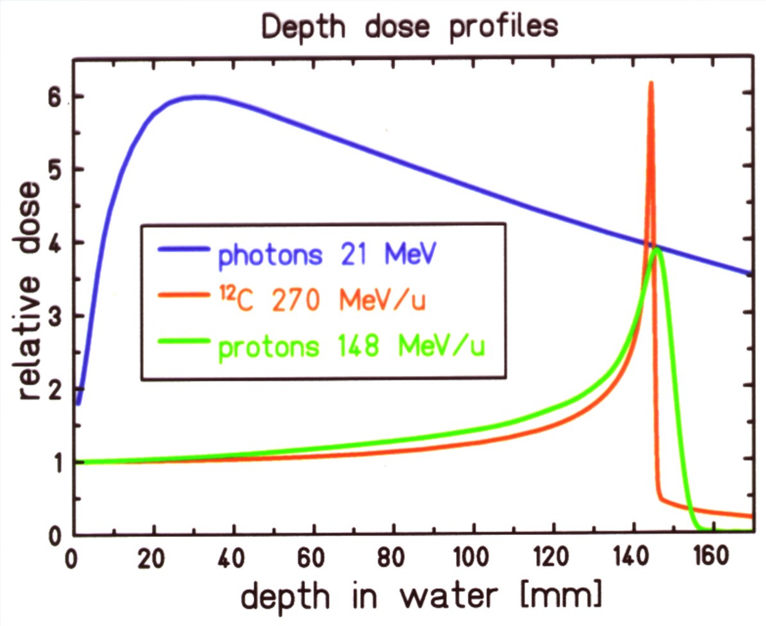


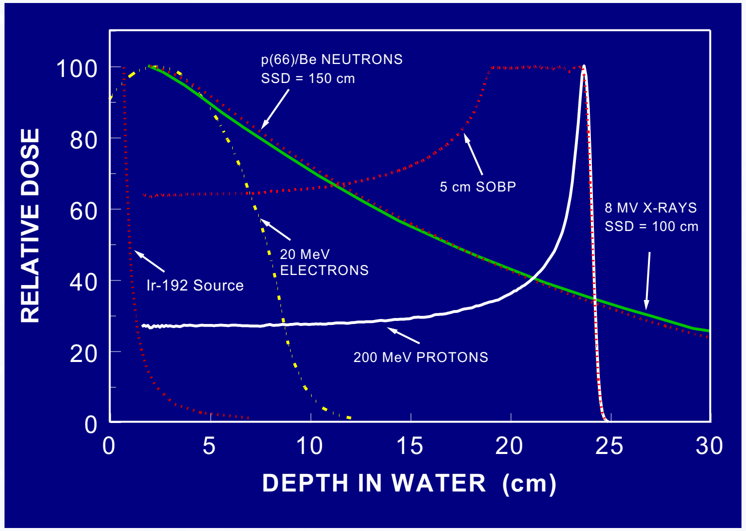
To scan the Bragg peak over the entire target volume, a Plexiglas propeller is used, which is moved in the beam path at 2000 revolutions per minute.



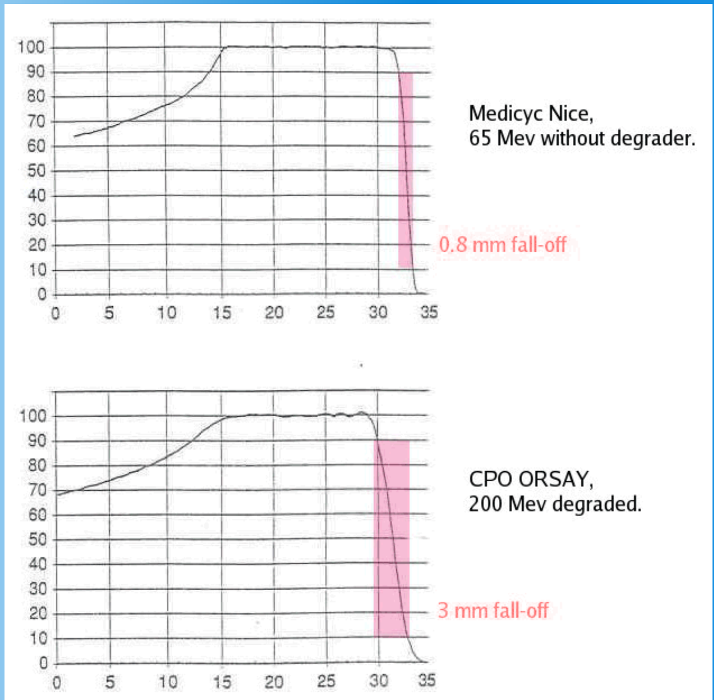
Dose distribution of charged particles

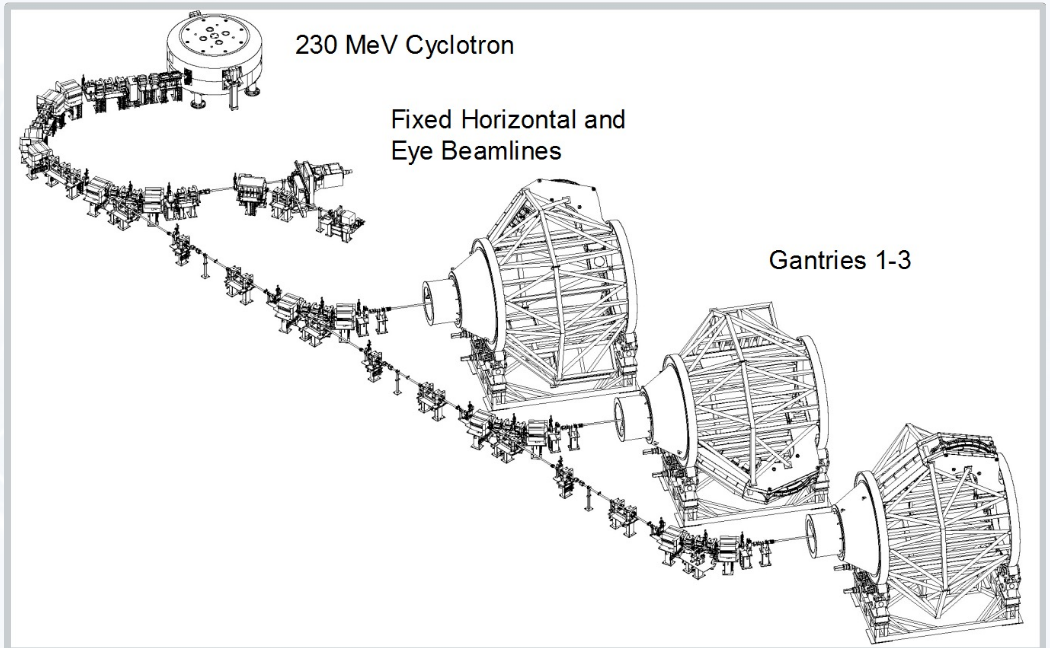
Better or different?





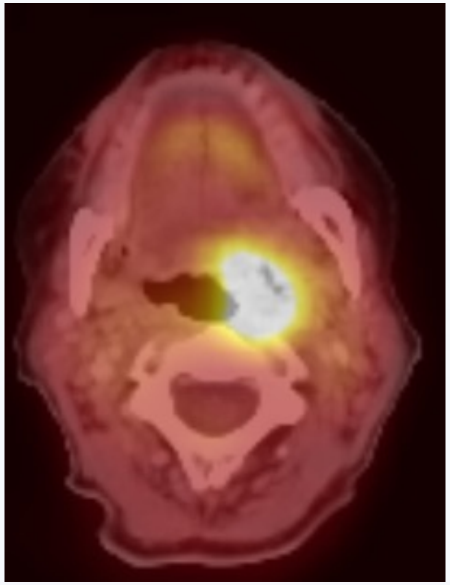
Protons = Protons ?





Why BNCT?
Inherent Challenges with Current RT Techniques

- Treatment is delivered to a volume of tissue
  → Normal tissue in target volume is damaged
- Physicians define target volume on a rather arbitrary basis
  → Target volume will vary with physician and imaging modalities

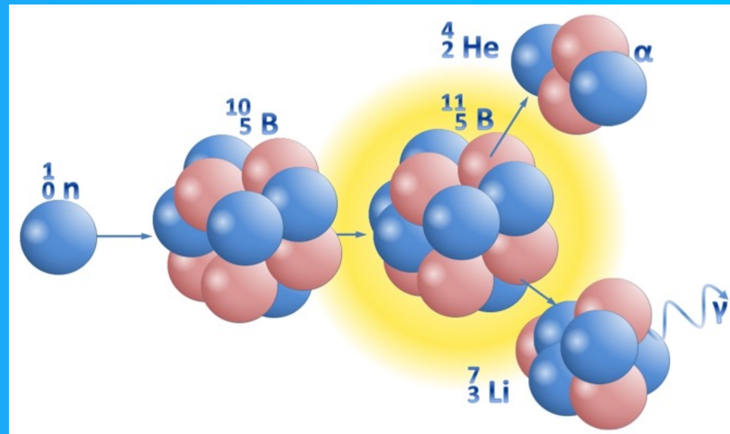


→ **Collateral damage inherently caused and cannot be avoided with conventional treatment methods**

→ **BNCT is effective on the cellular level. The target is defined by biology – not by humans.**

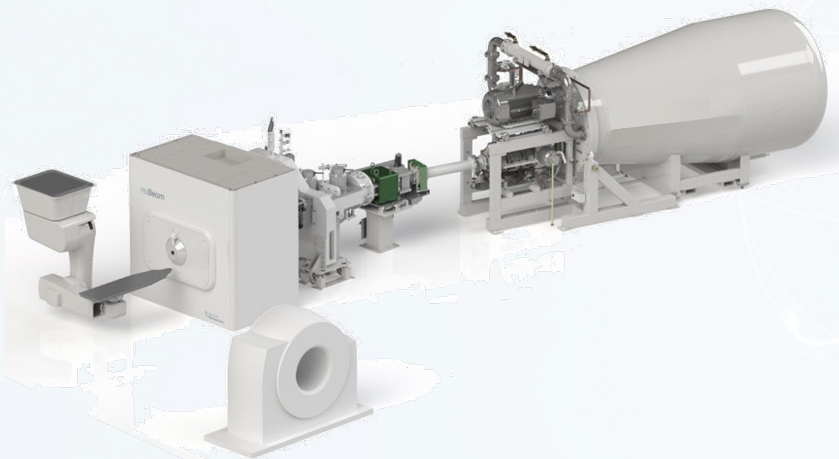
What is Boron Neutron Capture Therapy (BNCT) ?

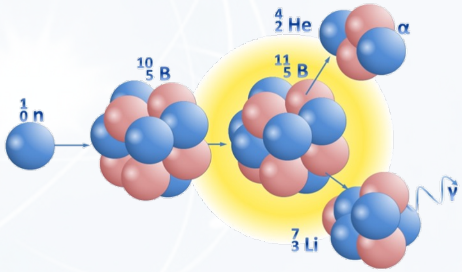
- BNCT uses the ability of the isotope ^{10}B to capture neutrons, resulting in two high-energy particles with short-range in tissue
- This allows the targeted destruction of single tumor cells without damaging directly adjacent normal cells



BNCT: A Binary Treatment Modality

Neutron Delivery System

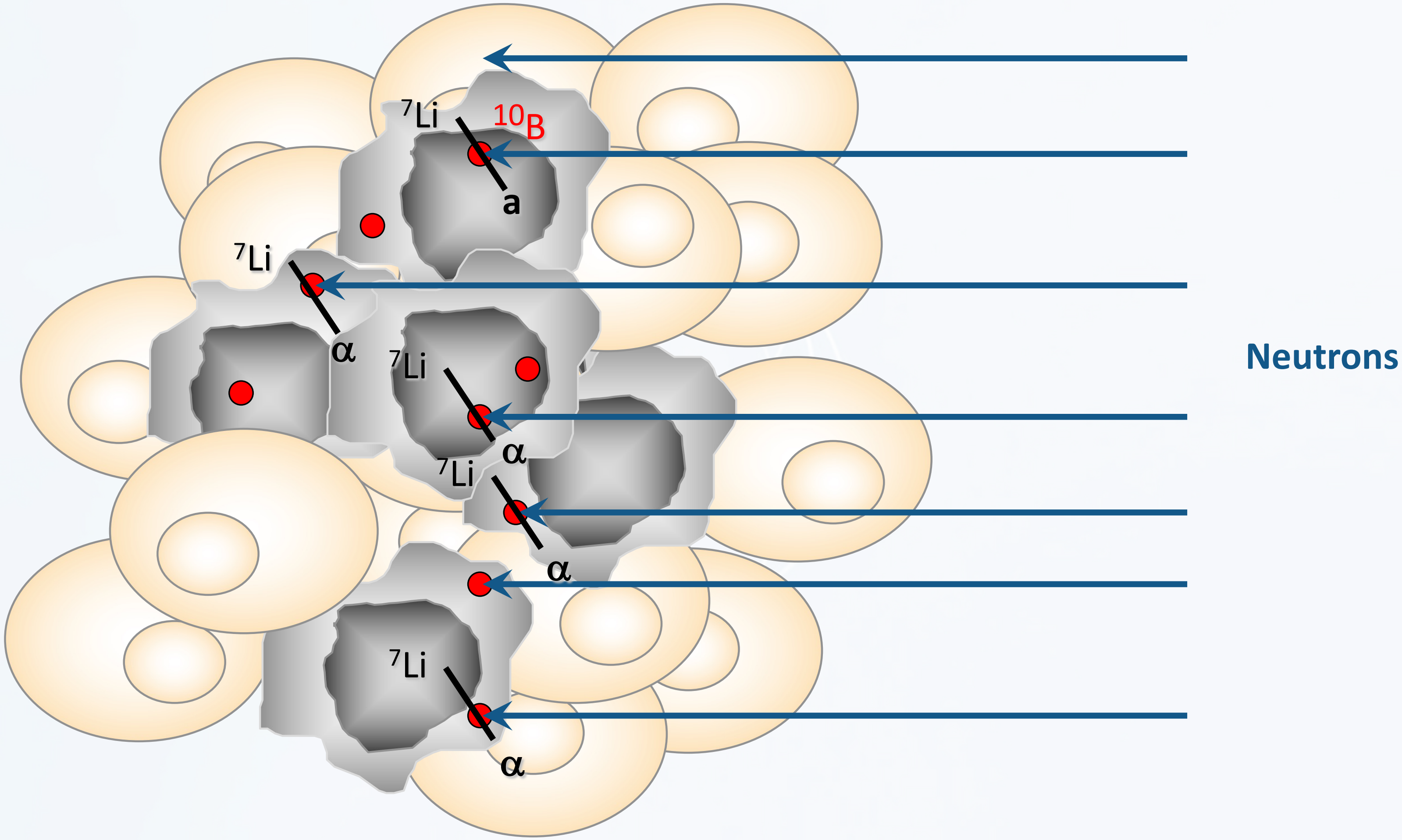




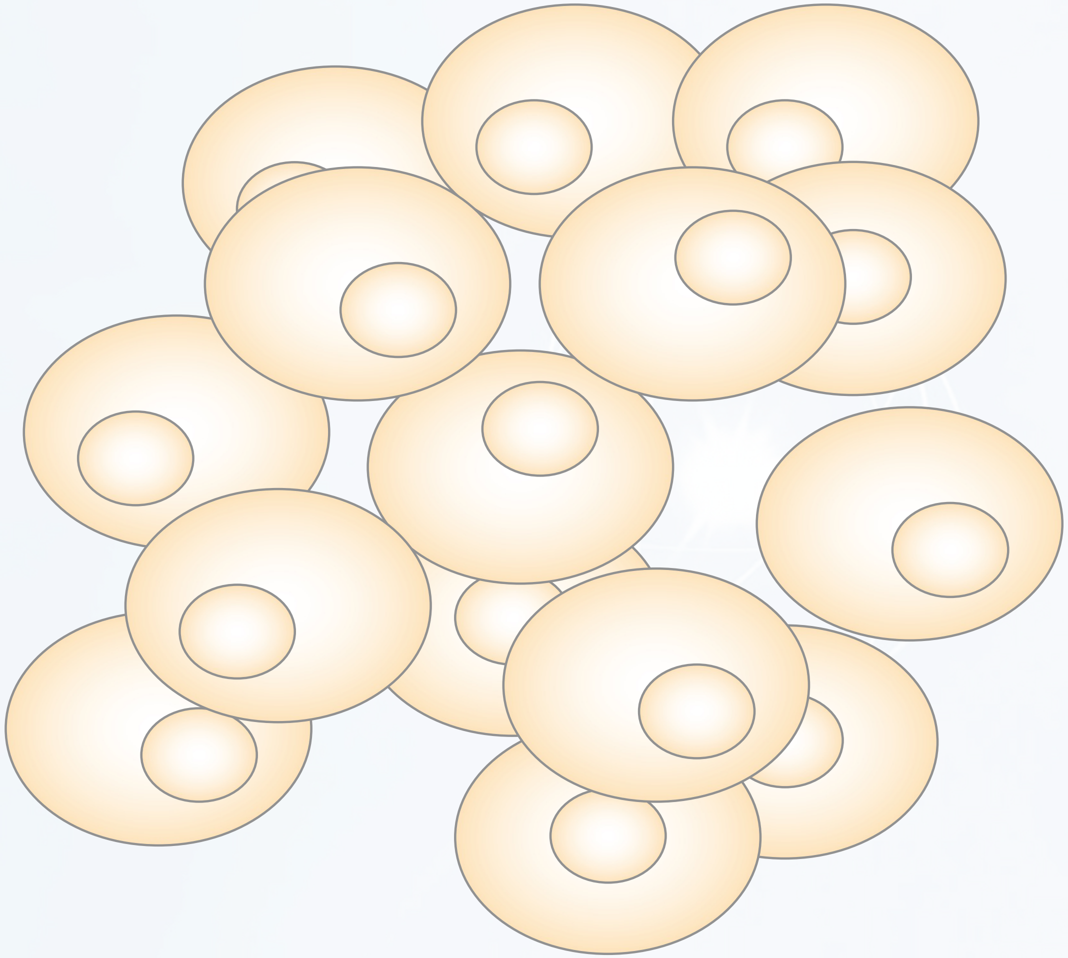
Drug

To be effective, neutrons and drugs must come together. Each of them alone is ineffective.

BNCT



BNCT



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Thank You

For Your Attention