Medicinsk Neutron Vetenskap

2. Neutron terapi
Snabba Neutroner

\[ p (66\text{MeV}) + ^7\text{Be} \rightarrow ^7\text{B} + n \]
\[ D^2 + ^7\text{Be} \rightarrow ^8\text{B} + n (48,5 \text{ MeV}) \]
\[ D^2 + T^3 \rightarrow ^4\text{He} + n (14 \text{ MeV}) \]

Neutroninfångning

Bor (BNCT)
Gd

Fissionsneutroner
Cf-252
Fast neutron therapy utilizes high energy neutrons typically greater than 14 MeV to treat cancer.

Most fast neutron therapy beams are produced from proton beams impinging upon beryllium targets.

\[ p + \text{Be}^7 = \text{B}^7 + n \]

Another alternative to produce fast neutrons is accelerating deuterons (D) in to about 150 keV and hitting a tritium target

\[ \text{D}^2 + \text{T}^3 = \text{He}^4 + n \text{ (14 MeV)} \]
University of Washington Cyclotron produces fast neutrons from directing 50.5 MeV protons onto a beryllium target and is equipped with a gantry mounted delivery system an Multi Leaf Collimator to produce shaped fields.

Photo of the MLC
Schematic of a treatment field delivery. The patient couch has been rotated, along with the gantry so the neutron beam will enter obliquely, to give maximum sparing of normal tissue.
Example of a treatment neutron field collimated using a neutron multi leaf collimator MLC.
$D^2 + Be^7 = B^8+ n(48.5 \text{ MeV})$
Table I: Fast neutron therapy facilities presently operating in the world.

<table>
<thead>
<tr>
<th>Center</th>
<th>Neutron Producing Reaction</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EUROPE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>U.K.</td>
<td>p(62)+Be</td>
<td>rotational gantry, variable collimator</td>
</tr>
<tr>
<td>Orléans</td>
<td>p(34)+Be</td>
<td>vertical beam</td>
</tr>
<tr>
<td>Belgium</td>
<td>p(65)+Be</td>
<td>vertical beam, (multileaf collimator and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>horizontal beam in preparation)</td>
</tr>
<tr>
<td>Germany</td>
<td>(d+T)</td>
<td>rotational gantry</td>
</tr>
<tr>
<td>Hamburg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heidelberg</td>
<td>(d+T)</td>
<td>rotational gantry</td>
</tr>
<tr>
<td>Munster</td>
<td>(d+T)</td>
<td>rotational gantry</td>
</tr>
<tr>
<td>Essen</td>
<td>d(14)+Be</td>
<td>rotational gantry</td>
</tr>
<tr>
<td>Garching-T.U. Münich</td>
<td>reactor neutrons (av. energy 2 MeV)</td>
<td>mixed beam</td>
</tr>
<tr>
<td><strong>UNITED STATES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Texas</td>
<td>p(42)+Be</td>
<td>rotational gantry, variable collimator</td>
</tr>
<tr>
<td>Ohio</td>
<td>p(43)+Be</td>
<td>horizontal beam</td>
</tr>
<tr>
<td>California</td>
<td>p(46)+Be</td>
<td>rotational gantry, variable collimator</td>
</tr>
<tr>
<td>Michigan</td>
<td>d(50)+Be</td>
<td>rotational gantry, multirood collimator</td>
</tr>
<tr>
<td>Washington</td>
<td>p(50)+Be</td>
<td>rotational gantry, multileaf collimator</td>
</tr>
<tr>
<td>Illinois</td>
<td>p(66)+Be</td>
<td>horizontal beam</td>
</tr>
<tr>
<td><strong>ASIA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>d(30)+Be</td>
<td>vertical beam, multileaf collimator</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>d(14)+Be</td>
<td>horizontal beam</td>
</tr>
<tr>
<td>Korea</td>
<td>d(50.6)+Be</td>
<td>rotational gantry</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>p(26)+Be</td>
<td>rotational gantry</td>
</tr>
<tr>
<td><strong>AFRICA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Africa</td>
<td>p(66)+Be</td>
<td>rotational gantry, variable collimator</td>
</tr>
</tbody>
</table>
Fast neutrons are high LET radiation and the damage done primarily by nuclear interactions.

In general fast neutrons can control large tumors because, unlike low LET radiation, neutrons do not depend on the presence of oxygen to kill the cancer cells.

In addition, the biological neutron biological effectiveness is not affected by the stage in the life cycle of cancer cells as it is with low LET radiation.

The required absorbed dose of neutrons to kill the same number of cancer cells is about one third the dose required with low LET radiation.

A full course of treatment consists of 12 treatments, three times a week for four weeks, compared to 340 treatments, five times a week for six weeks with photons, electrons, or protons.
Advantages of Neutron Therapy:

The biological effectiveness of neutrons is not affected by the growth stage of tumor cells. Most other forms of radiation are more effective on cells that are actively reproducing and on those that divide more rapidly than normal. They are less effective on cells that are in the resting phase or divide slowly.

The higher biological effectiveness of neutrons results in a required dose that is about one-third the dose required with photons, electrons or protons.

Fewer treatments (10-12) over a shorter period of time (~ 4 weeks) are necessary with the high LET neutron therapy as compared with the different forms of low LET radiation (30-40 over 6-8 weeks).

The damage done to the cell DNA structure is often irreparable permanently halting cell reproduction and tumor growth.

Unlike low LET radiation neutrons do not depend on the presence of oxygen to be effective. This is especially critical when considering large tumors that do not have good blood, and hence oxygen supply.
Unique, proven treatment option The Northern Illinois University Institute for Neutron Therapy at Fermilab is one of only two sites in the United States offering neutron therapy to cancer patients.

Neutron therapy blends advanced medical science with cutting-edge accelerator physics developed at Fermi National Accelerator laboratory, located in Chicago’s western suburbs.

The neutron therapy clinic at Fermilab has treated more than 3,100 patients and has been in operation longer than any other neutron therapy program in the nation.

In 2004, Northern Illinois University assumed management of the facility.
What is Neutron Therapy?

Neutron therapy is a highly effective form of radiation therapy. Long-term experience with treating cancer has shown that certain tumor types (histologies) are very difficult to kill using conventional radiation therapy. These histologies are classified as being "radioresistant."

Neutron therapy specializes in treating inoperable, radioresistant tumours occurring anywhere in the body.

- adenoidcystic carcinoma
- locally advanced prostate cancer
- locally advanced head and neck tumors
- inoperable sarcomas
- cancer of the salivary glands
Figure 6: Locally extended prostatic adenocarcinoma. RTOG randomized trial comparing a combination of fast neutrons and photons ("mixed-beam") and conventional photon irradiation alone. (a) The actuarial survival rates at 8 years are indicated, adjusted by exclusion of intercurrent non-cancer death ("determinental" survival rates). (b) The local control rates are indicated, combining clinical and biopsy criteria (Russell et al., 1987).
BNCT
(BORON NEUTRON CAPTURE THERAPY)

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• Institutionen för Radiofysik
• Institutionen för Neurokirurgi
• Institutionen för Kärnfysik
• Institutionen för Neuropatologi
• Institutionen för Biokemi
Behandling i två steg

1. Stabilt $^{10}$B ges Intravenöst som Bor-fenyl-alanin

2. $^{10}$B aktiveras i tumören

Termiska neutroner
Neutroninfångning i bor-10

Termiska neutroner infångas av $^{10}$B

Energin (2.3 MeV) deponeras mycket lokalt

Prompt gamma
Kärnreaktioner i hjärnan

Diagramm med elementer 4He och 7Li.
Forskningsreaktorn i Studsvik
BNCT Faciliteten

1. Clinical area
2. Patient rooms
3. Stepover area
4. Air lock
5. BNCT control room
6. Treatment room
7. Filter assembly
8. R2-0 reactor
9. Reactor pool
10. R2 reactor
Bestrålning
Dos vs. reaktor effekt

![Graph showing the relationship between Absorberad dos (Gy/h) and Reaktor effekt (kW). The graph shows a linear trend with data points.]
Relativa dosfördelningar
Bor-blod koncentration

Boron concentration [ppm] vs. Time after end of infusion [h]
Prompt-gamma spektroskopi (PGS)

• Mätning av infångningsgamma utsända från bor och väte i patient under bestrålning.
• Räknehastigheten i detektorn för linjerna kan relateras till borkoncentrationen in-vivo.
Figure 1. Kaplan–Meier plots of overall survival for the two Boron Neutron Capture Therapy studies. Curves plotted and median survival times calculated using the statistical package STATA: version 9.2 for Windows (College Station, TX, USA).
Figure 2. (A) Coronal whole brain section through frontal lobes showing a right-sided cavity, microscopically surrounded by tumor. The sizes of the surgical cavities seen on the whole brain sections correspond largely to those seen on pre-treatment CT images. Black arrow indicates site of microscopical view in fig. (2B), blue arrow that in fig. (2C). (hematoxylin and eosin). (B) Recurrence or remnant of original tumor outside of the central target area (at site of black arrow in fig. (2A)) showing high cell density with pleomorphism, malignant vessels but no necroses, as in a glioma grade III (hematoxylin and eosin). Magnification 170x. (C) Tumor within target area (at site of blue arrow in fig. (2A)) surrounding the complete necrosis displays scattered pleomorphic cells, moderate cell density and thin walled normal vessels and thus devoid of malignant features other than pleomorphism (hematoxylin and eosin). Magnification 150x. (D) Tumor within target area and surrounding the complete necrosis displays reduced cell density, moderate pleomorphism but no malignant vessels and thus devoid of malignant features other than pleomorphism (hematoxylin and eosin). Magnification 160x.
BNCT is a single-day treatment, with mild side effects, which would offer patients an initial 6 weeks with essentially undisrupted quality of life, compared with standard fractionated RT, which involves a total of 30 daily treatments over a period of 6 weeks. It is suggested that the efficacy of BNCT, with the prolonged infusion procedure used at Studsvik, should be assessed in a controlled trial, as an alternative to standard fractionated RT for GBM.
Californium is a radioactive metallic chemical element with the symbol Cf and atomic number 98. The element was first produced in the laboratory in 1950 by bombarding curium with alpha particles (helium ions) at the University of California, Berkeley.

\[ ^{242}_{96}\text{Cm} + ^{4}_{2}\text{He} \rightarrow ^{245}_{98}\text{Cf} + ^{1}_{0}\mu \]

Prolonged irradiation of americium, curium, and plutonium with neutrons produces milligram amounts of californium-252 and microgram amounts of californium-249.

Californium-252 decays with a half-time of 2.645 a:
- 96.9% alpha decay to form curium-248
- 3.1% of decays are spontaneous fission.

Californium-252 is a very strong neutron emitter, which makes it extremely radioactive and harmful but useful as a neutron source.

One microgram (μg) of californium-252 emits 2.3 million neutrons per second, an average of 3.7 neutrons per spontaneous fission.
Cf-252 is used as a brachiotherapy source for treatment of cervical cancer. 252Cf group. The dose at point in the paracervical space is about 56 Gy-eq – for patients treated intracavitarily with Cf-253 plus gamma radiation divided into two parts.

In the first week of therapy, 6 Gy (40 Gy-eq) of the 252Cf neutron component are applied.

In the fifth week of therapy 16 Gy absorbed dose of gamma radiation are given intracavitary

The clinical results of Cf-252 usage in tumor brachytherapy show that it is a highly effective method of treatment that is able to eliminate tumor cells resistant to conventional gamma radiation.

It should be noted that compared to external, fast neutron therapy, Cf-252 brachytherapy allows direct interaction of the neutrons with cells of the tumor population and thus the postradiation damage of healthy tissues is minimized.
Fig. 4. Local relapse-free survival comparison of stage IIIb cervical carcinoma.