ANTIPROTON CANCER THERAPY

Presented by the **AD-4/ACE** collaboration*

Poster available at http://www.phys.au.dk/~hk/ad4homepage.html

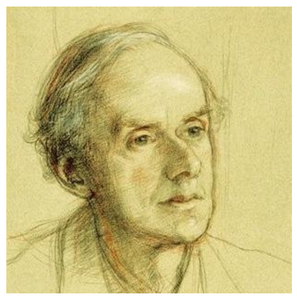
AARHUS PARTICLE THERAPY GROUP

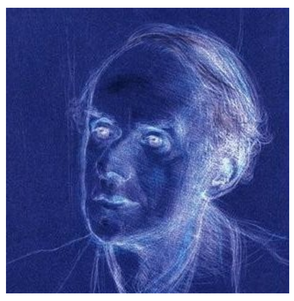
AARHUS UNIVERSITET

DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

ANTIMATTER

The existence of **antimatter** was first proposed by P.A.M. Dirac in 1928. He examined the wave equation of an electron in an arbitrary electron magnetic field. This **equation** had a **quadratic form**, and could be solved for an **electron with negative charge**, but also for a similar particle with **positive charge**. The **antielectron** was discovered 5 years later by C.D. Anderson. Similarly, the proton has an antiparticle, which is the **antiproton**. Antiprotons were already discovered in 1955 by Chamberlain et al.





Antimatter is similar to normal matter, just where the **charge sign is reversed.** Thus, the antiproton has a **negative** charge. When matter and antimatter meets, they **annihilate**, releasing their rest mass as energy according to $E=mc^2$. An antiproton annihilating on one proton results in **1.88 GeV** released energy. Thus, **one gram** of antihydrogen annihilating on matter releases energy corresponding to **3 Hiroshima** nuclear bombs.

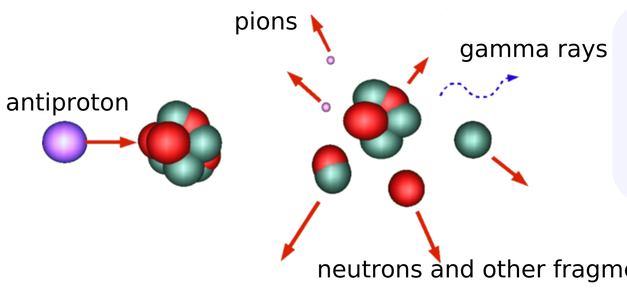
ANTIPROTON PRODUCTION

In spite of the popular perception of the availability of antiprotons (as in **Dan Brown's** bestseller "Angels and Demons"), it must be mentioned that the **production of antiprotons is very cumbersome.** Currently, only the European Organization for Nuclear Research **(CERN)** at Geneva, can provide a beam of antiprotons with low enough energy. Here, a 26 GeV proton beam from the proton synchrotron (PS) is dumped into an iridium target. For each spill, a few antiprotons are produced, which then are being collected and cooled at the **antiproton decelerator** (AD). The energy is reduced to almost **50 MeV**, giving a spill of **3e7** antiprotons (50 billionth of a nanogram!) every 90 seconds.

CERN. Geneva airport is seen to the right. The large ring is the LHC with a circumference is 26 km. For antiproton production, only the small PS and AD accelerators are used on the Meyrin site.

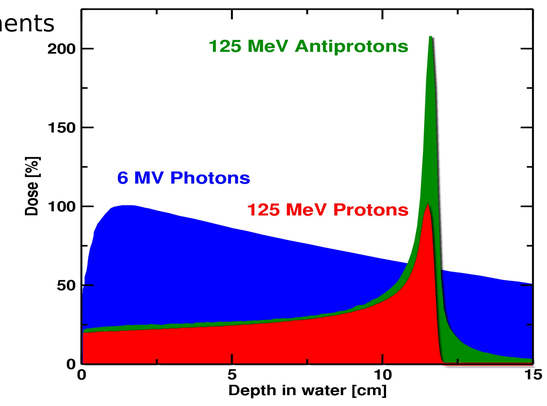
ANTIPROTON THERAPY

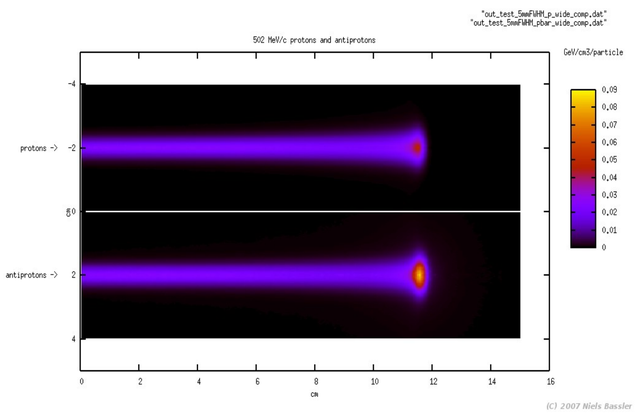
Antiprotons have some properties, which make them very relevant for radiotherapy:



1) When an antiproton stops, it will immediately annihilate on another nuclei. Most of the 1.88 GeV energy released is carried away by pions and gamma rays, but roughly **30 MeV** is **deposited locally** as kinetic energy from recoiling heavy nuclei.

2) Antiprotons behave like ordinary protons in the **plateau** region. Therefore the dosimetry is known. Also this is **Low-LET** radiation, just as protons, with known radiobiology. **Fractionation** benefits are **maintained**. **High-LET** radiation from the annihilation fragments is found at the **Annihilation-peak**. Antiprotons thus features low RBE in the plateau and high RBE in the peak.





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3) The pions and gamma rays emerging from antiproton annihilations can directly be used for **online monitoring** of the irradiation process with similar techniques known from PET. One may get an **instant** image of the dose deposition.

To the left : FLUKA calculation of the relative dose deposited by a ~126 MeV proton and antiproton beam in a water target. (iso-fluence)

THE AD-4/ACE COLLABORATION

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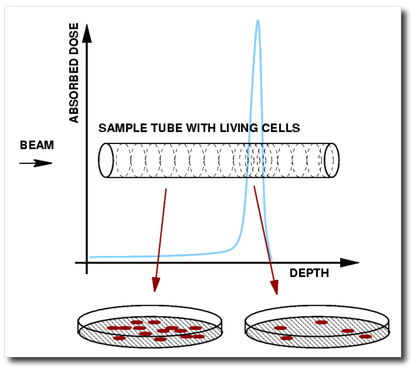
ANTIPROTON EXPERIMENTS AND RESULTS

In 2003 the **AD4/ACE collaboration** was formed in order to investigate the **biological effect** of the antiproton beam. We designed a setup, where a standard cell line (Chinese hamster cells, V79, WNRE) are irradiated with antiprotons.
We want to measure the **Relative Biological Effectiveness** (RBE) of the antiproton beam, which is the **ratio of dose** needed **to produce a certain biological effect** (such as killing 90.0 % of the cells) **for antiprotons and for a reference radition**, such as X-rays from a conventional radiotherapy unit. For instance, an RBE of 2 for antiprotons, means that ½ of physical dose deposited produces the same cell killing effect for antiprotons compared to conventional X-rays.

In order to measure the RBE, we need to understand the dosimetry of the antiprotons. The dosimetry is **complicated** by the **mixed radiation field** arising from the annihilating antiprotons and the sharp beam pulses of the antiproton beam from the antiproton decelerator.

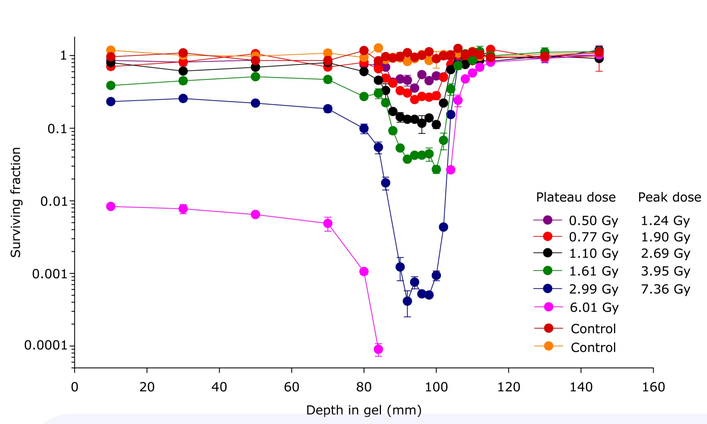


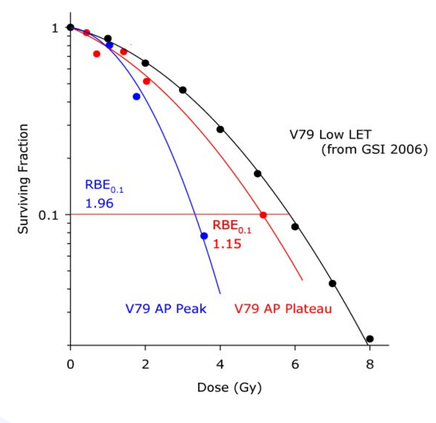
The AD4/ACE biology experiment.
The tube containing the hamster cells was irradiated with antiprotons. The gel matrix was extruded and cells were plated from several slices along the axis [1].

The most exact way of measuring absorbed dose, would be **calorimetry**, were the **radiation induced temperature increase** in the target medium (water or graphite) is measured. However, calorimetry is cumbersome and very difficult to setup.
Instead we relied on another dosimetry method with **ionization chambers**. Here, correction factors must be applied, but we found our experimental results to be in excelent agreement with theoretical predictions [2].

Finally several **solid state dosimeters** were tested, such as thermoluminescent detectors, radiochromic films and alanine detectors. **Alanine** is an amino acid, which forms a stable radical (unparied electron) upon irradiation. The **amount of radicals can be read out** with by electron spin resonance (ESR). Alanine pressed to small pellets have proven to be most reliable, and are now used in our group as an **redundant antiproton dosimeter** [3].

PRELIMINARY RESULTS





Several tubes of V79 hamster cells cooled down to 4 ˚C are irradiated with various amounts of antiprotons. After irradiation, the tubes are flown to a **radiobiology laboratory** in Aarhus, Denmark, where the tubes are sliced and the amount of **surviving cells are counted**. This figure clearly shows that **less cells survive** in the peak region.

(The peak region was widened to 1 cm width by using multiple energies of antiprotons for irradiation.)

Our results indicate almost a **doubling of the RBE** in the peak region from the entry region. However, these data are not final yet since more data sets are needed.

RBE_{01} -peak = 1.96
RBE_{01} -plateau = 1.15

Data points extracted from the figure to the left, here plotted for the **plateau region** (at 2 cm penetration depth) and **peak region** (at 9 cm penetration depth) and a reference radiation (Co-60 gamma rays).

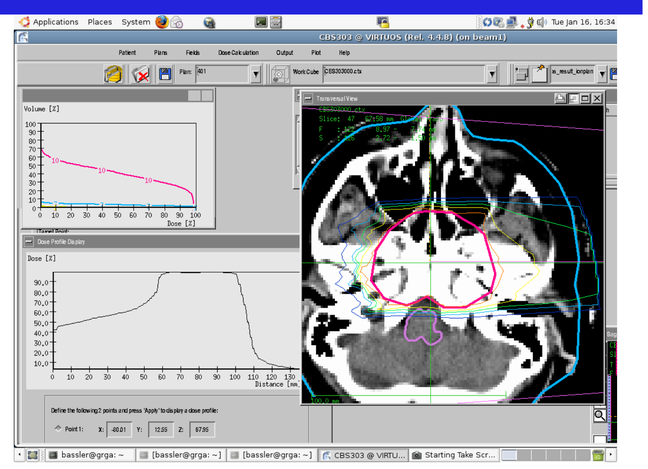
This figure also summarizes our **interdisciplinary** efforts: **biologists** are responsible for the y-axis, **physicists** for the x-axis...

CURRENT DEVELOPMENT

The goal is to do planning studies with antiprotons using the knowledge gained about the dosimetry, the particle spectrum of annihialtion products, and the **RBE** in the annihilation peak. The dose planning system **TRiP**, which is used by the DKFZ for carbon ion beams, is modified to **feature antiproton beams as well**.
Planning studies may give a clearer picture of the anticipated benefits of antiproton radiotherapy.

The cell experiment was repeated with **carbon ions** at **GSI in Darmstadt**, Germany for comparison with antiprotons.

In addition we are measuring the effect of the **secondary particles** which leave the target region. Again, both **dosimetric** and **radiobiologic** experiments are performed.



Above: The very first treatment plan with antiprotons using TRiP. The input data for the antiprotons are based on benchmarked Monte Carlo simulations. Currently only physical dose is modeled, but work is done to include the radiobiology**!**.

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