

Editorial

Antiprotons for radiotherapy?

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The paper by Holzscheiter et al. in the current issue [5] reports the first measurement of the biological consequences of antiproton irradiation. This paper takes one back to the days when the science of a new exotic particle could generate great excitement, untarnished by the need to address the practicality or the economics of translating the basic discovery into routine clinical practice! What is certain is that antiproton facilities are unlikely to appear on every street corner any time soon, but the idea is intriguing.

Radiation oncology in its first 100 years has been dominated by technological advances in physics and engineering. It is true that there have been a few key insights from biological research, but not many. Technology has rapidly and completely outpaced the biology. Armed with a computer, dose contours can be tailored by the physicist and planning dosimetrist far more accurately than the extent of the disease can be delineated by the physician – while the biologist looks on in awe. During the life-time of many radiation oncologists practicing today, X-ray energies have escalated from 250 kVp to 20 MV, computers have revolutionized treatment planning, 3D-CRT has given way to IMRT with the advent of dynamic multileaf collimators. The latest trend is for free-standing proton facilities (*with or without the availability of carbon ions*) which promise the ultimate ability to conform the dose to the tumor volume, while sparing normal tissue. As it turns out however, protons are not the summit of achievement; there are antiprotons! [4].

The excitement of this particle, in a nutshell, stems from the fact that antiprotons share all the dose distribution advantages of protons, but in addition the dose in the Bragg peak region is amplified because as it stops the antiproton annihilates with a neutron or a proton, and deposits as energy some of the rest mass of both particles [4]. Annihilation occurs, of course, because an antiproton cannot exist at rest in our universe. It all sounds too good to be true!

A closer look at the process of annihilation soon makes it clear that the picture is much more complicated than at first appears. When an antiproton annihilates with a proton or a neutron, their combined rest mass (about 2 GeV) is radiated away by π -mesons (Fig. 1). On average, one pion in five is absorbed by the nucleus in which the annihilation takes place and the resultant excited nucleus releases energy

via the emission of protons, neutrons or heavier fragments [1,2]. It is these low energy charged particles, especially the heavy fragments that deposit energy at high LET, close to the annihilation point that amplify the Bragg peak. This expectation is confirmed by the radiobiological measurements of Holzscheiter et al. [5]. However, the charged mesons (π^\pm), the neutrons, and the γ -rays resulting from the decay of the neutral mesons transfer their energy further away from the annihilation and most escape the body [1,2]. In other words, the picture is not quite as rosy as it appears at first sight since only a *small fraction* of the rest mass of the annihilating pair is deposited locally at high LET. The bulk of the energy results in a total body dose of pions, γ -rays and neutrons, and many particles escape from the body. This represents good news and bad news.

The *good news* is that, since the pions all originate from the point at which annihilation occurs, they can be detected and used for real-time imaging to check the accuracy of the dose distribution. This is not something that can be done with protons, but it is a property shared with carbon ions. In this case some of the stable ^{12}C ions are stripped to positron-emitting ^{11}C and ^{10}C , which can be detected in a PET scanner, thus verifying the treatment plan.

The *bad news* is that the patient will receive a total body dose of pions and neutrons which have a high RBE for radiation carcinogenesis and will contribute to the induction of second cancers. There are not much data available at present concerning the magnitude of this total body dose but it tends to negate the putative advantage of antiprotons, namely to concentrate dose in the tumor and minimize the exposure of normal tissues.

The prediction that clinical antiproton facilities are unlikely to appear any time soon is borne out of the statement in the paper by Holzscheiter et al. [5] that exposures in the experiments described were as long as 16 h! The experiments were performed at CERN, but even this massive machine is hard pressed to produce sufficient antiprotons since the process is so inefficient.

Antiprotons were discovered more than half a century ago [3] and their possible use in radiotherapy first suggested more than 20 years ago [4]. It is likely to be some years, if ever, before antiproton beams of sufficient intensity for clinical use can be generated, but Holzscheiter et al. [5] have shown the proof of principle by these fascinating radiobiological experiments.

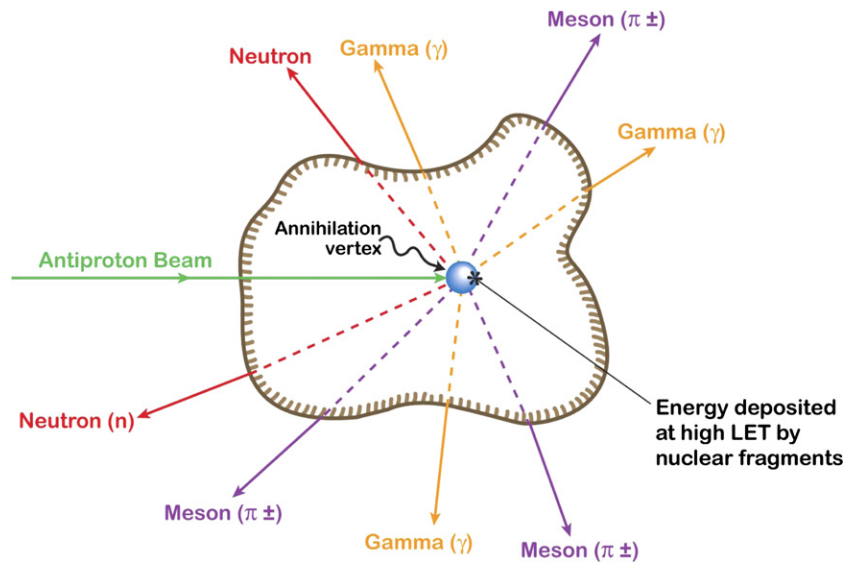


Fig. 1. Representative annihilation event produced by an antiproton stopping in matter. The energy of annihilation (about 2 GeV) is released through the emission of several pions. On average three charged pions (π^\pm) are emitted, which have a long range and deposit energy outside the local volume, for every neutral pion (π^0) that decays into two γ -rays, which also have a long range. On average about one pion in five is absorbed by the nucleus on which the annihilation takes place. The excited nucleus releases energy via protons, neutrons or heavier fragments. The low energy charged particles, particularly the nuclear fragments, deposit energy locally at high LET. The neutrons, on the other hand, have a long range (based on Gray and Kalogeropoulos [4]).

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