Physica Medica 31 (2015) 601–606

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Microbeam radiosurgery: An industrial perspective

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ARTICLE INFO

Article history:
Received 18 December 2014
Received in revised form
1 April 2015
Accepted 7 April 2015
Available online 30 April 2015

Keywords:
Microbeam
Radiosurgery
Radiotherapy
Cancer

ABSTRACT

In spite of its long demonstrated potential, microbeam radiosurgery (MBRS) has yet to be developed into a clinical tool. This article examines the problems associated with MBRS, and potential solutions. It is shown that a path to a clinically useful device is emerging.

Introduction

In conventional radiotherapy, the ability to destroy a cancerous tumor is limited by normal tissue toxicity. Typically, a total dose between 50 and 100 Gy is delivered to malignant tissue. While higher doses would certainly lead to greater tumor control, such higher doses are not possible because of damage to surrounding healthy tissue.

A number of scientific studies on small animals over the past two decades have demonstrated the astonishing fact that healthy tissue can tolerate an enormous amount of dose (>300 Gy) when delivered in small diameter beams or thin planes of radiation (<700 μm), termed microbeam radiation [1–5]. Although cells in the direct paths of the microbeams are killed, the adjacent non-irradiated tissues mount a healing response. Studies have also demonstrated that malignant tissue can be destroyed by microbeam radiation via cross-firing from several directions [5–8]. Thus, MBRS appears to have tremendous potential to control internal disease with little or no toxicity to surrounding healthy tissue.

In spite of its extraordinary potential, MBRS has yet to become available to the clinic. The problems which have kept MBRS from the clinic, along with potential solutions, are examined herein.

Discussion

From an industrial perspective, there are five major problems associated with the current state-of-the-art of MBRS. These are use case, photon energy, targeting method, radiation source, and biology. Each of these problems is discussed below.

Use case

Although several small animal models have been used (mice, rats, rabbits, and piglets), nearly all pre-clinical MBRS studies to date have focused on brain tissue. While a device that would cure brain cancer is greatly desired, such a device would command a small market from the perspective of an industrial manufacturer of radiotherapy equipment. Cancer statistics for the USA in the year 2013 show that brain cancers accounted for 1.4% of all cancers [9]. See Fig. 1. To warrant the long and expensive route of product development, it is necessary to show that MBRS is effective in destroying many more types of malignant tissue while still sparing the corresponding many more types of healthy tissue.

For conventional radiotherapy, lung cancer is a large (14% of all cancers) but woefully underserved market because radiation often induces pulmonary fibrosis. Pulmonary fibrosis alone can lead to death. Recently, Varian Medical Systems, Inc. (USA), in collaboration with the European Synchrotron Radiation Facility (France), launched a study to determine whether or not microbeam radiation induces fibrosis in the lungs of rats. The results of this study are pending, and will be reported at a later date.

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http://dx.doi.org/10.1016/j.ejmp.2015.04.003

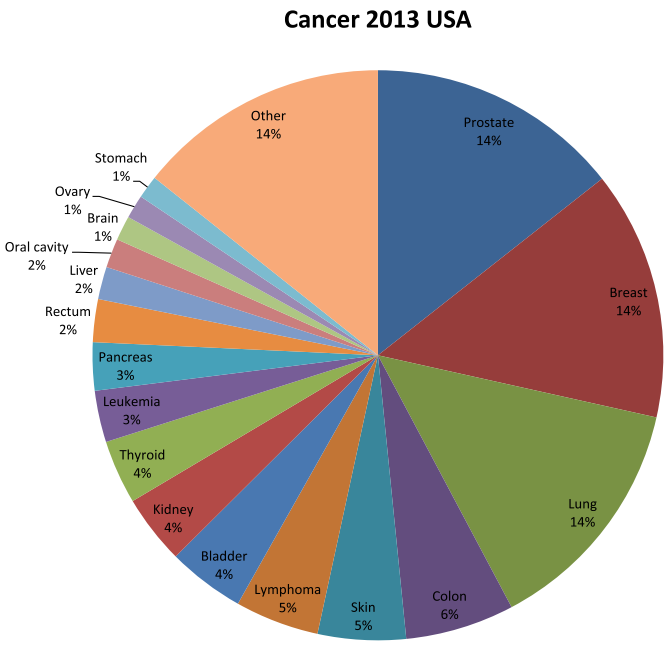

Figure 1. Distribution of cancers, by anatomical site, presented in the USA during the year 2013.

By way of this article, the MBRS research community is respectfully called upon to explore the effects of microbeam radiation on yet more types of tissue and cancers; e.g., liver, pancreas, kidney, bladder, etc.

Photon energy

All MBRS studies have employed spectra of low energy photons which peak between 50 and 150 keV. While such photon energies are sufficient for small animals, they are not sufficient to provide dose at depth in human patients. Figure 2 shows the percentage depth dose curves for 500 μm diameter pencil beams of monochromatic 200 keV and 2 MeV photons. At 20 cm depth, which is half-way into the wide portions of a human patient, 200 keV photons supply only 5% of incident dose. The lower energy photons used in MBRS provide even less. 2 MeV photons, such as used in conventional radiotherapy, provide 35% of incident dose at 20 cm depth.

Figure 2 also shows that peak dose deposition for low energy photons occurs at the surface of the patient; i.e., at the skin. This is important because there are many nerve endings in skin, and damage to the skin is very painful. Even though damage created by microbeams at the skin may be expected to heal nicely, such damage will likely be painful during the healing process. Peak dose deposition for high energy photons, however, occurs below the skin, allowing for pain-free experience.

The primary reason low energy photons have been used in MBRS studies up to now is that it has been the thinking of researchers in the field that the lateral dose deposition profile (i.e., in the direction orthogonal to the direction of beam propagation) must have a square wave shape [4]. That is, the dose in the valley regions of the microbeam array must be low and flat, the dose in the peak regions must be high and flat, and the transition between the two regions must be sharp. This dose profile assures that there is no damage to healthy tissue in the valley regions, thereby allowing such undamaged tissue to provide a healing response to the destruction generated in the peak regions. Because of the phenomenon of Compton scattering, high energy photons yield a rounded lateral dose deposition profile. Figure 3 shows the lateral dose deposition profiles for 500 μm diameter pencil beams of 200 keV and 2 MeV photons. The 2 MeV photon case clearly does not meet the square wave profile requirement. Because of dose tails extending into the valley regions, microbeams with photon energies above 200 keV have been considered unacceptable.

With this article, a shift in thinking is proposed. It is herein argued that the shape of the lateral dose deposition profile is immaterial. Rather, what is important is that the biological damage zone created by a microbeam be sufficiently narrow that the undamaged regions on either side are able to induce healing. It is proposed that the Compton scattering of high energy photons be

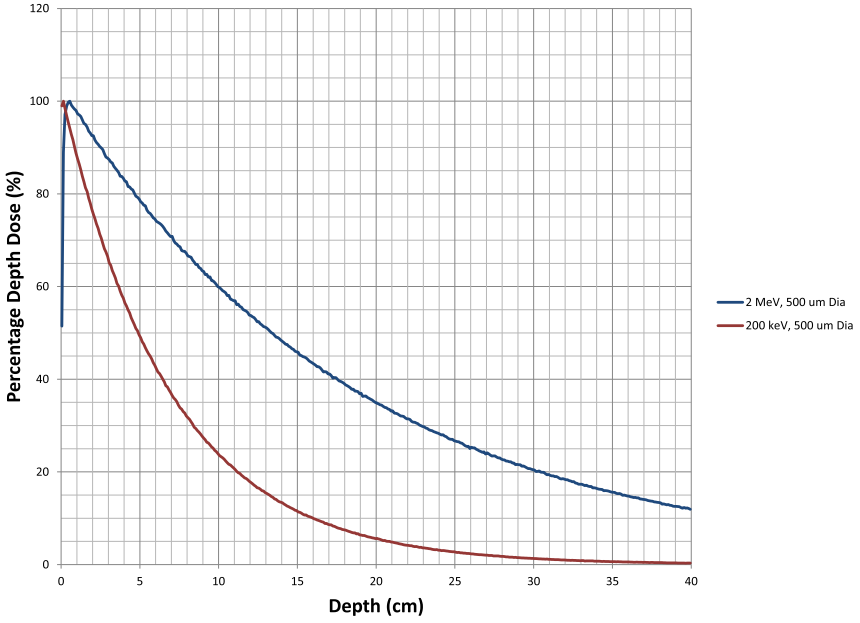

Figure 2. Calculated percentage depth dose curves for 500 μm diameter microbeams of monochromatic 200 keV and 2 MeV photons.