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LINEAR ACCELERATOR FOR DEMONSTRATION OF X-RAY RADIO-THERAPY WITH FLASH EFFECT*

S.V. Kutsaev†, R. Agustsson, S. Boucher, K. Kaneta, A.Yu. Smirnov, V. Yu
RadiaBeam Technologies, LLC, Santa Monica, CA, U.S.A.
A. Li, K. Sheng, Department of Radiation Oncology, University of California,
Los Angeles, CA, U.S.A.

Abstract

Emerging evidence indicates that the therapeutic window of radiotherapy can be significantly increased using ultra-high dose rate dose delivery (FLASH), by which the normal tissue injury is reduced without compromising tumor cell killing. The dose rate required for FLASH is 40 Gy/s or higher, 2-3 orders of magnitude greater than conventional radiotherapy. Among the major technical challenges in achieving the FLASH dose rate with X-rays is a linear accelerator that is capable of producing such a high dose rate. We will discuss the design of a high dose rate 18 MeV linac capable of delivering 100 Gy/s of collimated X-rays at 20 cm. This linac is being developed by a RadiaBeam/UCLA collaboration for a preclinical system as a demonstration of the FLASH effect in small animals.

INTRODUCTION

Ultra-fast radiation delivery, also known as FLASH radiotherapy, may become a breakthrough technology for oncology treatment. Compared to conventional radiotherapy with dose rate ~ 0.1 Gy/s, FLASH radiotherapy markedly reduced the normal tissue toxicity without compromising tumor response [1]. The FLASH effects have been consistently observed across different animal species, using different modalities including electrons, X-rays, and protons. Moreover, the FLASH effect was recently demonstrated in a human study for treating skin lesions [2].

It is believed that with a sufficiently high dose rate, depleted oxygen cannot be replenished via diffusion before the full radiation dose is given, reducing the cell damage and leading to the hypothesized FLASH effect [3]. Other mechanisms, including inflammatory response, were also indicated [4]. Regardless of the FLASH-therapy mechanism, the promising initial results warrant further investigation and human clinical trial studies.

One possibility for delivering FLASH would be an X-ray system [5]. However, there are significant technical challenges to achieving the ~500× greater dose rate for FLASH in human patients. Unfortunately, the physical process for generating X-rays is not very efficient, therefore a high-power accelerator is needed. Conventional 6 MV medical linacs produce a flattening filter free dose rate of around 0.2 Gy/s at one meter from the X-ray target –3 orders of magnitude too low – however they are on the low end of the spectrum of linac powers [6]. A typical medical linac has a beam power on the order of 1 kW, while industrial accelerators for sterilization of food and medical products can achieve beam powers of several hundred kW.

Another factor that allows for improvement in dose rate is increasing the beam energy. The conversion efficiency from electron beam power to X-ray power scales approximately with E^3, so a small increase in energy can make a large difference in X-ray intensity. The increased X-ray energy also allows greater penetration.

RadiaBeam and UCLA are working on a clinical solution for X-ray FLASH therapy that takes advantage of a single linac based on already-demonstrated technology and an innovative, yet straightforward, method for intensity modulation [7, 8]. This linac will be capable of producing 18 MV X-ray radiation with 100 Gy/s collimated dose rate in the tumor, located at 80 cm from the source. Such dose will be achieved by accelerating a >300 mA beam with 2.5% duty factor. Since the complexity of this linac is extensive, the expected timeline for its completion is estimated to be several years. Therefore, in parallel to a clinical system, we are developing a scaled linac that can be used for demonstration of the FLASH effects in small animals. The linac will benefit from using the infrastructure of a 9 MeV NDT linac (FLEX) [9] available at RadiaBeam, and therefore can be developed and fabricated in a much shorter time scale by only replacing the accelerating structure.

LINAC CONCEPT

The goal of this project is to design and build an inexpensive linac for demonstration of gamma FLASH therapy. The following considerations are taken into account. The designed accelerator must be able to provide at least 100 Gy/s dose, collimated, at 20 cm from the target. This corresponds to 16.5 cGy/s uncollimated dose at 1 m from the target. Second, the accelerator must be able to utilize the existing FLEX linac RF power system, available at RadiaBeam, based on 5 MW peak power klystron, operating at 2.856 GHz frequency with 0.4% duty factor.

The other consideration is to maximize the X-ray dose conversion from the accelerated electron beam. In order to do this, we pursued two approaches. First, the dose yield scaled linearly with the beam current I and cubically with the energy W as:

$$D = k \cdot I \cdot W^{2.7-3.0}$$

Where k is a yield factor that depends on the particular X-ray conversion target design. For example, we know that for 6 MeV linacs produced at RadiaBeam, k=10.6 cGy/min/μA [10] and k~30 cGy/min/μA for a Varian 9 MeV Linatron.

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† kutsaev@radiabeam.com

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At the same time, for the available RF power, a linear accelerator can roughly produce a beam with the current and energy that scales as

$$P = \frac{W^2}{R \cdot L} + I \cdot W$$

Here R is the shunt impedance of the structure that depends on the geometry of the accelerating structure and the conductivity of the material. Therefore, it is obvious that for a given amount of RF power, P=5 MW, it is possible to find an optimum between beam energy and current that produces a maximum dose yield.

ACCELERATING STRUCTURE

First, we had to choose the accelerating structure for the linac. We considered several types of the RF structures that are typically used in industrial accelerators, each of which have their pros and cons [11].

The side-coupled linac (SCL) is a standing wave (SW) structure that is used in all medical accelerators produced at RadiaBeam. It has smallest longitudinal footprint because the coupling cells are located off the axis of the structure. At the same time, larger transverse dimensions complicate the possibility of using a focusing solenoid, which could be very important to avoid beam losses (and therefore, minimize power waste). The on-axis coupled structure (OCL) has slightly lower shunt impedance, because the coupling cells with zero accelerating fields are located on axis. At the same time, it is easier to put a solenoid because of smaller transverse dimensions.

The disk-loaded structure (DLS) is a travelling wave (TW) structure that is used in high-current accelerators. In the case of ~10 MeV it has lower shunt impedance compared to SW structures, but it is very simple and robust. The problems with DLS could be solved by using a magnetic-coupled DLS, also known as backward TW (BTW) structure [12, 13]. Thanks to the coupling via magnetic field, its beam iris could be made very small, and the shunt impedance high. However, in this structure the power propagates (and dissipates) from the end of the structure towards its beginning, which makes the bunching (front-end) section, and therefore the beam parameters, very sensitive to the operational conditions.

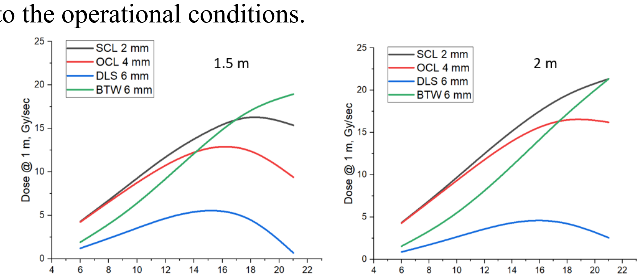

Figure 1: Dependence of maximum dose rate yield (at 1 meter) achievable in different structures as a function of beam energy and linac length.

The comparison of the performance of different structures is provided in Fig. 1. These results were obtained using analytical expressions for the energy gain in TW and SW structures [14]. We see that only 2 structures (OCL and BTW) are worth considering. SCL was dismissed because of the solenoid placement infeasibility, and DLS provides much lower dose rate compared to the other options. We consider OCL a safer choice.

We see that longer structures (1.5-2 m or more) can provide higher doses. This is an expected result, because the dissipated power scales with the gradient. It should be noted that for 1.5 m or longer length, the SW structures need to be split in two sections to avoid overlap of neighboring resonances [15]. The BTW structure seems to be more efficient but has more challenging beam dynamics due to the strong sensitivity of bunching cells to beam loading. Both structures will need solenoid.

Another observation is the existence of an optimal energy for each structure, due to the above-mentioned tradeoff between energy and current. This optimum is located between 16 and 20 MeV, depending on the structure. Therefore, we decided to design a linac with 18 MeV energy. According to these preliminary simulations, we can expect ~375 Gy/sec at 0.2 m.

BEAM DYNAMICS

We decided to proceed with the OCL option with 2 mm aperture. Beam dynamics simulations were performed in Parmela for 18 MeV average energy. We used a 30 kV electron gun identical to the one used in the FLEX linac (Fig. 2). The initial buncher geometry is very similar to cargo inspection OCL linacs [16] and consists of 3 cells with the reduced phase velocities.

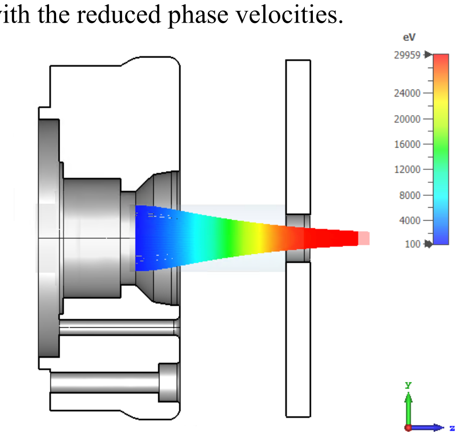

Figure 2: Geometry and beam profile of the 30 kV electron gun.

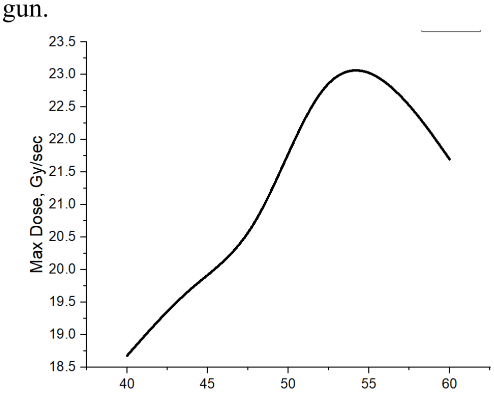

Figure 3: Dose yield as a function of number of cells.

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Beam dynamics simulations were performed for different numbers of accelerating cells (i.e. the total length of the structures) from 40 to 60 and the results are shown in Fig.3. According to these results, the optimal number of cells is around ~50-55. However, keeping in mind the modes separation problem for SW structures, which are typically limited to ~20 cells per section, we decided to proceed with 48 cells (2 sections of 24 cells, fed by a 3 dB splitter [17]).

As space charge and small aperture can affect higher current beams, we also decided to use a solenoid. The required solenoid field strength was found by performing beam dynamics simulations in a 2m OCL structure with an external magnetic field applied. These studies demonstrated that the beam transmission is maximized if >1000 Gs solenoidal field is applied. It is important to mention that the cathode must be demagnetized to avoid emittance growth.

Finally, the buncher was optimized in order to maximize beam transmission and minimize energy spread [18]. The following parameters were considered during the optimization: phase velocities of cells #1-3 and field amplitudes in these cells. Two criteria were used for the optimization quality: beam transmission should be maximized, and beam spectrum width should be minimized. The best configurations of the bunchers and corresponding beam parameters are summarized in Fig. 4. The same plot demonstrates the simulated energy spectrum of the accelerated beam, the quality of which is very good (narrow beam head and thin low-energy tail).

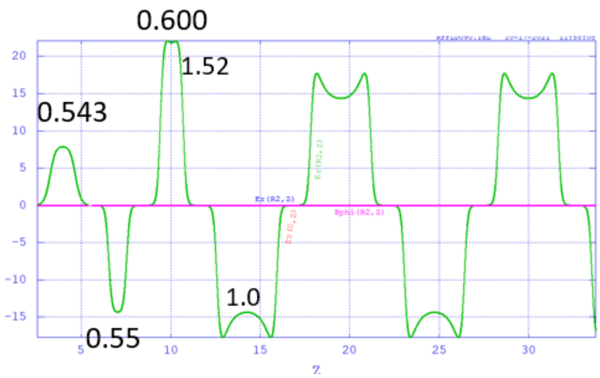

Figure 4: Optimal configuration of accelerating field in the bunching section.

The parameters of the optimized linac simulated in Parmela are presented in Table 1. These numbers demonstrate that we were able to increase the beam current by ~50% thanks to the deep redesign of the buncher, application of solenoid, and due to the decision to operate with longer sections (almost 2.4 m). The expected dose meets the requirements for FLASH therapy.

CLINICAL VERSION

As mentioned in the Introduction, the clinical version of the linac must provide the same dose, being located 4 times further away, and therefore the dose at the X-ray converter must be 16 times higher. To solve this problem, we plan to increase the accelerated current by almost a factor 3: to 325 mA, and the duty factor by a factor of 6, to 2.5%.

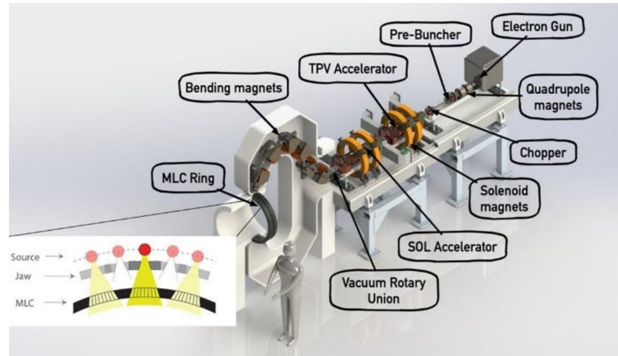

Figure 5: Rendering of the clinical 18 MeV X-ray FLASH therapy linac.

In order to realize this, we plan to design a linac (Fig.5) that will consist of a 1.3 A, 140 kV electron gun, prebuncher, tapered velocity buncher and 2 TW constant gradient sections, powered by a commercially available 10 MW L-band klystron with 170 µs pulses at 150 Hz, to bring an 8.14 mA average current electron beam to 18 MeV. Assuming a dose conversion factor of 2,000 Gy/min/mA at 18 MeV, such a linac will be able to provide an uncollimated dose rate of 271 Gy/s at 1 m, which is equivalent to ~100 Gy/s collimated dose at 80 cm, assuming ~25% dose delivery efficiency. The beam is transported through a rotary vacuum joint into a rotating magnetic gantry that brings the beam to a rotating X-ray target directed at the patient [2], [7], [8].

Table 1: Beam Parameters of the Designed Linac

Linac	FLEX	Demo	Clinical
Structure[#]	TW CI	SW OCL	TW CG
Frequency, MHz	2856	2856	1300
Length, m	0.85	2.6	4.5
RF power	5 MW @ 0.4% duty		10 MW @ 2.5%
Beam energy, MeV	9	18	18
Beam current, mA	100	130	325
X-ray dose rate, Gy/sec at 1 m	4.4	17.5 ± 2.0	271

SUMMARY

We have designed an 18 MeV S-band linac consisting of 2 sections of 24 cells of on-axis coupled accelerating structure, powered from the 5 MW klystron, and capable of delivering the 100 Gy/sec collimated X-ray dose into the tumor at 20 cm distance to the irradiated patient. The linac is currently being fabricated and will be used for the demonstration of FLASH effect in small animals. The clinical version is also being designed and anticipated to be available several years after the demonstration one.

[#]CI – constant impedance, CG – constant gradient

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