

Dosimetric characterization of the laser-accelerated high-energy electron beam for radiotherapy applications

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Radiotherapy utilizing very-high-energy electron (VHEE) beams in the range of 50–300 MeV has gained significant interest over the past two decades due to their advantageous dose characteristics, deep tissue penetration capabilities, and potential for ultrahigh dose-rate treatments. Laser wakefield accelerators (LWFAs) are particularly well suited for generating VHEE beams in a compact setup, thanks to their substantially higher accelerating gradients compared to conventional radio-frequency accelerators. To meet the demands of clinical applications, a comprehensive dosimetry study of LWFA-generated VHEE beams in a preclinical treatment configuration is essential. In this study, a VHEE beam with a maximum energy over 160 MeV was produced using a compact and stable LWFA prototype operating at 1 Hz. The beam was subsequently transported through a quadrupole triplet to eliminate low-energy components and reduce pointing jitter, followed by a scatterer and collimator to create a uniform circular radiation field with an 8-mm diameter. Using this beam, we measured the three-dimensional dose distribution within a solid-water phantom and evaluated the feasibility of multifield intensity-modulated irradiation by delivering 400 VHEE beams from 20 different angles into the phantom. This resulted in a 16-mm-diameter dose plateau peak, with the relative uniformity of approximately 2.8%, and the entrance dose was only 20% of the peak value. These findings demonstrate the feasibility and robustness of LWFA-based VHEE beams for treating deep-seated tumors, highlighting the need for dedicated engineering and preclinical studies in this promising direction.

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I. INTRODUCTION

Cancer remains one of the most significant challenges to human health. Radiation therapy, utilized in over half of cancer patients, constitutes a vital component of cancer treatment, relying on the use of ionizing radiation such as photons, electrons, and hadrons to locally deposit doses for the destruction of cancer cells. Presently, widely employed radiation therapy facilities predominantly depend on high-energy photon beams (x-rays) generated from standard radio-frequency linear accelerators. More recently, hadron

radiotherapy has gained attention due to its beneficial dose deposition characteristics, particularly the Bragg peak, which allows for high-dose deposition at the distal end of the beam with minimal downstream doses. However, hadron beams are highly sensitive to inhomogeneities such as air gaps [1,2], limiting their applicability in treating moving targets and necessitating high-precision image-guided preprocessing. Additionally, the synchrotron/cyclotron machines used for accelerating hadron beams are bulky and expensive, posing limitations on the widespread adoption of this radiation therapy technique.

In recent years, there has been growing interest in utilizing very-high-energy electron (VHEE, in the energy range of 50–300 MeV) beams for radiation therapy [3,4]. This interest is driven by their high penetrative capability, limited penumbra diffusion [3], ease of magnetic steering [5–7], and insensitivity to tissue inhomogeneities [8,9]. Previous numerical studies have shown potential benefits for VHEE in the treatment of various tumor models,

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including those in the lung, prostate, pediatric brain, and head, by depositing lower doses in healthy organs compared to high-energy x-rays [10–12].

Over the past two decades, the rapid advancement of laser wakefield acceleration (LWFA) has brought promising prospects for space-efficient and cost-effective VHEE radiotherapy machines [13,14]. This concept was originally proposed by Tajima and Dawson [15], where a strong plasma wave can be excited by an ultrashort, ultraintense laser pulse propagating through a low-density gaseous medium. Due to the absence of material breakdown, LWFA can sustain acceleration fields more than 3 orders of magnitude stronger than conventional radio-frequency accelerators, enabling the acceleration of electron beams to several hundreds of MeV over a distance of only several millimeters [14,16–18]. Additionally, the ultrashort nature of the produced VHEE beam [19–21] makes it an attractive option for radiobiology studies at ultrahigh dose rates. It is worth noting that laser-accelerated proton beams have also recently shown their potential for radiotherapy in terms of ultrahigh dose-rate irradiation, with the detailed radiobiology studies on cells [22] and mice tumors [23].

Numerous research groups worldwide are actively exploring the feasibility of radiation therapy employing laser-accelerated high-energy electron beams. Significant progress has been made in key areas, including dose measurement methodologies [6,24,25], treatment planning optimization [6,26], and the characterization of radiobiological effects [27,28]. Very recently, our research team

has developed a compact LWFA-based radiotherapy prototype capable of stably generating collimated VHEE beams exceeding 100 pC at a repetition rate of 1 Hz. Preclinical validation of this system was achieved through successful irradiation of mice tumor models [29]. However, a comprehensive dosimetry study for such a system has remained absent. In this work, we present a detailed characterization of the three-dimensional (3D) dose distributions generated by the VHEE system. Furthermore, we evaluated a simplified intensity-modulated treatment planning approach utilizing multifield irradiation, validating the prototype's robustness for targeting tumors of finite sizes while significantly reducing entrance and exit doses.

II. EXPERIMENTAL SETUP

The dosimetry experiment was conducted using our recently developed LWFA-VHEE prototype for radiotherapy [29], which consists of a self-built compact 20-TW laser system, a LWFA module, a beam transport module, a beam shaping module, and a final platform for dose measurements. As depicted in Fig. 1, the LWFA module is achieved by focusing a 20 TW, 25 fs laser pulse to a full width at half maximum (FWHM) diameter of around 11 μm and impinging it onto a 2-mm supersonic gas jet filled with 99% helium and 1% nitrogen. Electron beams are stably generated through ionization injection [30–32] and then accelerated up to around 160 MeV with continuous spectra.

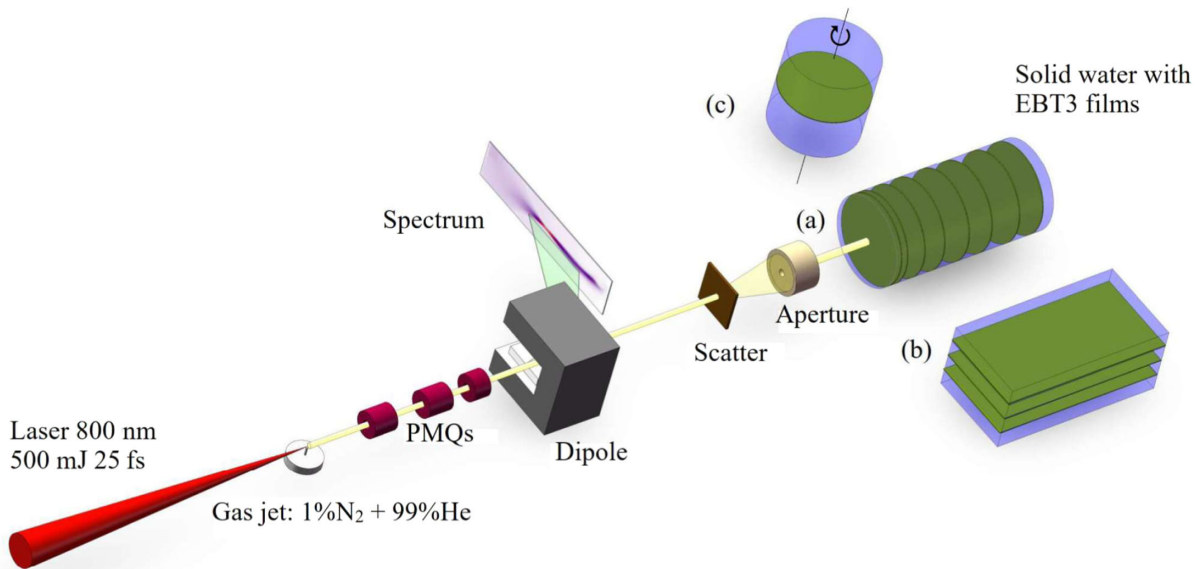


FIG. 1. The experimental setup. A 20 TW, 25 fs laser was focused into a 2-mm-diameter gas jet and accelerated electrons through its launched wakefield. After exiting the plasma source, the electron beam passed through a triplet of magnetic quadrupoles to remove the low-energy components and stabilize its pointing jitter. A movable dipole magnet together with a scintillation screen was used to measure the beam's energy spectra. Afterward, a copper scatterer and stainless steel collimator aperture were used to shape the beam's profile to be uniform. Finally, the beam was delivered into three types of solid-water phantom (in blue) embedded with EBT3 films (in green), labeled as (a) and (b) to measure its lateral and longitudinal slice dose distribution, respectively, and as (c) to model the multifield irradiation configuration.

Afterward, a set of three permanent magnetic quadrupoles (PMQs) is positioned 8.5 cm downstream of the nozzle. These PMQs serve as a beam transport module to filter out low-energy electron components and minimize the beam's pointing jitter. Subsequent to the PMQs, an energy spectrometer—comprising a 1 T dipole magnet and a calibrated scintillation screen—is employed to analyze the beam. Upon exiting the PMQs, the electron beam displays a characteristic butterfly-shaped energy spectrum, with its central waist near 70 MeV [Fig. 2(a)]. Figure 2(b) shows 300 consecutive measurements of the electron energy spectra after traversal through the PMQs, revealing a mean beam energy of 82 ± 2.3 MeV and a charge of 160 ± 18.7 pC (accounting for all electrons with energies above 40 MeV from the energy spectrometer). Notably, the low-energy portion below 50 MeV exhibited significant divergence. Additionally, the PMQ configuration reduced beam pointing fluctuations by nearly an order of magnitude from ~ 2.4 to ~ 0.3 mrad through the imaging relay technique [29].

Subsequently, the high-energy electron beam exits the vacuum chamber through a 100- μm -thick polyimide window and is scattered by a 1.45-mm-thick copper plate to achieve a much larger size of nearly 20 mm in FWHM. In the meantime, bremsstrahlung x-rays could also be produced. To assess its contribution to the overall dose distribution, Monte Carlo simulation using the code TOPAS [33] was performed, which demonstrates that the dose from bremsstrahlung x-rays constitutes less than 1% of the total absorbed dose, confirming that its influence is negligible in our experiment. After getting scattered, the electron beam is then shaped to an 8-mm-diameter size with a nearly flattop distribution by a 30-mm-thick stainless steel aperture of the same size. The above scatter and aperture constitute the beam shaping module, which tailors the beam to have a relatively large and uniform irradiation field to cover certain tumor regions of small animals. EBT3 Radiochromic films and solid water blocks, consisting of epoxy resins and powders, density equal to water, were placed behind the aperture to characterize the dose deposition of

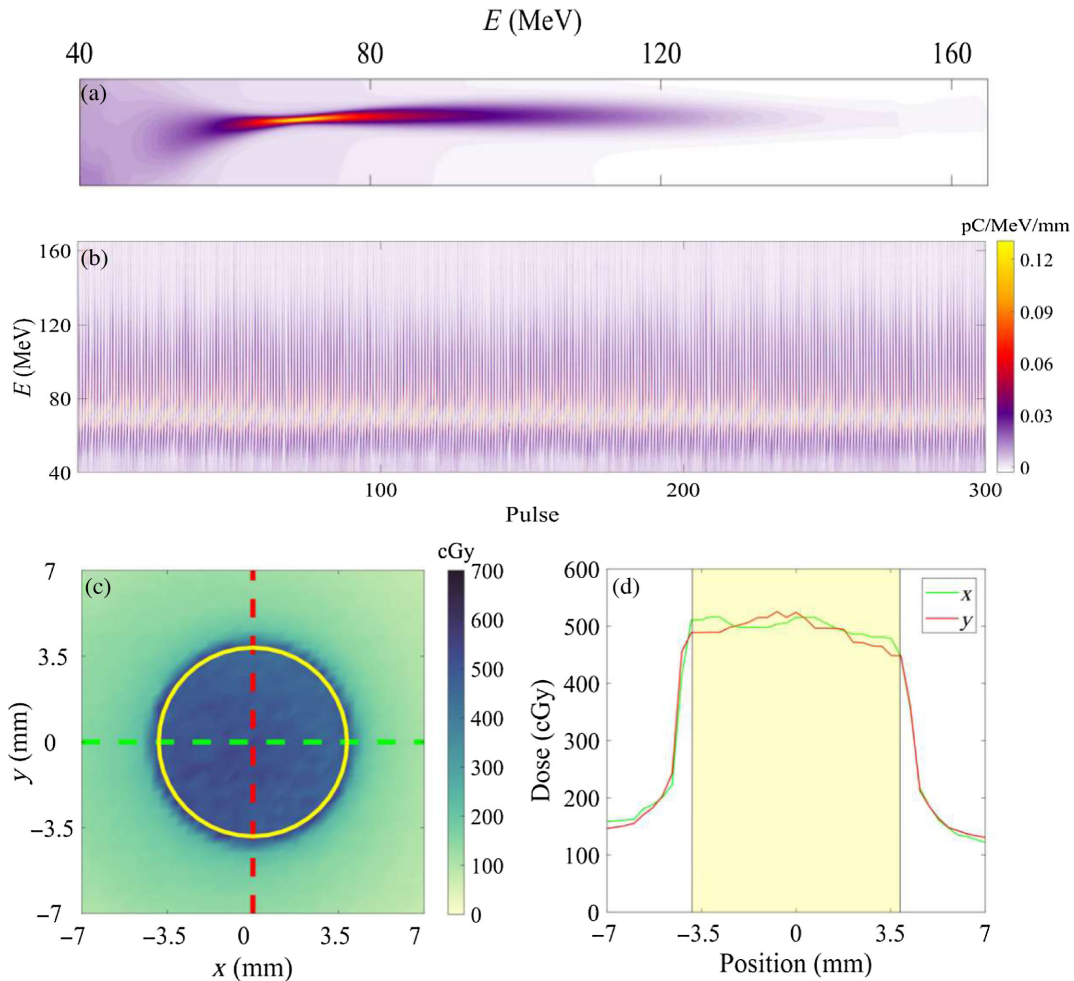


FIG. 2. Measured properties of the delivered electron beams. (a) One example energy spectrum of the electron beam after passing through the triplet. (b) Consecutive 300 shots of the electron spectra under the same condition as in (a). (c) The transverse dose distribution of the beam after passing through the aperture. (d) The lineout dose distributions along the two dashed lines of (c).

the LWFA electron beam. In the experimental setup, EBT3 films with only a few hundred micrometers thickness were embedded between solid water blocks for measuring the dose deposition of the electrons. The 2D spatial dose distribution was assessed by varying the EBT3 film's orientation, specifically in the transverse and longitudinal directions, to obtain profiles along the corresponding axes. All EBT3 films were scanned 24 h after irradiation using an Epson 12000XL Photo scanner (Epson, Suwa, Japan) in transmission mode with no color correction, at 72 dpi. Prior to the experiment, a medical x-ray radiotherapy machine (Varian Edge series) was utilized to calibrate the film coloration, and the Film QA Pro 2016 software was used for calibrating the dose-response curve and reading the dose results. The transverse dose distribution of the LWFA electron beam just after the aperture was measured with 300 shots, and the result is presented in Fig. 2(c) with vertical and horizontal central lineouts shown in Fig. 2(d). A flattop dose distribution of approximately 5 Gy with a radius of approximately 4 mm is observed, as marked within the yellow circle of Fig. 2(c), and the relative uniformity fluctuation of this region was about 4.8%.

III. RESULTS AND DISCUSSIONS

For the dose deposition measurement, we have employed two types of configurations. The first configuration consisted of 18 blocks of cylindrical solid water, with EBT3 films inserted in between, to measure the 2D lateral slice of the dose at different depths [see Fig. 1(a), where EBT3 films are colored with green and solid water colored with blue]. The second configuration, as shown in Fig. 1(b), consisted of four layers of rectangular solid water, with three EBT3 films inserted in between, to measure the longitudinal slice dose distributions. In both cases, 600 shots were delivered, and the results are presented in Fig. 3. Figures 3(a)–3(h) present the measured lateral dose distributions at different depths based on the first configuration, with lineout distributions along the axis of $y = 0$ and $x = 0$, respectively. It is observed that at shallower depths < 20 mm, the lateral dose maintains a circular and relatively uniform profile with similar sizes as the dose just after the aperture. Subsequently, the dose decreases, and its distribution becomes closer to a Gaussian profile due to the multiple Coulomb scattering of the electron beams by the

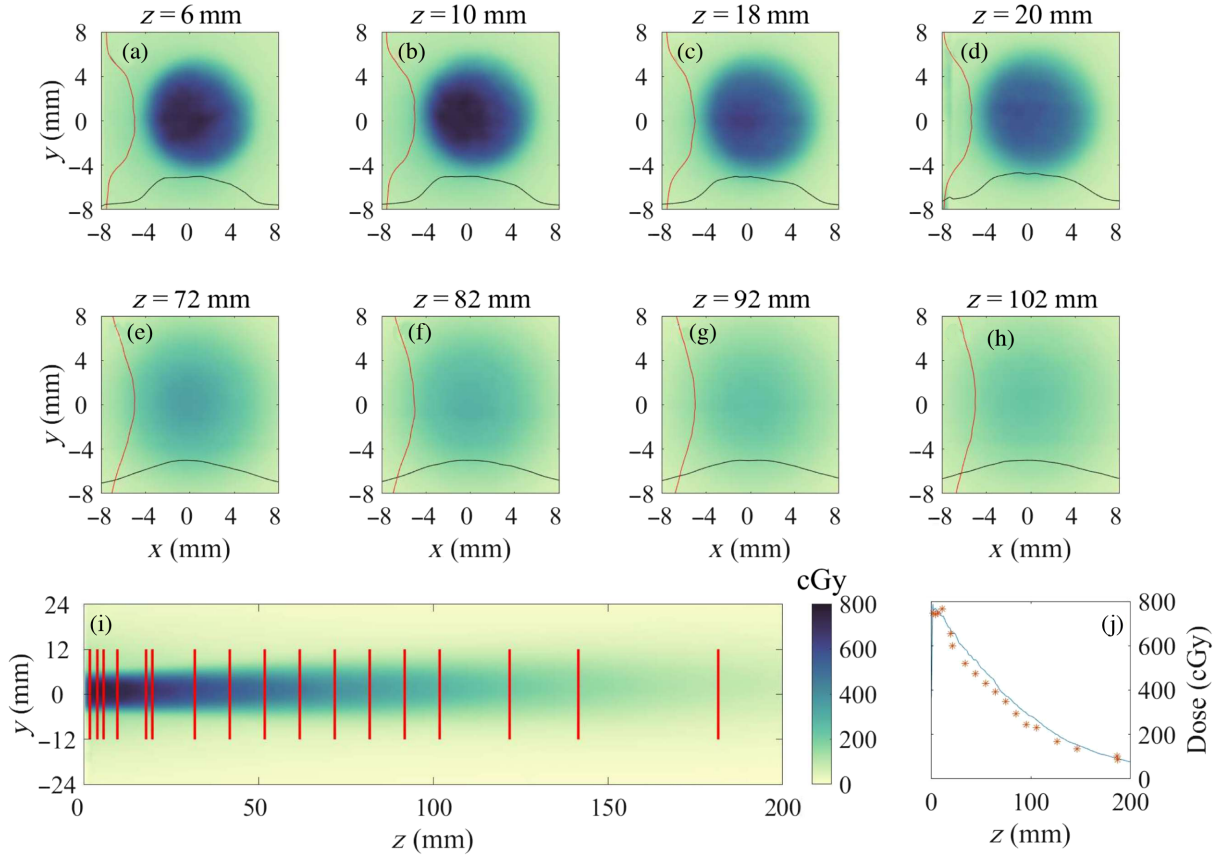


FIG. 3. Results of the dose measurements. (a)–(h) The measured lateral slice dose distributions at different depths using the configuration of Fig. 1(a), where the red and black solid curves represent the lineout profiles along the $x = 0$ and $y = 0$ axes, respectively. (i) The measured longitudinal slice dose distribution along the beam propagation using the configuration of Fig. 1(b), where the red lines represent the positions of EBT3 films of (a)–(h). (j) The on-axis lineout dose distributions, with the orange stars representing the measurements from (a) to (h) and the blue solid curve representing the dose on axis ($y = 0$) in (i).

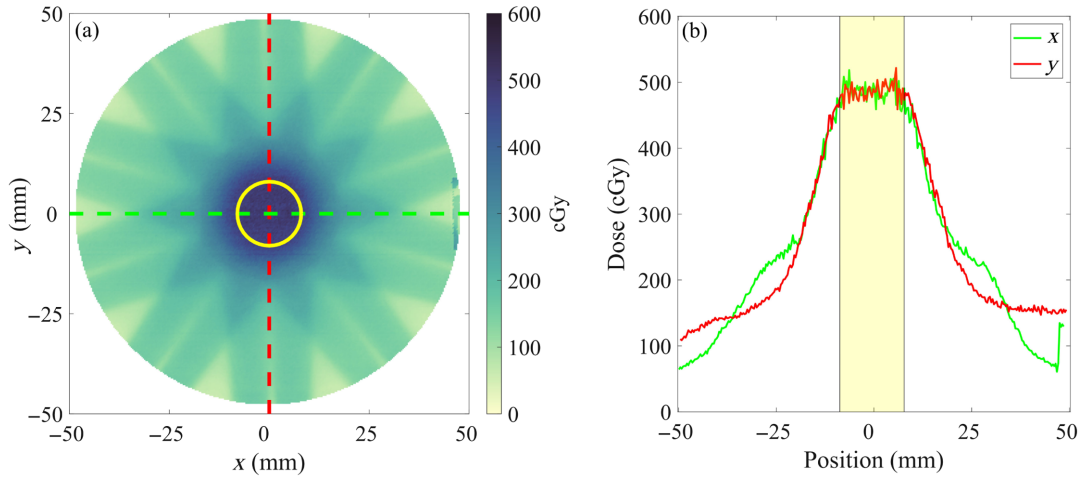


FIG. 4. The multifield irradiation onto a cylindrical solid-water phantom using the configuration of Fig. 1(c). (a) The slice dose distribution of the EBT3 film inserted in the middle of the phantom, which is created by rotating the phantom and displacing it simultaneously and irradiating it with a total of 20 irradiation fractions with 20 shots per fraction. (b) The lineout dose distributions along the two dashed lines of (a). By this approach, a circular dose plateau with a diameter of 16 mm at a depth of 50 mm was formed with the entrance dose approximately 20% of the central peak value.

solid water medium. Figure 3(i) shows the longitudinal slice of the electron beam dose deposition based on the EBT3 film positioned in the center of the second configuration of Fig. 1(b), with red solid lines representing the inserted positions of the EBT3 films from Figs. 3(a)–3(h). It is evident that the absolute dose together with its distribution is similar to the measurement of the first configuration. This can be further confirmed by the on-axis dose comparison shown in Fig. 3(j), where orange stars represent the on-axis dose at different depths from Figs. 3(a)–3(h) and the blue solid curve represents the dose lineout along the central axis of Fig. 3(i), demonstrating the stability of the continuous operation of the prototype machine. We note that the electron beam delivered here is more akin to a pencil beam with only a few mm width, which generally deposits the maximum dose near the entrance and then decreases along its propagation. In our setup, as shown in Fig. 3(j), at around 70 mm depth, the dose decreases to about 50% of the entrance dose, denoted as $R_{50} = 70$ mm. For much wider beams (e.g., over 50 mm), the in-depth dose will become more flat, as side scattering gets compensated [24]. Nevertheless, the pencil beam strategy is considered to be more flexible and precise in treatment planning by using electromagnetic scanning to create a dose maximum at the deep-seated tumor region [34,35].

To further investigate the current capabilities of the LWFA-based VHEE prototype for treating tumors, we conducted multifield irradiation onto a cylindrical solid-water phantom to imitate intensity-modulated radiation treatment (IMRT) [36]. An EBT3 film was inserted between two blocks of solid water with a diameter of 100 mm and a thickness of 50 mm, all installed on a rotational motor stage [see Fig. 1(c)]. Similar to the procedure of [25], for each two fractions, we first rotated

the phantom by 36° and shot one fraction, and then displaced it by 5.4 mm and shot the second one. After a total of 20 irradiation fractions, with 20 shots each, a flattop dose region located 50 mm away from the entrance with a 16-mm-diameter was formed, and the maximum dose reached approximately 5 Gy [see Fig. 4(a)]. The dose fluctuation within the flattop area was approximately 2.8%. Additionally, as shown in Fig. 4(b), the entrance and exit doses of the VHEE beam were only 20% of the peak dose in the target area. This simple exploration confirms that the LWFA-based machine is capable of stably delivering VHEE pencil beams, holding great potential for precise treatment planning designs.

In summary, we present a detailed characterization of the dose deposition of VHEE beams based on our compact LWFA-based radiotherapy prototype, which is capable of delivering a collimated VHEE pencil beam with a uniform irradiation field at 1 Hz operation. The two types of dose measurements demonstrate that the VHEE pencil beam can penetrate over 200 mm with an R_{50} value of approximately 70 mm. Furthermore, we explored the potential of using VHEE for IMRT to create a dose flattop region. With 400 shots, the dose reaches ~ 5 Gy within a 16-mm-diameter circular region, and the relative uniformity is about 2.8%. It should be noted that our imitation of IMRT planning is still quite coarse and a more sophisticated treatment planning system is yet to be developed, involving the control of beam irradiation direction/position, beam numbers, and beam focusing conditions to achieve more precise dose deposition into targeted tumors.

To advance LWFA-based very-high-energy electron beams toward clinical applications, in addition to initial tumor model irradiation and dosimetry studies, we are dedicated to pursuing three critical parallel objectives. First,

the design of a compact dose delivery system dedicated to LWFA-based VHEEs. It is known that LWFA-based electron beams generally exhibit relatively large energy spreads when achieving high charges and high stability. However, most beam transport modules are chromatic. One possible approach could be to first reduce the electron beam's energy spread without substantial charge loss via an energy spread compression module [37] and then transporting the beam, which, however, would potentially increase the complexity and size of the entire system. Alternatively, we recently proposed a simple dose delivery system using only two dipoles that can directly transport VHEE beams with large energy spreads and create a maximum dose deeply inside the body [35]. Second, the development of a robust treatment planning system algorithm specifically tailored for VHEE beams with broadband spectra. It is known that the VHEE dose distribution is not highly sensitive to the beam's energy spread due to the fact that its deposited energy is not localized (in contrast to ion beams). Nevertheless, for ensuring precise dose conformity for complex tumor geometries, it is still necessary to integrate advanced optimization frameworks that account for energy-dependent scattering and penetration dynamics. Third, designing a rotational gantry prototype which integrates a compact and stable laser acceleration module equipped with advanced diagnostics [21,38,39] and optimization tools [40–43], together with a compact LWFA-based VHEE beam delivery system. Once these components are fully integrated and validated, our goal is to conduct preclinical testing of VHEE-based intensity-modulated radiation therapy delivery. This phase will focus on irradiating deep-seated tumors in mid-to-large animal models, with an emphasis on quantifying therapeutic efficacy, normal tissue sparing, and practical gantry performance under clinically relevant conditions. Success in these studies will mark a pivotal step toward translating LWFA-VHEE technology into human trials.

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B. Z., Z. G., and S. L. contributed equally to this work.

DATA AVAILABILITY

Source data supporting this work are now deposited in WPS cloud, [44].

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