Bayesian optimization of a laser-plasma accelerator aiming the production of high-energy electron beams for VHEE radiotherapy

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Abstract. *Radiation therapy aims to maximize tumor dose while minimizing exposure to healthy tissues. Despite advances, normal tissue toxicity remains a significant obstacle. While proton therapy shows promise, its high cost limits widespread adoption. Very high-energy electrons (VHEE, 50-250 MeV) represent an alternative with deep tissue penetration suitable for conventional and FLASH radiotherapy, which enables higher curative doses while reducing normal tissue toxicity. Laser-plasma accelerators (LPAs) offer a compact and cost-effective approach to generating electron beams for VHEE radiotherapy, a modality with dosimetric advantages comparable to proton therapy but without requiring the large cyclotrons typically used for ion acceleration. This work implements Bayesian optimization to systematically tune particle-in-cell (PIC) simulations modeling an LPA, aiming to produce optimal electron beams for VHEE radiotherapy. Key findings include achieving a spectrum with two charge peaks at different energies and total integrated charge of 1.9 nC. Additionally, the Institute of Energy and Nuclear Research (IPEN) has recently received approval to acquire a 15 TW laser, making it the most powerful in the Southern Hemisphere. The framework developed in this work can be scaled to IPEN's laser system parameters to guide future VHEE radiotherapy experiments.*

1. Introduction

Radiotherapy (RT) is essential to treat most of malignant tumors, with the aim of providing enough radiation to eradicate cancer cells while minimizing damage to normal tissues [Lv 2022, Abdel-Wahab 2021]. Despite advances, dose-limiting toxicity to normal tissues remains a significant challenge [Lv 2022]. Although proton therapy shows promise, its high cost limits widespread adoption [Bulanov and Khoroshkov 2002, Kokurewicz 2017]. Current megavoltage electron beams (4-22 MeV) are limited to treating superficial tumors within 5 cm depth [IAEA 2005], however very high-energy electrons (VHEE, 50-250 MeV) offer superior tissue penetration for conventional and FLASH RT, with elevated dose rates that potentially improves normal tissue tolerance while addressing tumor radiation resistance [Corsini 2021].

VHEE therapy provides reduced sensitivity to tissue heterogeneity, superior focusing capabilities, and flatter depth-dose profiles compared to X-rays and protons [Whitmore 2021]. Research shows that VHEE beams above 100 MeV provide uniform depth-dose distributions comparable to transmission proton beams, with VHEE energies of 150+ MeV achieving equivalent dosimetric quality to 250 MeV proton plans [Böhlen 2024], and can also be precisely focused at depths up to 15 cm [Kokurewicz 2021, Whitmore 2021]. Despite these advantages, VHEE technology remains in the developmental stage, with no commercially available clinical systems yet on the market. Laser-plasma accelerators (LPAs) represent a promising technology for generating VHEE beams more compactly and cost-effectively than conventional LINACs [Kokurewicz 2017, Corsini 2021]. While conventional accelerators are limited to gradients of 100 MeV/m, LPAs can achieve up to 100 GeV/m, with experimental results demonstrating 8 GeV electron beams in just 20 cm of plasma [Gonsalves 2019].

Given the complex dynamics governing LPA electron beam acceleration, this work proposes applying Bayesian Optimization (BO) to laser-plasma acceleration for generating electron beams suitable for VHEE RT, using Particle-in-Cell simulation data to optimize LPA parameters with an objective function that rewards the accumulation of charge at energies close to a selected target value. Although in a previous work an LPA operating in the self-modulated regime was optimized for the production of medical radioisotopes, prioritizing beam energy and charge over quality [Nunes 2025], this study specifically explores the bubble regime, aiming to produce high-quality beams suitable for RT applications.

The Institute of Energy and Nuclear Research (IPEN) has recently received approval to acquire a 15 TW laser, making it the most powerful in the Southern Hemisphere [Vieira Junior and Samad 2024]. This work will be scaled to IPEN's laser system parameters to guide future VHEE radiotherapy experiments.

2. The Model

In order to generate quasi-monoenergetic electron bunches for potential clinical applications, this study investigates VHEE acceleration in the bubble regime using the FBPIC code [Lehe 2015] to perform PIC simulations with fixed laser parameters and BO to optimize the simulation target. The internal parameters of the PIC simulations are presented in Table 1.1 and the laser pulse parameters are listed in Table 1.2, which are kept constant [Böhlen 2024]. The optimization aims to identify, within the intervals specified in Table 1.3, the values of the laser focal position (z_{foc}), the gas jet density profile (rising ramp, R_1; plateau, L_1; and falling ramp, R_2), and its composition (helium density, n_{He}, and nitrogen density, n_{N}) that maximize the electron charge with energies close to a predefined target value. These parameters physically characterize the LPA configuration.

The optimization process begins with a set of random experiments (n=5) with parameters assigned within specified ranges, then follows an iterative approach of selecting new sampling locations, collecting observations, and updating the model. In this study, the BO algorithm was employed through the Botorch library [Balandat 2020], with the objective of maximizing a function F_{obj}, defined in relation to the energy and charge of

Table 1. Laser-plasma interaction simulation parameters.

Parameter	Value or interval	Unit	Description
1.1. PIC Parameters			
z_{min}	-33	μm	Initial boundaries of the longitudinal simulation domain
z_{max}	0		
r_{max}	80	μm	Simulation domain radius
Δ_z	$\lambda_0/32$	nm	Spatial resolution in z
Δ_r	$\lambda_0/12$	nm	Spatial resolution in r
$N_{m,pz,pr}$	2	—	Number of modes
$N_{p\theta}$	8	—	Number of particles per cell along θ
1.2. Laser Parameters			
P_L	92.6	TW	Initial peak power
λ_0	800	nm	Wavelength
z_0	-15	μm	Pulse centroid
τ	30	fs	Pulse length (FWHM)
w_0	30	μm	Waist
1.3. Input Parameters			
z_{foc}	25 , 1100	μm	Laser focal position
n_{He}	$0.25, 0.55$	$10^{19} cm^{-3}$	Helium density
n_{N}	$0.0, 0.3$	$10^{19} cm^{-3}$	Nitrogen density
R_1	50 , 350	μm	Up-ramp length
L_1	600 , 1400	μm	Plateau length
R_2	50 , 350	μm	Down-ramp length

the beam accelerated by LPA. The upper confidence bound (UCB) acquisition function has been adopted. Figure 1 shows the details of this process.

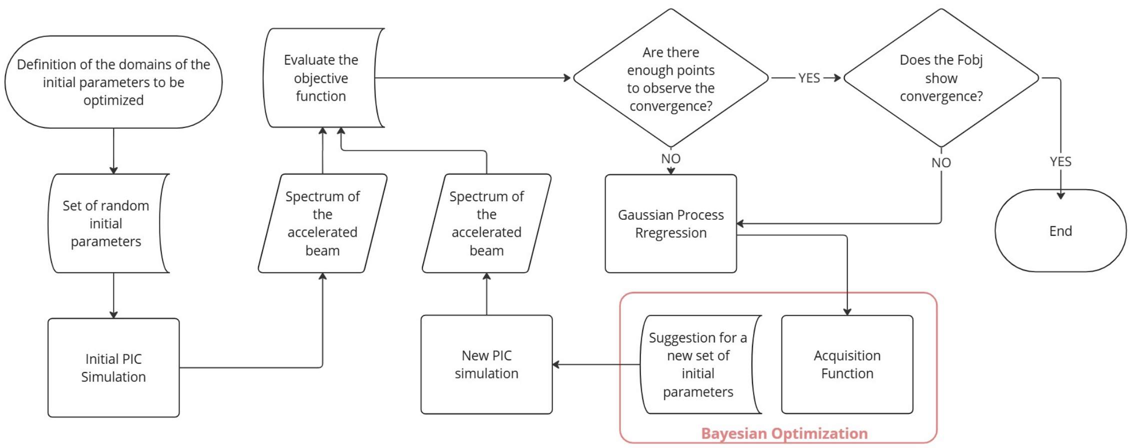

Figure 1. Flowchart of the BO process in PIC simulations.

Output parameters were derived from the energy spectrum of the accelerated electron beam generated by the simulations. The proposed F_{obj} combines the charge (Q) with a term that evaluates how closely obtained energies (E_i) match the target energy $E_t = 200\,\text{MeV}$, chosen to provide sufficient penetration depth for treating deep-seated tumors. This approach allows the search for optimal parameters that result in a quasi-monoenergetic bunch centered at the target energy. For analysis, the energy spectrum was discretized by dividing the selected energy interval into N bins. If the i-th bin contains a nominal energy E_i and a given amount of charge Q_i, then the aforementioned quantities can be calculated as follows,

$$F_{obj} = \sum_{i=1}^{N_{bins}} Q_i \, e^{-0.1|E_i - E_t|} \quad . \tag{1}$$

3. Results and Discussion

Figure 2(j) presents the achieved electron energy spectrum, spanning 50 to 450 MeV with a total charge of 1.9 nC. The spectrum features a bimodal distribution, with quasi-monoenergetic peaks at 150 MeV and 200 MeV, each reaching 15.0 pC per energy bin. This optimal spectrum results from the optimization based on the defined objective function F_{obj}, with $E_t = 200$ MeV, leading to a quasi-monoenergetic peak centered at E_t. Additionally, a second peak around 150 MeV was obtained. Magnetic fields could be employed to select which peak will be utilized, and their energies could be adjusted through attenuation.

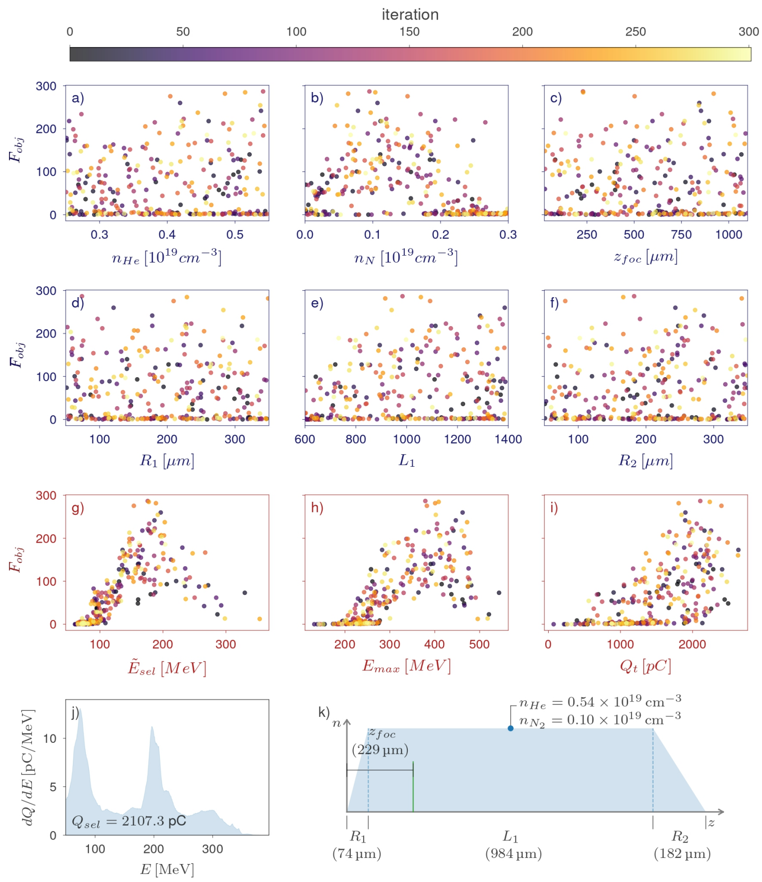

Figure 2. Bayesian Optimization Results, with a color scale indicating the algorithm iteration.

The FWHM energy spread per peak is 20–30 MeV (13–20% relative spreads for primary peaks) and a substantial high-energy tail extends beyond 300 MeV, reaching nearly 450 MeV. This spectrum is particularly relevant for VHEE radiotherapy, where energies above 100 MeV ensure effective tissue penetration. The 1.9 nC charge supports high-dose or single-shot FLASH therapy, while energy-specific selection via magnetic filtering could optimize treatment planning. The observed spectral complexity underscores the advanced laser-plasma dynamics in the helium-nitrogen target, demonstrating the feasibility of LPAs for medical applications.

Figure 2 illustrates a systematic exploration of parameter space through BO across approximately 300 iterations. Panels a-f display the relationship between input parameters and the objective function value, which effectively weights charge by proximity to the selected energy. The helium density (n_{He}) distribution panel (a) shows peak objective function values around 0.5×10^{19} cm^{-3}, though significant variations suggest complex parameter interdependencies. For nitrogen doping panel (b), lower concentrations yield better results, indicating nitrogen acts as a controlled injection mechanism rather than a primary accelerator. The focusing position (z_{foc}) in panel c displays a non-monotonic trend, emphasizing the importance of precise laser focusing relative to plasma structure.

Geometric parameters R_1, L_1, and R_2 panels (d-f) exhibit scattered distributions, highlighting sensitivity to target geometry. In panel e, the plateau (L_1) at 1000 μm corresponds to peak objective function values. However, up-ramp (R_1) and down-ramp (R_2) optimizations panels (d, f) lack convergence, suggesting ramp configurations do not significantly affect final LPA optimization in the bubble regime.

Panels (g-i) reveal the direct proportional relationship between performance metrics and objective function values. Panel (g) shows a strong positive correlation between the selected energy ($\tilde{E}_{\mathrm{sel}}$) and the objective function up to 200 MeV, beyond which the performance declines, indicating an optimal energy window. Panel (h) displays a similar trend for the maximum energy (E_{max}), peaking at 300-400 MeV. The total charge (Q_t) in panel (i) reveals a clear positive correlation with the objective function throughout the explored range, with the highest values at charges exceeding 2000 *pC*.

4. Conclusions

The primary contribution of this study lies in optimizing simulation parameters using BO to produce clinically relevant electron beam characteristics for VHEE radiotherapy. By focusing on the bubble regime, the research demonstrated the production of quasi-monoenergetic electron bunches, resulting in an optimal spectrum with two quasi-monoenergetic peaks centered at 150 MeV and 200 MeV, respectively, which are appropriate for medical applications. The optimization approach yielded electron beams with approximately 1.9 nC total charge and distinctive spectral features.

Systematic exploration through 300 BO iterations revealed complex interdependencies between input parameters and beam characteristics. Future optimization efforts will prioritize the most influential parameters by analyzing their correlation with the objective function F_{obj}, while exploring alternative objective function formulations to enhance convergence and beam quality. Additionally, we plan to conduct a series of simulations with a 15TW laser system to prepare for experimental validation at IPEN, where this technology is expected to be operational by 2027.

These findings represent significant progress toward the practical implementation of compact laser-plasma-based accelerators for radiotherapy. The beam parameters achieved, particularly the high charge at energies exceeding 100 MeV with reasonable energy spread, satisfy key requirements for the potential implementation of radiotherapy. The BO approach offers a powerful tool for navigating the complex parameter space of laser-plasma acceleration, potentially accelerating the development and clinical translation of this promising technology for cancer treatment.

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