Original Article

Optimization of Ion Energy for the Treatment of Cancerous Tumors

Ghaforyan Hossein*, Mohammadi Bilankohi Sara , Khalilpour Habib
Department of Physics, Payame Noor University (PNU), Tehran, Iran

Abstract

Background & Objectives: For over 60 years, proton beams and heavy ions have been a powerful ion therapy method for treating cancerous tumors. It is an inherent ability of high-energy ions to discharge their energy at a certain depth with high doses, which is impossible for other beams such as X-rays, gamma rays, and electron beams. Moreover, it is an excellent way to protect healthy tissues in ion therapy.

Materials & Methods: Scientists have used radio frequency (RF) accelerators to generate high-energy ions. However, due to the high price and large devices, laser-plasma accelerators have received much attention. This paper has studied the best conditions for producing high-energy argon ions. For this purpose, the interaction of high-intensity laser pulses with argon nanoclusters is simulated. This simulation is based on the nanoplasma model by the particle in cell method (PIC).

Results: The simulation results show that the ion energy is dependent on the parameters of the irradiated laser and the parameters of the target cluster.

Conclusions: The energy of the ions increases with the intensity of the laser and the duration of the laser pulse. Access to higher energy ions is also possible by changing the radius of the cluster. The density of the initial atoms of the cluster is also an important parameter that influences the energy of ions.

**Keywords:** laser-cluster interaction, accelerated ions, nanoplasma model, ion therapy, particle in cell method

Introduction

Approximately 4% of the world's population is diagnosed with cancer each year, and more than half of these patients receive radiation therapy. Radiation therapy with surgery is the most ordinary and best kind of cancer treatment. Although radiotherapy is mainly performed using photons, proton therapy has been considered because of its ability to irradiate high doses on tumors and focus on a smaller area. With protons (and other ions), healthy tissue is less damaged during radiation than when photons or electrons are used. Nevertheless, due to high prices and limited availability, patient access to treatment of heavy protons and ions (C $^{+6}$) is limited. Ionized hadrons was first used in 1932 to treat cancer. In 1946, Bob Wilson made the first proposal in this field (1). In 1954, the

*Corresponding Author: Ghaforyan Hossein, Department of Physics, Payame Noor University (PNU), Tehran, Iran
Email: hghaforyan@pnu.ac.ir
https://orcid.org/0000-0002-3384-175X

Mohammadi Bilankohi Sara: https://orcid.org/0000-0002-8477-1210
Khalilpour Habib: https://orcid.org/0000-0002-2911-0305

first patients were treated. As of 2012, there were 39 particle therapy centers in the world, more than half of which are in the United States and Japan (2). Approximately 100,000 patients have been treated with hadrons (protons and carbon ions). Higher energy protons are needed to treat deeper tumors. Nevertheless, radiotherapy using accelerator-based hadron beams is well established. A number of good researches in this field are given in the sources (3-14). It shows how effective Hadron therapy is in treating cancer. Initially, accelerators were dedicated to research in nuclear physics. Ionic radiation was soon used in other fields such as materials analysis, materials science, geology, and biology. Therefore,

accelerators were used in hospitals and industry. Most of these accelerators use low and medium energies. Radioactive isotopes produced by accelerators are used in medical imaging and therapeutic applications. For example, ^{11}C, ^{13}N, ^{15}O, and ^{18}F are used for PET imaging, and ^{103}Pd is used to treat tumors. In this case, they are located near the tumor. Ionic radiation therapy is very important because healthy tissues near the tumor are at serious risk. One of the advantages of ion beams is that they disappear entirely in the area away from the Bragg peak and have only a slight deviation from the peak. Chart 1 shows the relative radiation dose for treatment in terms of tissue depth (2).
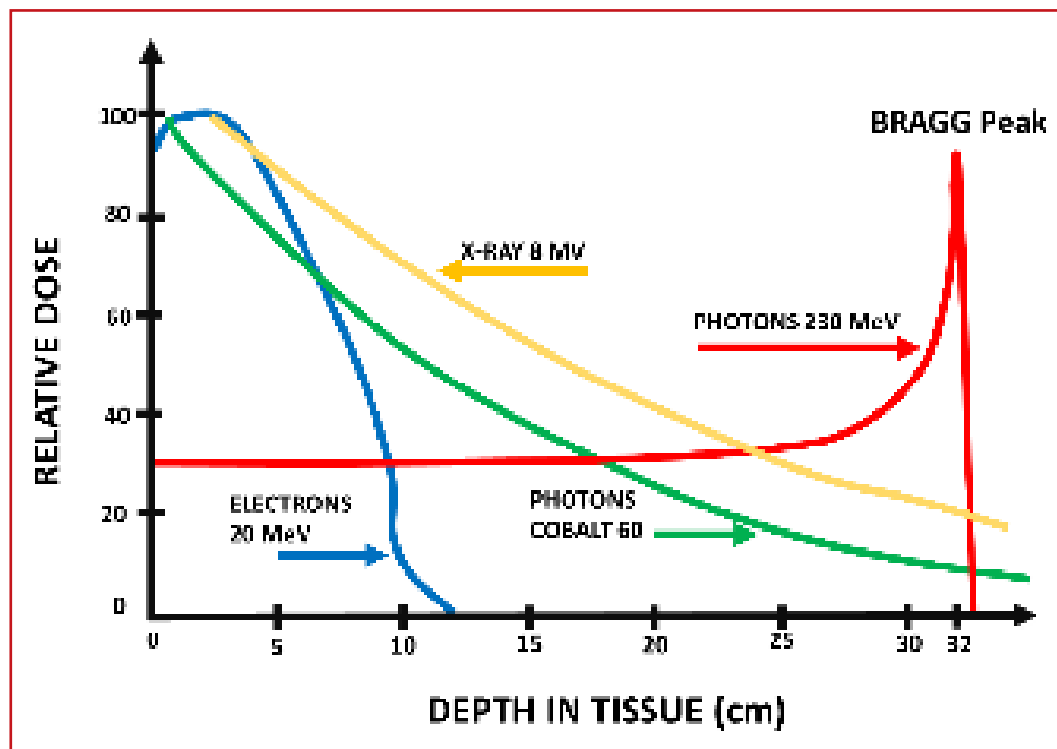

Chart 1. The relative radiation dose deposited as a function of tissue depth for various particle and photon beams (2)

It is observed that X-rays, which are commonly used, reduce the radiation dose by penetrating the tissue. The same thing happens with other photon beams. However, the maximum release of proton energy occurs at a deeper distance in the tissue, which can coincide with the depth of the tumor by selecting the appropriate energy for the proton. In this method, healthy tissue located upstream

in the last few decades, outstanding progress has been made in high-power laser technology, with laser powers reaching the petawatt (PW) level. With adequate focusing, petawatt lasers can generate peak electric fields of order 10^{12} V/cm with relatively efficient conversion to relativistic electrons with energies over 1 GeV. These electrons can create beams of protons,

heavy ions, neutrons, and high-energy photons. Given the potential for energetic laser-driven particles, we can now consider experiments in laser laboratories that are normally associated with conventional nuclear accelerators and reactors.

Recently, many researchers have studied the interaction between femtosecond lasers with clusters, both theoretically and experimentally (15-17). Clusters effectively absorb the energy of laser pulses. The absorbed energy yields cluster explosions to create high-energy particles, ions and electrons, and soft X-rays (18). Numerous theoretical models have been proposed to justify the experimental results (19-22). The nanoplasma model is one of these models. Many phenomena, such as the process of cluster expansion, and the production of energetic ions and electrons, can be described with this model. This model considers a high-density plasma ball with a uniform density and temperature (23). Many scientists have studied the interaction of femtosecond lasers with atomic clusters to produce energetic particles.

Researchers have done different work to investigate the emission of ions in the interaction of lasers with clusters. Zhong et al. studied the energy of Ar ions emitted from Ar clusters irradiated by intense femtosecond laser pulses. Therefore, laser-cluster interaction as a relatively small and low-cost system for the production of high-energy ions has been introduced.

Zamith et al. experimentally investigated the optimization of charged ion production due to the interaction of an intense laser field with xenon clusters (24). By studying the energy of ions obtained from the explosion of clusters irradiated by intense femtosecond laser pulses and experimental measurements, they discovered that the consequences were in good agreement with the heating mechanisms of the nanoplasma model (25). Because the production of high-energy ions is important in medicine and industry, in this work, we study the production of high-energy ions in laser-cluster interaction and discuss in detail the dependence of ion energy on effective parameters.

Materials & Methods

This work's main aim is to simulate the interaction of high-intensity femtosecond laser pulses with argon gas nanoclusters to obtain high-energy ions. The simulation code based on the particle in cell method has been modified for our aim. The main used code is written in C^{++} and solves the differential equations using a fourth-order Runge–Kutta method. After successfully running the code, the charts are plotted using Matlab. In this way, first, the Eqs. (2) and (3) are solved using initial values, and then the electron density and temperature are calculated for use in obtaining the results.

The electric field in the cluster increases after irradiating a high-intensity laser pulse. The relationship between the laser field (E_0) and the electric field inside the cluster (E_c) is as follows

$$E_c = \frac{3E_0}{|\varepsilon + 2|} \qquad (1)$$

E_0 is the amplitude of the laser field in vacuum and $\varepsilon = 1 - \frac{\omega_P^2}{\omega(\omega + iv)}$ is the plasma dielectric constant using Drude model, $\omega_P = \sqrt{\frac{4\pi n_e e^2}{m_e}}$ is the plasma electron frequency, e, me are the electron charge and electron mass respectively, and v is electron-ion collision frequency. In Eq. (1), When $n_e = 3n_{crit}$, $|\varepsilon + 2|$ has minimum value, and the inner field inside the cluster becomes greater than the laser field which is called resonance point.

With variation in the field inside the cluster, according to the nanoplasma model, three processes of ionization, heating, and expansion of the cluster occur, respectively. The ionization mechanism in nanoplasma model starts with field ionization and continues with collisional ionization. The cluster is first ionized by laser field, which is expressed in the model with ADK tunnel ionization rate and produces a small number of electrons, and the interaction of the produced electrons with other particles creates collision ionization which is very important. Heating is the second process that occurs in the nanoplasma model. The laser transfers its energy to the cluster through reverse bremsstrahlung absorption (26). In this case, a fraction of

electrons finds enough energy to escape the cluster, and positive ions are created inside the cluster.

Finally, the cluster expands in response to coulomb pressure and hydrodynamic forces. Coulomb pressure results from of the repulsive ions that occur in clusters. The hydrodynamic pressure created by the expansion of hot electrons is the second factor for cluster expansion. The important equations related to the processes mentioned in the nanoplasma model are presented below.

a. The time evolution of the ion density n_i and electron temperature T_e (26):

$$\frac{dn_i(Z)}{dt} = -[W(Z) + \alpha_3(Z)n_e^2]n_i(Z) + W(Z-1)n_i(Z-1) + \alpha_3(Z+1)n_e^2 n_i(Z+1)$$

$$(2)$$

$$\frac{dT_e}{dt} = \frac{2}{3}\frac{Q}{n_e} - \frac{T_e}{n_e}\frac{dn_e}{dt} + \frac{2}{3}\sum_{Z=0}^{\infty}\varepsilon_i(Z)[\alpha_3(Z+1)n_e n_i(Z+1) - S(Z)n_i(Z)]$$

$$(3)$$

where the relation between the electron density and ion density is given by $n_e = \sum_{Z=0}^{\infty} Zn_i(z)$.
In Eq. 2, the coefficients W and α3 describe, respectively the total ionization rate from a charge state Z to a charge state Z + 1, and the three-body recombination rate. S is the collisional ionization coefficient which will be discussed in the partial review of Lotz formula (27).

b. The inverse bremsstrahlung (IBS) absorption rate for a clustered plasma is given by (26):

$$Q = \frac{\omega_p^2 \nu}{\left[\omega - \frac{\omega_p^2}{3\omega}\right]^2 + \nu^2} \frac{|E_0|^2}{8\pi} \qquad (4)$$

Here, (ω) is the collision frequency, and E_0 is the intensity of the laser.

c. The hydrodynamic pressure due to the expansion of hot electrons is given by (28):

$$P_e = n_e k_B T_e \qquad (5)$$

the coulomb pressure is given by (28):

$$P_{coul} = \frac{q^2 e^2}{8\pi r^4} \qquad (6)$$

where q is the built-up charge on the cluster due to electron escape. It is noticed that coulomb pressure is important only for very small cluster and its role in our calculation will be ignored.

d. during the laser interaction with cluster, the energy of the laser first is absorbed by the electrons and then this energy is transformed to the kinetic energy of the cluster ions. With this assumption that the velocity of the radial motion of the ions is the linear function of radius of the cluster, the mean kinetic energy of the ions can be written by (29):

$$\bar{E} = \frac{3}{10}m_i \left(\frac{dr}{dt}\right)^2 = 0.3 m_i v_i^2 \qquad (7)$$

where $m_i = 40 m_p$ (m_p is the mass of a proton) is the mass of Ar ions and v_i is the cluster expansion velocity.

Results

In this interaction, we considered the radius of the argon cluster to be 15nm and the density of its initial atoms to be $n_{io} = 2.63 \times 10^{22}$ cm^{-3}. We used a laser with an intensity of 5×10^{14} Wcm^{-2} to 1×10^{16} Wcm^{-2}, a wavelength of 825nm, and FWHM=40 fs.

The problem of high temperatures and energetic particles in the laser cluster interaction is of fundamental importance in many applications. So, access to high-energy ions seems to be essential in these interactions. In the present study, we tried to obtain higher energy ions by changing the interaction conditions, and this capability can lead to significant development in medical science and industry. To this end, we investigated the role of laser intensity, laser pulse duration, the initial radius of the cluster, and the density of the initial atoms of the cluster in the ion energy resulting from the interaction.

Also, to investigate the physics of the problem and find the reasons for the changes in the important interaction parameters, we first simulated the time evolution diagram of the applied laser electric field and the internal field of the cluster, which is shown in chart 2.
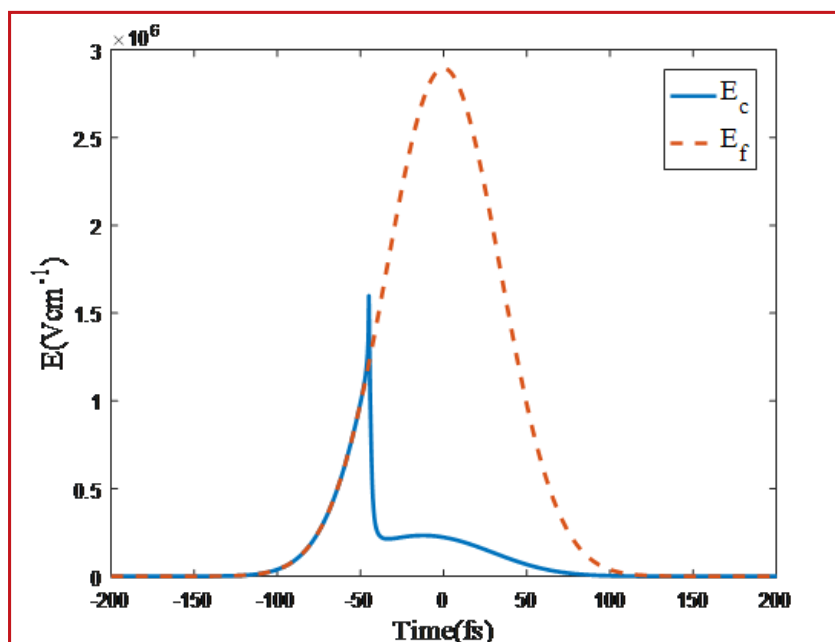
Chart 2. The laser's electric field with 40fs pulse duration, 825 nm wavelength, and with intensity 1×10^{15} Wcm^{-2} (dashed) and electric field inside the cluster in laser interaction(solid)

It is necessary to pay attention to the fact that the time origin in the time diagrams is selected so that the maximum external field corresponds to t = 0. Chart 2 shows that the laser field is Gaussian with a maximum value at t = 0fs and starts to increase from t = -110fs and tends to zero at almost 110fs.This field leads to the production of an internal field inside the cluster. The internal field of the cluster at the moment t = -33fs has the second maximum, which will play an important role in subsequent processes,

particularly the beginning of the ion energy increase. The cluster's internal field starts to increase simultaneously as the laser field increases and reaches a maximum at t = -50fs. It is clear from the Chart that the internal field at t = -50fs is larger than the external field. Increasing the energy of the electrons and their escape from inside the cluster causes a rapid decrease in the internal field of the cluster.

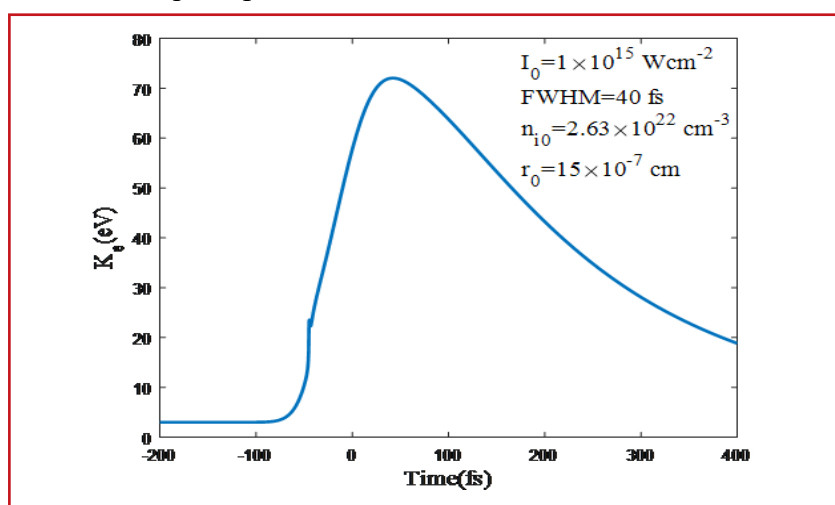For further investigation, we have shown the time evolution of electron energy in chart 3.

Chart 3. Time evolution of the electron energy during laser cluster interaction with 40fs pulse duration, 825 nm wavelength, and intensity 1×10^{15} Wcm^{-2}

To study the energy of ions and explain the time evolution of ion energy, we first obtained the time evolution of electron energy in the interaction of a laser with an intensity of 1×10^{15} Wcm^{-2} with an argon cluster, shown in chart 3. It is clear from chart 2 that at the moment t = -50fs, at the same time, as the internal field of the cluster increases, the energy of the electrons begins to increase, and this increase continues until the internal field does not reach zero. After the internal field disappears, the energy of the electrons begins to decrease. This process is similarly imaginable for subsequent pulses.

Because the principal purpose of this study is to obtain the energy of ions and to obtain the optimal conditions for the production of energetic ions, for this purpose, we have calculated the time evolution of ion energy at four different intensities for laser interaction with argon clusters shown in chart 4.
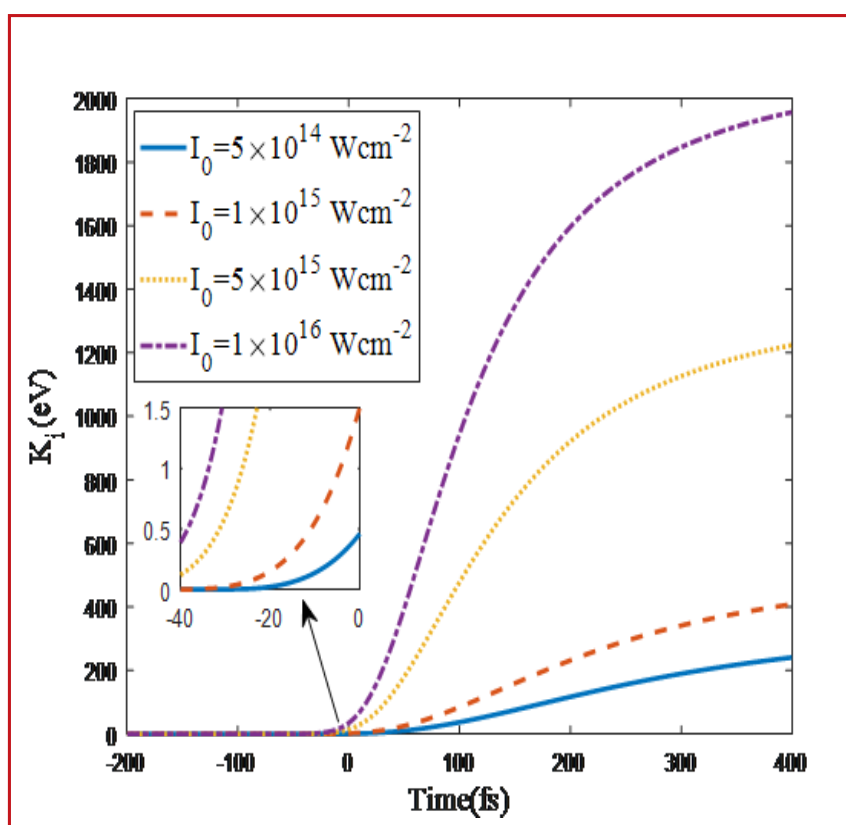

Chart 4. Time evolution of the ion energy during laser cluster interaction with 40fs pulse duration laser, 825 nm wavelength for four different laser intensity values

A closer look at chart 4 reveals that the ions' energy increases dramatically as the laser intensity increases. Further details of chart 4 for the initial moments of ions energy increase show that, for example, for the intensity of 1×10^{15}Wcm^{-2}, the energy of the ions starts to increase from t = -33fs. Examining the simulation results, it is clear that the second maximum in the internal field of the cluster coincides with the beginning of the increase in the energy of the ions.

Another influential parameter that researchers have studied in previous papers for electron energy is the laser's pulse duration. Therefore, to investigate the effect of this parameter on ion energy, we have simulated the time evolution of ion energy for different pulse durations, shown in chart 5.
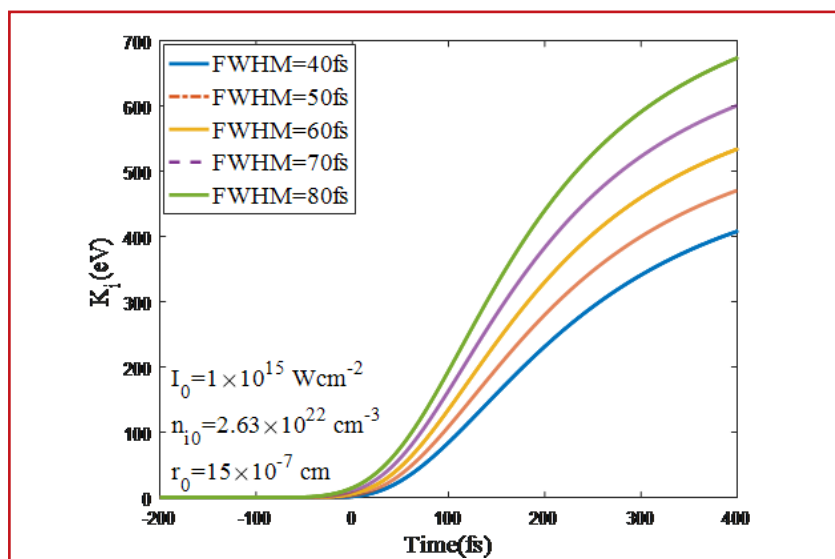
Chart 5. Time evolution of the ion energy during laser cluster interaction with 40fs pulse duration laser, 825 nm wavelength, and intensity 1×10^{15} Wcm^{-2} for five different pulse durations

Further investigation reveals that the energy of the ions resulting from the interaction depends on the laser's pulse duration, and increasing the pulse duration leads to an increase in the energy of the ions. In previous articles, the temperature dependence of electrons on laser pulse duration has been reported. Therefore, it can be said that as the energy of the electrons leaving the cluster increases, the energy of the ions also increases subsequently.

To investigate other interaction parameters in increasing ion energy, we simulated the time evolution of ion energy in the laser interaction with argon clusters in different radii, as shown in chart 6.
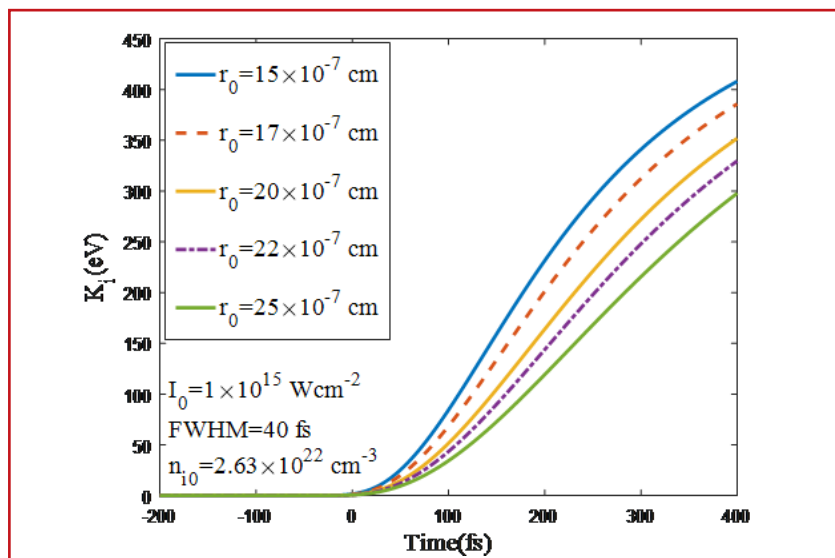

Chart 6. Time evolution of the ion energy during laser cluster interaction with 40fs pulse duration laser, 825 nm wavelength, and intensity 1×10^{15} Wcm^{-2} for five different radii of the cluster

It is clear from chart 6 that by reducing the cluster radius at a constant initial atoms density, the ion energy increases, so the cluster radius is introduced as a parameter affecting the ion energy under this type of interaction. When the density of the initial atoms is constant and the radius of the cluster increases, more atoms are exposed to laser radiation. Therefore, most of the laser energy is spent on ionization, and the energy of electrons leaving the cluster is reduced; consequently, the energy of the ions also decreases.
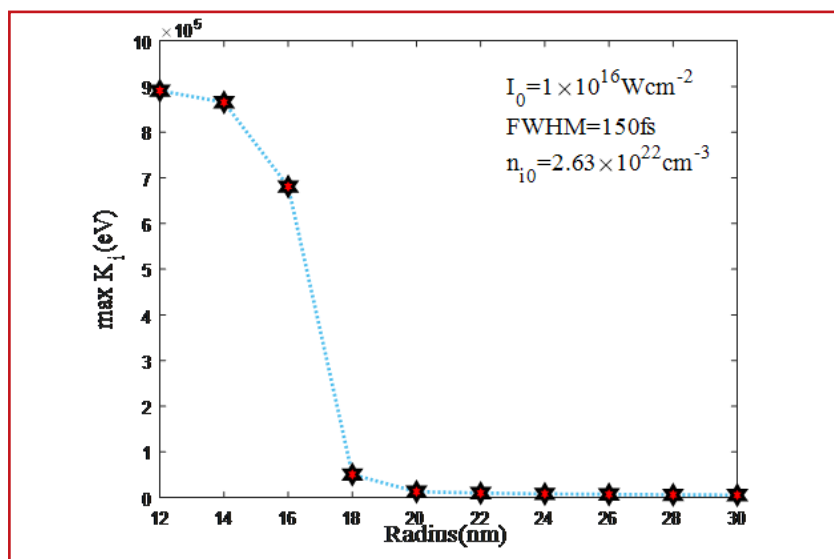
Ghaforyan H, et al.

Chart 7. Maximum energy of the ions in terms of the radius of the cluster in the laser-argon cluster interaction with 150fs pulse duration and 780 nm wavelength

To further investigate ion energy's dependence on the cluster's radius in chart 7, the maximum ion energy in terms of the radius with the different pulse duration is plotted. As seen from this chart, the energy of ions decreases with increasing radius. The remarkable point in this chart is that as the radius decreases and the pulse duration increases, the ion energy increases significantly (up to 900 KeV).

The density of the initial atoms of the cluster is also one of the effective parameters in the laser-cluster interaction. To investigate its role in ion energy, we obtained the time evolution of ion energy for three different initial atom densities, as shown in chart 8. The increasing density of initial atoms of the cluster causes most of the laser energy to be spent on ionization. As the density of the initial atoms increases, the density of electrons and ions increases, but the ions' energy decreases, as shown in chart 8.
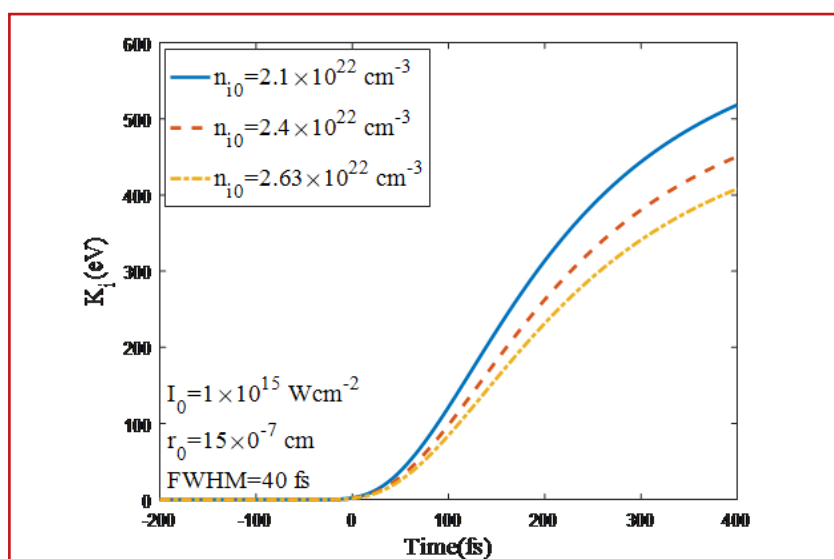
Chart 8. Time evolution of the ion energy during laser cluster interaction with 40fs pulse duration laser, 825 nm wavelength, and intensity 1×10^{15} Wcm^{-2} for three different initial densities of atoms

Discussion

Since ion therapy is one of the appropriate methods for treating cancerous tumors and treating tumors at a deeper distance in the body tissues requires the production of high-energy ions. In this paper investigates the interaction of high-intensity femtosecond laser pulses with atomic clusters of argon gas to obtain high-energy ions. By considering the changes in the electric field inside the cluster after interacting with the laser, it becomes easier to analyze the behavior of the produced particles. The occurrence of two maxima in the inner field of the cluster plays an essential role in the acceleration of electrons and ions. When the internal field of the cluster reaches the first maximum, the energy of the electrons increases sharply, which causes them to leave the cluster. When the internal field of the cluster reaches the second maximum, the energy of the ions begins to increase. The simulation results showed that increasing the laser intensity causes a significant increase in ion energy. The laser pulse duration was another parameter that increased the energy of the ions. When the density of the initial atoms of the cluster is constant, the energy of the ions increases as the initial radius of the cluster decreases. The density of the initial atoms of the cluster is another influential parameter that, with proper selection, ions with higher energy can be obtained. Therefore, we conclude that without increasing the intensity of the laser, other effective parameters can increase the energy of the ions. Since the increase in ion energy co-occurs with the increase in the cluster radius and the decrease in the cluster ion density, confirming the nanoplasma model and the simulation results. In addition to the benefits presented for this study, the choice of the cluster as a target in laser interaction is one of the important advantages compared to the results of other researchers. Because in the interaction of lasers with solids, higher laser intensities are required to accelerate ions. But, ions can be accelerated at low intensities in the interaction of lasers with atomic clusters. Also, the absorption of laser energy in the clusters is larger than in the gas and solid targets, so it can be said that the clusters have the advantage of the solid and gas phases.

In the laser-cluster interaction to produce energetic electrons and ions, if the laser intensity is greater than 1×10^{18} Wcm^{-2}, relativistic equations must be used to study the dynamics of electrons and ions (30-33). However, if laser intensity is less than that, for example, in the range 1×10^{14} Wcm^{-2} to 5×10^{17} Wcm^{-2}, the classical equations must be used to study the dynamics of electrons and ions. In recent years, some researchers have investigated laser-cluster interactions for laser intensities higher than 1×10^{19} Wcm^{-2}, which has led to the production of ions with energies of 2MeV to 90MeV. Smith (34), Fukuda (35), and Tajima (36) were researchers who, from 2009 to 2020, were able to produce ions with an energy of 90MeV by radiant 5×10^{19} Wcm^{-2} lasers. Nevertheless, some scientists have tried to produce high-energy ions using low-intensity lasers, the classical region. Taguchi (37), Kumarappan (38), Krishnamurthy (39), and zhu (29) produced ions with energies of 10KeV to 100KeV using radiate lasers with intensities of 1×10^{15} Wcm^{-2} to 1×10^{16} Wcm^{-2}. In this study, considering all conditions, we obtained ions with energy of about 900Kev in the classical range (intensities of 1×10^{15} Wcm^{-2} to 1×10^{16} Wcm^{-2}. It can be seen that the energy of the ions, in this case, increased nine times compared to the previous works (See chart 7).

Conclusion

The results showed that the energy of the ions obtained from the interaction of femtosecond lasers with Argon clusters is dependent on the parameters of the irradiated laser and the parameters of the target cluster. As the intensity of the laser and duration of the laser pulse increase, the energy of the ions increases. Also, the cluster's radius and density of the cluster's primary atoms are important parameters that affect the energy of the ions. Based on the obtained results, it seems that using high-power lasers; desktop accelerators can be made that take up little space and also have a low price. Achieving this will allow ion therapy technology

to treat cancerous tumors in most hospitals.

Acknowledgments

Conflict of interest

The author(s) declare(s) that there is no conflict of interest.

References

1. Wilson RR. Radiological use of fast protons. Radiology. 1946; 47: 487–491.

2. Ledingham Ken W. D, Bolton Paul R, Shikazono N, Charlie Ma CM. Towards Laser Driven Hadron Cancer Radiotherapy: A Review of Progress. Applied Sciences. 2014, 4(3): 402-443.

3. Ledingham KW, Bolton PR, Shikazono N, Ma CM. Towards laser driven hadron cancer radiotherapy: A review of progress. Applied Sciences. 2014;4(3):402-43.

4. Jones B. The case for particle therapy. The British Journal of Radiology. 2014; 79: 937.

5. Chang-Ming C. M, Maughan R. L, Colin G.O. Within the next decade conventional cyclotrons for proton radiotherapy will become obsolete and replaced by far less expensive machines using compact laser systems for the acceleration of the protons. Medical Physics. 2006; 33: 571-573.

6. Hamatani N, Tsubouchi T, Takashina M, Yagi M, Kanai T. Commissioning of carbon-ion radiotherapy for moving targets at the Osaka Heavy-Ion Therapy Center. Medical physics (Lancaster). 2022; 49 (2): 801.

7. Min Y, Hekai L, Xiaoya W, Jianyun Y, Long G, Yinyan H, et al. Ion Therapy: A Novel Strategy for Acute Myocardial Infarction. Advanced science, 2020; 7 (10): 2000544-n/a.

8. Inaniwa T, Abe Y, Suzuki M, Lee S.H, Mizushima K, Nakaji T, et al. Application of lung substitute material as ripple filter for multi-ion therapy with helium-, carbon-, oxygen-, and neon-ion beams. Physics in medicine & biology. 2021; 66 (5): 55002.

9. Horst F, Schardt D, Iwase H, Schuy C, Durante M, Weber U. Physical characterization of 3He ion beams for radiotherapy and comparison with 4He. Physics in medicine & biology. 2021;66 (9): 95009.

10. Zhang H, Zhang Y, Yang H, Qian C, Li X, Sun X. Hi'Beam-A: A Pixelated Beam Monitor for the Accelerator of a Heavy-Ion Therapy Facility. IEEE Transactins on Nuclear Science. 2021; 68: 2081.

11. Ghaforyan H, Sadighi-Bonabi R, Irani E. The Effect of Chirped Intense Femtosecond Laser Pulses on the Argon

Cluster. Advances in High Energy Physics. 2016; 2016: 2609160.

12. Ghaforyan H. Energy of electrons at the interaction of femtosecond laser with argon nanocluster. Pramana. 2019;92(5):1-9.

13. Khalilpour, H., Ghaforyan, H. The Study of Simulation of the Interaction of Intense Femtosecond Laser with Neon Nanocluster. Biquarterly Journal of Optoelectronic. 2021; 3(2): 9-18. [In Persian]

14. Ghaforyan, H. Studying Simulation of Effective Parameters on Charge State of Ions in Interaction of High Power Laser with Argon Nano - Cluster. Biquarterly Journal of Optoelectronic, 2017; 1(3): 27-34. [In Persian]

15. Ditmire T, Smith R. A, Tisch J.W G, Hutchinson M.H. High Intensity Laser Absorption by Gases of Atomic Clusters. Phys Rev Lett. 1997; 78: 3121.

16. Gleitsmann T, Bernhardt T.M, Wöste L. Luminescence properties of femtosecond-laser-activated silver oxide nanoparticles embedded in a biopolymer. Applied Physics A. 2006; 82: 125.

17. Forster M, Égerházi L, Haselberger C, Huber C, Kautek W. Femtosecond laser interaction with pulsed-laser deposited carbon thin films of nanoscale thickness. Applied Physics A. 2010; 102: 27 (2010).

18. Ditmire T, Zweiback J, Yanovsky V.P, Cowan T.E, Hays G, Wharton K.B. Nuclear fusion from explosions of femtosecond laser-heated deuterium clusters. Nature. 1999; 398: 489–492.

19. Brun R, Urban L, Carminati F, Giani S, Maire M, McPherson A, Bruyant F, Patrick G. GEANT: detector description and simulation tool. CERN; 1993.

20. Ditmire T, Donnelly T, Rubenchik AM, Falcone RW, Perry MD. Interaction of intense laser pulses with atomic clusters. Physical Review A. 1996;53(5):3379.

21. Rose-Petruck C, Schafer KJ, Wilson KR, Barty CP. Ultrafast electron dynamics and inner-shell ionization in laser driven clusters. Physical Review A. 1997;55(2):1182.

22. Last I, Jortner J. Multielectron ionization of large rare gas clusters. The Journal of Physical Chemistry A. 1998;102(47):9655-9.

23. Bornath Th, Hilse P, Schlanges M. Interaction of Dense Nanoplasmas with Intense Laser Fields: Ionization Dynamics in Large Silver Clusters. Plasma Phys. 2007; 47: 402.

24. Zamith S, Martchenko T, Ni Y, Aseyev SA, Muller HG, Vrakking MJ. Control of the production of highly charged ions in femtosecond-laser cluster fragmentation. Physical Review A. 2004;70(1):011201.

25. Springate E, Hay N, Tisch JW, Mason MB, Ditmire T, Hutchinson MH, Marangos JP. Explosion of atomic clusters irradiated by high-intensity laser pulses: Scaling of ion energies with cluster and laser parameters. Physical Review A. 2000;61(6):063201.

26. Gao X, Arefiev A.V, Korzekwa R.C, Wang X, Shim B, Downer M.C. Spatio-temporal profiling of cluster mass fraction in a pulsed supersonic gas jet by frequency-

domain holography. Applied Physics. 2013;114: 034903.

27. Lotz W. Electron-impact ionization cross-sections for atoms up to Z=108. Phys. A. 1970; 232: 101.

28. Milchberg HM, McNaught SJ, Parra E. Plasma hydrodynamics of the intense laser-cluster interaction. Physical Review E. 2001;64(5):056402.

29. Zhu P, Liu L, Xu Z. Theoretical investigation of high-energy ions produced from laser-cluster interactions. Laser and Particle Beams. 2003; 21: 593.

30. Ma WJ, Kim IJ, Yu JQ, Choi IW, Singh PK, Lee HW, Sung JH, Lee SK, Lin C, Liao Q, Zhu JG. Laser acceleration of highly energetic carbon ions using a double-layer target composed of slightly underdense plasma and ultrathin foil. Physical review letters. 2019;122(1):014803.

31. Liu M, Gao X, Wang W.M, Li Y.T. Theoretical Study of the Efficient Ion Acceleration Driven by Petawatt-Class Lasers via Stable Radiation Pressure Acceleration. Appl Sci. 2022; 12: 2924.

32. Wang P, Gong Z, Lee S.G, Shou Y, Geng Y, Jeon C, et al. Super-Heavy Ions Acceleration Driven by Ultrashort Laser Pulses at Ultrahigh Intensity. Physical Review X. 2021; 11: 021049.

33. Wagner F, Brabetz C, Deppert O, Roth M, St¨ohlker T, Tauschwitz An. Accelerating ions with high-energy short laser pulses from submicrometer thick targets. High Power Laser Science and Engineering. 2016; 4: e45.

34. Smith JR, Orban C, Morrison JT, George KM, Ngirmang GK, Chowdhury EA, Roquemore WM. Optimizing laser–plasma interactions for ion acceleration using particle-in-cell simulations and evolutionary algorithms. New Journal of Physics. 2020;22(10):103067.

35. Fukuda Y, Faenov AY, Tampo M, Pikuz TA, Nakamura T, Kando M, Hayashi Y, Yogo A, Sakaki H, Kameshima T, Pirozhkov AS. Energy increase in multi-MeV ion acceleration in the interaction of a short pulse laser with a cluster-gas target. Physical review letters. 2009;103(16):165002.

36. Tajima T. Laser Acceleration of Ions for Radiation Therapy. Reviews of Accelerator Science and Technology. 2009; 2:201.

37. Taguchi T, Antonsen Jr T.M, Palastro J, Milchberg H, Mima K. Particle in cell analysis of a laser-cluster interaction including collision and ionization processes. Optics Express. 2010; 18: 2394.

38. Kumarappan V, Krishnamurthy M, Mathur D. Asymmetric High-Energy Ion Emission from Argon Clusters in Intense Laser Fields. 2001; 87: 085005.

39. Krishnamurthy M, Mathur D, Kumarappan V. Anisotropic "charge-flipping" acceleration of highly charged ions from clusters in strong optical fields. Physical Review A. 2004;69(3):033202.