Dosimetric Analysis of a Laser Accelerated Electron Beam and Optimization of FBX Chemical Dosimeter

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A thesis presented for the degree of
Doctor of Philosophy

University of Szeged
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Szeged
2020

1 Introduction

Cancer is the second leading cause of death worldwide, and it has become a global social and economic problem due to the continuous rise in incidence and mortality. In the last few decades impressive progress has been made in the understanding and early detection of cancers, and in the various treatment modalities. These achievements have made many cancer types curable.

Traditionally, there are three major treatment modalities for cancer diseases: surgery, radiotherapy and systematic therapy. Due to their ionization potential, high-energy ionization radiation (such as X-ray or high-energy particle beams) damages the genetic material of cells, which leads to cell death by blocking the cell's ability to divide and proliferate further.

Therefore, the importance of radiotherapy is evident and the number of radiation treatments have been growing thanks to increasingly efficient treatment methods, as well as precise and homogenous dose delivery. Radiation therapy is applied in most cancers. In fact, we may claim that the number of treated cases is limited by the quantity of available radiotherapy equipment and/or the relative costs of treatment.

More than 90% of the current external radiation therapies is based on photon beams due to their greater penetration compared to electron beams, which are also commonly used as a source in everyday external radiation therapy treatments. The former is used to treat deeper tumours, while electron beams are mainly used to treat tumours situated close to the body surface. However, *in silico* studies have shown that very high energy electron (VHEE) beams (50-60 MeV) have a more favourable dose distribution than advanced photon techniques, and in some situations, the results approach the charged particle therapy values.

In general, photon and electron beams are generated by linear particle accelerators (LINACs). LINACs accelerate electrons which are used directly for treatments or indirectly for the generation of X-ray radiation. The available LINAC technology has an acceptable cost and offers a compact setup with appropriate flexibility in adjusting the beam parameters (beam energy, direction, intensity etc.), which ensures the worldwide accessibility of

photon based radiotherapy techniques.

In the last few years, a new technology seems to be emerging using powerful lasers to accelerate particles. It is expected that this technology will significantly reduce the size of accelerators and make operation more cost-effective. Considering the present state of the art, the laser-driven electron acceleration to energies suitable for radiation therapy is well established. This technology is capable of producing monoenergetic electron beams with small divergence and dose rates suitable for practical clinical applications. However, there is still a lot to do regarding the efficiency, stability and reliability of the acceleration process.

The success of radiation therapy crucially depends on the accuracy of dose delivery to the target volume and on how much the dose absorbed by the surrounding healthy tissue is minimized. To realize this, a consistent dosimetry system is needed.

Dosimetry in radiation therapy has two important tasks: to supply the necessary dosimetric data for treatment planning calculations (radiotherapy machine commissioning) and to verify the delivered dose. Both tasks require a proper calibrated dosimetry system capable of measuring absorbed doses with high precision, sensitivity and accuracy at high spatial and dose resolution.

Measuring the absolute value of the absorbed dose for a clinical beam would be a sophisticated procedure, necessitating expensive instrumentation and very careful analysis and control of the measurement conditions. In practice, professionals follow a dosimetry protocol, published by national and international organizations. These procedures are based on the use of a reference dosimeter (usually an ionization chamber) which has a calibration factor, traceable to a Primary Standard Dosimetry Laboratory (PSDL) and ensures consistency in dose determination.

There are three methods currently known as sufficiently accurate for measurements of absorbed dose to water: calorimetry, chemical dosimetry and ionization dosimetry. The most commonly used instrument is the ionization chamber due to its good reproducibility and stability. However, chemical dosimeters presents some favourable properties which make it extremely useful in such situations where common dosimetry tools are not suitable.

The laser-driven radiation beam has some features which dif-

fer from the LINAC based beams which make the dosimetry a challenging task. To date, no dosimetric protocols have been established for the absolute dosimetry of radiation beams with such high instantaneous dose rates due to the lack of knowledge related to the response of dosimeters to such high dose rate radiation. My effort was to prepare the necessary methodology for future dosimetric measurements in such radiation fields using a modified version of the Fricke type chemical dosimeter, as an alternative to ionization chambers.

2 Aims of the thesis

In this thesis I investigate the dosimetric properties of an 1 kHz repetition rate LWFA electron beams. High repetition rate electron beams can be generated by commercially available 1 kHz laser systems (multi-TW power & few-cycle pulse duration); one such system is currently operational at ELI-ALPS Research Institute. Using the PIC and Monte Carlo simulation techniques the following statements were examined:

1. The energy spectra of an 1 kHz repetition rate LWFA electron beams generated with a 1 kHz laser system with parameters of the laser system currently operational at ELI-ALPS Research Institute are suitable for radiotherapy applications.

2. With the achievable radiation dose and dose rate and depth dose characteristics such particular LWFA systems could be used to address different practical needs (irradiate large target volumes, intensity or energy modulations etc.).

3. The high repetition rate compensate for the shot-to-shot reproducibility issue.

Furthermore, an enhanced chemical dosimetry system was developed to be used in various irradiation arrangements where common dosimetry tools are not suitable (for example in case of LWFA electron beams) or are difficult to use (like in radiobiological experiments where the standard reference conditions cannot

be provided in most cases). The main aim of this work was to develop such a dosimetry tool, capable of measuring the absorbed dose with high precision and accuracy in reference conditions. To achieve this aim, the following statements were examined:

1. With appropriate modification of the composition the FBX chemical dosimeter can be further optimized considering its dosimetric properties and capabilities as well as accuracy and precision.

2. With full characterization of the technique and developing the necessary tools and accessories for radiation dose measurements in reference conditions, as well as establishing the dosimetry methodology necessary to assure the desired accuracy and precision, the optimized FBX chemical dosimeter can be used as an absolute dosimetry technique suitable for measurements of radiation dose in the clinical dose domain (up to 20 Gy).

3 Methods

3.1 Feasibility study of 1 kHz LWFA electron beam

The electron beam source was simulated based on the electron beam characteristics obtained from 3D particle-in-cell (PIC) simulations, which were performed using the EPOCH open source code with the parameters of the SYLOS II laser system available at ELI-ALPS. To assess the dosimetric characteristics, Monte Carlo simulations were performed based on the Geant4.

The position, energy and direction of each electron in the beam were derived from a data file generated by the 3D PIC simulation, taking into account the correct weighting factor, as well as the position and momentum of each pseudo-electron. These parameters were then used to set up the initial electron parameters in the MC simulations.

3.2 Imporved FBX chemical dosimeter system

The dosimetric solutions were prepared from pre-prepared stock solutions, based on the following preparation procedure:

- Sulphuric acid stock solution – All stock solutions were made with 25 mM H_2SO_4, which was prepared before use from 0.5 M analytical grade sulphuric acid solution (5 ml 0.5 MH_2SO_4 dissolved in 100 ml HPLC water). The latter was obtained from concentrated H_2SO_4 solution (an ampoule contains 49.04 g H_2SO_4, Firma Chempure) and stored in dark screw-cap bottles at room temperature.

- The ferrous ammonium sulphate stock solution (FS) – ammonium Fe^{2+} sulphate hexahydrate ($(NH_4)_2Fe(SO_4)_2{\times}_6H_2O$, 3.921 g, Sigma-Aldrich) was dissolved in sulphuric acid (H_2SO_4, 25 mM, 50 mL). This was further diluted with 25 mM H_2SO_4 (100 mL). The resulting solution of ferrous ammonium sulphate (100 mM) was stored in a refrigerator to prevent the thermal oxidation of iron ions.

- The benzoic acid stock solution (BA) – benzoic acid ($C_7H_6O_2$, 1.974 g, Sigma-Aldrich) was dissolved in sulphuric acid (H_2SO_4, 25 mM, 900 mL). This was further diluted with 25 mM H_2SO_4 (100 mL). The final solution was 16.16 mM benzoic acid. (Dissolution can be accelerated by heating.)

- The xylenol orange stock solution (XO) – xylenol orange disodium salt ($C_{31}H_{30}N_2Na_2O_{13}S$, 179.16 mg, Sigma-Aldrich) was dissolved in sulphuric acid (H_2SO_4, 25 mM, 50 mL) and was then further diluted with 25 mM H_2SO_4 (100 mL).

All irradiation was performed in reference conditions using an in-house made PMMA slab phantom and different beam qualities. A conventional LINAC ($SSD = 100$ cm, field size 15 cm × 15 cm) was used for 6 MV and 15 MV photon beams and for 6 MeV, 9 MeV and 12 MeV electron beams, respectively. A cell and small animal irradiator facility was used (Xstrahl, RS320 type self-contained X-Ray irradiator) for 250 kVp X-ray beams ($HVL = 1.53$ mm Cu equivalent).

After irradiation, 0.1 mL xylenol orange stock solution (XO) was added to each 0.9 mL of irradiated dosimetric solution. The final solution contained 0.25 mM xylenol orange disodium salt. After waiting at least ten minutes for the xylenol orange to form complexes with the Fe^{3+} ions, we measured the solution's absorbance at 560 nm against the xylenol orange blank solution. The blank sample was prepared in a sample vial from the XO stock solution (0.1 mL) and sulphuric acid (0.9 mL 25 mM), in the same manner as the dosimetric samples.

Absorption measurements were performed using an UV-VIS spectrophotometer (Lambda 35, Perkin Elmer, double light path) and a quartz cuvette with a 1 cm path length. The recommendation of the ISO/ASTM 51026:2014 standard was followed to ensure the reproducibility and accuracy of the measurements.

4 Results and discussion

1 kHz Laser Accelerated Electron Beam Feasible for Radiotherapy Uses

As stated in the Introduction, our main aim is to assess the possibility of using a 1 kHz laser driven electron beam for radiotherapy and radiobiology applications. Reliable radiotherapy applications require 6 MeV or greater electron energies. Based on our PIC simulation, such beams can be produced with the parameters of the SYLOS II laser system available at ELI-ALPS.

The SYLOS II laser is a 1 kHz repetition rate "few-cycle" laser with Optical Parametric Chirped Pulse Amplification (OPCPA), which generates 5 TW, few-cycle laser pulses at a high repetition rate, with a central wavelength of 880 nm. The pulse energy is over of 35 mJ with less than 8 fs pulse duration combined with remarkable long-term stability. SYLOS II is the first laser system to have demonstrated multi-TW, few-cycle laser pulses at a high repetition rate.

For accurate estimate of the dose rate I performed Monte Carlo simulations using the electron beam parameters (electron position,

Laser beam pulse length (FWHM)	8 fs
Peak power	4 TW
Repetition rate	1 kHz
Focal spot diameter (FWHM)	2.2 μm
Peak intensity	$2 \cdot 10^{19}$ Wcm^{-2}
Target	He gas jet
Max. e- density	$4 \cdot 10^{19}$ cm^{-3}
Expected e- pulse charge	3–10 pC
Mean kinetic energy	35.97 MeV
Angular distribution (FWHM)	1.13 $^{\circ}$
Expected dose rate for 100 cm SSD	6 Gy/min/pC
Instantaneous dose rate	$3.9 \cdot 10^{6}$ Gy/s/pC
Depth of dose maximum in water	1.9 cm

Table 1: Dose rate at different distances from source obtained from MC simulations using the LWFA electron beam parameters taken from the PIC simulation.

direction and kinetic energy) obtained with the PIC simulations. At the distance of 100 cm, the depth of dose maximum is 1.9 cm and the amount of dose delivered by a single electron bunch with 1 pC charge is 97.1 μGy. From the 3D PIC simulations we can conclude that the electron bunch charge is 3 pC and the amount of dose delivered by a single electron bunch totals $\sim$ 0.3 mGy. This very small amount of dose can be enhanced dramatically by operating the LWFA at 1 kHz repetition rate, which results in a mean dose rate of 0.3 Gy/s or 18 Gy/min which is comparable with the achievements of medical LINACs.

However, through the adjustment of laser and gas target parameters, the electron bunch charge can be increased, and is expected to reach charges exceeding 10 pC. This means that the

above calculated dose rate can be increased by a factor of ten. With this high dose rate the LWFA acceleration technique becomes the rival of today's LINAC systems.

On the other hand, it is well known that the LWFA electron acceleration process is particularly sensitive to laser system stability in terms of energy, focus point position and other optical parameters, as well as plasma generation from gas jets. The major uncertainty comes from fluctuation in the beam pulse charge.

I have proved that operating the LWFA at 1 kHz repetition rate provides precise control over dose delivery. With a constant pulse charge of 1 pC and with a standard deviation of $\sigma = 30\,\%$, for a dose of 1 Gy, we need approximately $n = 10^4$ shots which permits the delivery of 1 Gy with an uncertainty of 0.30 %.

Based on our MC simulations, we can demonstrate that with the available dose rate obtained with 1 pC pulse charge, the spot scanning system can produce a beam size of 20 cm × 20 cm in a few tens of milliseconds, with a central axis depth dose of about 0.275 mGy at the depth of dose maximum. This means that the dose rate which can be achieved with the spot scanning method is 1.65 Gy/min/pC. Considering the pulse charge of 3 pC, obtained from PIC simulations, the dose rate improves to a modest but usable value of 4.95 Gy/min. These results were obtained by simulating the spot scanning technique using the previously generated depth dose data.

Improved FBX chemical dosimeter system with enhanced radiochemical yield

To improve the sensitivity of the FBX dosimeter, attempts have been made to increase the chemical yield of ferric ions and to enhance the photometric measurement techniques. We performed a series of experiments varying the chemical composition to increase the sensitivity of the FBX dosimetric solution.

By using a concentration of 16 mM benzoic acid, and by irradiating an FB solution instead of an FBX solution, the radiochemical yield can be increased from a mean literature value of $6.89 \cdot 10^{-6}$ mol/J to $9.08 \cdot 10^{-6}$ mol/J, which equals to a 24 % en-

hancement. We named this system enhanced FBX (eFBX).

Beam	$G(Fe^{3+})$ $molJ^{-1}$
6 MV photon	$9.08 \pm 0.17 \cdot 10^{-6}$
15 MV photon	$9.10 \pm 0.17 \cdot 10^{-6}$
6 MeV e^-	$8.98 \pm 0.15 \cdot 10^{-6}$
9 MeV e^-	$9.03 \pm 0.08 \cdot 10^{-6}$
12 MeV e^-	$8.97 \pm 0.26 \cdot 10^{-6}$
250 kVp X-ray	$6.46 \pm 0.08 \cdot 10^{-6}$

Table 2: The radiochemical yield of the eFBX dosimetric solution for different beam qualities.

We established a standardized measurement protocol to ensure that eFBX is an easy-to-handle chemical dosimeter. For this purpose, we started out from the ISO standard on the practice for using the Fricke reference standard dosimetry system. Our protocol describes the preparation, handling and storage of the solution; irradiation in reference conditions; the photometric measurements and subsequent data processing.

Table 3 summarizes the uncertainty budget for eFBX dosimeter calibration, made using the recommendations of IAEA. The combined standard uncertainty can be considerably improved by eliminating uncertainty type B assigned to temperature correction. Temperature correction was not considered in this study, but on the basis of the spur theory and the increased amount of ferrous sulphate in the final composition, a similar relation can be assumed between temperature and radiochemical yield as in case of the Fricke dosimeter. The same connection is true for the temperature correction of absorbance measurements, which is related to the associated volume change with temperature. Correction for this variation means that the combined standard uncertainty becomes 1.0 %.

Source of uncertainty	Relative standard uncertainty (%)	
	Type A	Type B
Reference dose rate		
N_k secondary standard	—	0.20
Positioning	—	0.02
Temperature and pressure correction	0.03	0.10
Measurement of current	0.05	0.10
Calibration of OFBX solution		
Positioning of dosimeter	—	0.02
N_{pw} plexi-water conversion	0.20	—
Photometric and volumetric correction	0.35	0.61
G value determination	0.6	—
ϵ determination	0.2	—
Temperature correction	—	0.50
Quadratic summation	0.75	0.83
Combined standard uncertainty	1.12	
Extended uncertainty (k=2)	2.24	

Table 3: Uncertainty budget of the eFBX solution. Temperature correction was calculated based on the relations used for the Fricke dosimeter as the temperature dependence measurement has not yet been performed. The combined standard uncertainty without this term becomes 1.0 %.

5 Conclusion and new scientific resutls

Laser-driven particle acceleration represents a long-awaited breakthrough in the development of novel radiotherapy facilities. The feasibility and suitability of real particle beam parameters can be investigated using currently available high power laser systems. One of the main objective of this work was to theoretically investigate the potential application of high repetition rate LWFA electron beams for radiotherapy.

Electron beams produced in plasma by 1 kHz high repetition rate laser system may provide a promising alternative for conventional accelerators. In this study I have demonstrated that this laser system can produce electron beams with high energies (35.97 MeV mean kinetic energy) and acceptable dose rates (18 Gy/min considering the electron bunch charge of 3 pC obtained by PIC simulations) and dose delivered with very high precision, due to the high repetition rate of the system.

This results suggest that this LWFA acceleration technique can be a promising alternative for RF-based conventional LINAC electron accelerators. The beam energy and charge can be controlled by modifying the target length and plasma density via changing the gas jet pressure, even during the operation. This will enable researchers to perform intensity and energy modulated irradiation. The energy modulation and the spot scanning technique together could open extremely important application spectra for electron irradiation of superficial targets with uneven thickness, providing significant normal tissue protection.

Further efforts are needed to choose the best beam steering solution as well as to develop the suitable beam monitoring and dosimetry system. Taking advantage of their particular future (very short pulse length, high instantaneous dose rate, narrow beam size etc.) we may be able to develop novel radiotherapy techniques such as microbeams, FLASH techniques etc. The results of this in silico study represent a promising start for further scientific work on laser-driven electron source development.

In this work I have also studied some of the properties of the well-known FBX dosimetric solution in terms of sensitivity and dose range. The main motivation was the fact that the success

of radiation therapy crucially depends on the accuracy of dose measurements. However, to date, no dosimetric methods have been established for the absolute dosimetry of radiation beams with very high instantaneous dose rates. My effort was to prepare the necessary methodology for future dosimetric measurements in such radiation fields using a modified version of the Fricke type chemical dosimeter, as an alternative to ionization chambers.

The photometric determination of ferric ions is one of the major obstacle to obtaining good results with low uncertainties. This problem can be eliminated by improving the sensitivity of the solution, which I achieved by increasing the benzoic acid concentration and by adding xylenol orange dye after irradiation. Nonlinearity, a hallmark of an FB system, was eliminated by increasing the ferrous sulphate concentration from the original 0.2 mM value to 1 mM.

For reference irradiation, I constructed a special, multipurpose PMMA slab phantom to hold Eppendorf tubes filled with dosimetric solutions. This phantom can also be used for irradiation under the same conditions as those used for biological and/or chemical samples kept in cell culture dishes or multi-well plates. Moreover, one can perform the cross-calibration of the eFBX dosimeter with other dosimeters, such as films, ionization chambers etc.

Further improvements to the system can be made by studying the influence of temperature on chemical yield and absorbance measurements. If there is indeed a relation between chemical yield and temperature, and between absorbance and temperature, the obtained 1.12 % combined standard uncertainty can be further reduced to 1.0 %.

I am planning to conduct further experiments to make our reference dosimetry system more widely accepted. Our aim is to further optimize and refine the dosimetric characteristics and measurement practices and to ensure the reliability of this system as a reference dosimeter. It is also crucial to prove its suitability in various practical situations, especially in the dosimetry of radiobiological experiments, as well as in radiotherapy measurements. Furthermore, its suitability for measurements of beams with high instantaneous dose rate is still an open question.

New scientific results

1. With PIC simulations I have demonstrated that this laser system can produce quasi-monoenergetic electron beam with high mean kinetic energies (35.97 MeV) at 1 kHz repetition rate which may provide a promising alternative for conventional accelerators;

2. Using Monte Carlo simulations I have demonstrated that this type of 1 kHz LWFA system is capable of generating a sufficient dose rate for practical radiobiological or medical applications (18 Gy/min or even higher);

3. I proved that the operation of LWFA at 1 kHz repetition rate provides precise control over dose delivery (with an estimated uncertainties of 0.3 %);

4. With further developments it is possible to obtain electron beams with depth dose characteristics suitable for real radiotherapy applications (active scanning, microbeams etc.);

5. With proper control of laser and gas target parameters we may be able to perform energy and intensity modulated irradiation, as well as the combination of them even in real time;

6. I have outlined some practical issues and pitfalls which need to be addressed before such systems are used in real applications;

7. I have conducted detailed investigations on the dosimetric properties of the FBX dosimetric solution in terms of sensitivity and dose range;

8. I have improved the precision and accuracy of the dosimeter by increasing the benzoic acid concentration and by adding xylenol orange dye after irradiation;

9. Nonlinearity, a hallmark of an FB system, was eliminated by increasing the ferrous sulphate concentration;

10. I adapt the classical radiochemical model to the new chemical formula which qualitatively explains the enhanced radiochemical yield;

11. For reference irradiation, I constructed a special, multipurpose PMMA slab phantom. This phantom can be used for irradiation under the reference conditions of the dosimetric solution as well as biological or chemical samples in Eppendorf tubes, or for the cross-calibration of our chemical dosimeter with other dosimeters;

12. A standard operational procedure has been established and validated to guarantee the necessary accuracy and precision.