

Characterization of x-rays pulses from a hundred joules plasma focus to study its effects on cancer cells.

J. Jain^{1,2,3,*}, J. Moreno^{1,2}, G. Avaria^{1,2}, C. Pavez^{1,2}, B. Bora^{1,2}, M. J. Inestrosa Izurieta^{1,2}, D. Diez⁴, O. Alvarez⁴, J. Tapia⁴, K. Marcelain⁴, R. Armisen⁴ and L. Soto^{1,2,*}

¹Comisión Chilena de Energía Nuclear, Casilla 188-D, Santiago Chile

²Center for Research and Applications in Plasma Physics and Pulsed Power, P4

³Universidad de Talca, Chile

⁴Instituto de Ciencias Biomédicas & Centro de Investigación y Tratamiento del Cáncer, Facultad de Medicina, Universidad de Chile, Chile

**E-mail:* jajain83@gmail.com, lsoto@cchen.cl

Abstract. With the purpose to study the effects of pulsed x-rays radiation on cancer cells, the total doses of x-ray pulses and the temporal duration of the pulse has been characterized in a hundred joules plasma focus device (PF-400J, 130 kA achieved in 300ns, 30 kV, 880 nF, 38 nH). TLD dosimeters were located outside of the discharge chamber, at 96 mm from the anode top. In addition, two photomultipliers with plastic scintillator were located in axial and radial directions. From the statistical analysis of the TLD and photomultiplier signals, was possible to estimate that a single shot has a total dose of the order of $30 \pm 15 \mu\text{Sv}$ with a duration of the order of $12 \pm 3.6 \text{ ns}$ at FWHM. Preliminary experiments using MCF7, a breast cancer cell line, were performed. Cells were irradiated at 96 mm from the anode top with 300 cumulative x-ray shots and cell proliferation was evaluated at 24, 48 and 72 hours later.

1. Introduction

Plasma focus devices (PF) have been paid attention due to their usefulness for fundamental as well applied studies [1, 2, 3]. On one hand, PF devices could be used for basic science [1, 2], including astrophysical plasma research [4, 5] and on the other hand they have various applications in material and biological sciences [6-11]. Indeed, during different phases: breakdown, rundown, compression, pinch and axial plasma shock of PF discharges; various phenomena take place [1, 3]. Pinch and axial plasma shock are considered as rich phases as a point of view of application as well as fundamental studies. Moreover, recently it has been discovered that the axial plasma shock phase [12] have application in the field of interaction of powerful plasma with the first wall of fusion reactor wall like Tokamaks and inertial fusion [13]. On the other hand, many groups have been studied the pinch phase [14] in order to understand the basic physical processes to make it more applied in nature: magnetic field reconnection [15], filaments [16, 17], plasma jets [18]. During the pinch phase there is emission



of soft and hard x-rays [18] as well as neutrons if the filled gas is deuterium. The emission of various types of radiation during pinch phase makes PF devices applicable to material [19] and biological sciences [7]. In this work the effects of pulsed x-rays radiation on cancer cells, using a table-top plasma focus device is explored.

Radiation is used for the treatment of cancers. In radiation therapy, tumors are exposed to high doses of radiation from a continuous source. The amount of dose delivered to cancerous tumor depends upon the type and the stage of the cancer. For example, solid epithelial tumors can be treated with dose range 60 – 80 Gy while lymphomas can be treated with 20 – 40 Gy. Total radiation dose can be fractionated over a long time. Fractionate dose can be kept as 1.5 – 2.0 Gy per day, five days a week [20]. Fractioning the total dose allows healthy cells (which are also exposed to the radiation along with cancer cells) to recover themselves. Also fractionation may help to re-oxygenate the chronically or acutely hypoxic cells, which are more radio-resistance.

The effect of high dose exposure on cancerous cells is well characterized. Nonetheless, low doses effects cannot be predicted by extrapolating linearly from higher to lower dose effects. Given that decreasing radiation dose would have lower side effects on healthy cells. Now days many groups are trying to study the behavior of cancer cells under the action of low doses. N.V. Litvyakov et. al. [21] used pulsed periodic x-rays at pulse frequency 10 – 16 Hz on cultured cells from tumors of different histogenesis. They claimed that the pulse periodic x-rays exposure to the cells induces apoptosis in 20 – 40 % of cells. In their work the total absorbed doses were 30 – 120 mGy. Since the study done in [12] showed positive results of low dose irradiation on cancer cell, devices that can produce such low doses need to be studied.

Low energy plasma focus devices may be a good choice considering radiation emission. The plasma focus devices emit radiation (x-rays, neutrons) in pulse form. The advantage to choose plasma focus over other devices for this study is that they can produce the pulses of x-rays and neutrons depending on the filled gas. For example if the filled gas is hydrogen only x-rays are produced and if the deuterium is used as a filled gas, x-rays as well as neutron emission takes place. In addition, the size and cost of low energy plasma focus devices are lower than that of conventional radiation sources like-linear accelerators (LINAC) [22]. Therefore low energy plasma focus devices may provide an option of portable radiation emitting source for low dose radiation therapy applicable to cancers. Although, a lot of scientific efforts are needed in order to transfer pulse radiation technology of plasma focus devices to clinical trials.

In section 2 we will describe the experimental setup. The results are discussed in section 3 and the work is concluded in section 4.

2. Experimental setup

2a. Pulsed x-ray characterization and equivalent dose

Pulsed radiation of X-rays was produced using dense plasma focus device PF400J ($C_0 = 880$ nF, $L_0 = 38$ nH, 30 kV charging voltage, 130 kA of peak current achieved in 300 ns) [23]. A schematic of plasma focus PF-400J is shown in figure 1. The device PF400J consists of 8 copper cathodes and a central stainless steel hollow anode, which has an effective length of 8 mm. Rest of the length of anode is covered by an insulator (alumina, shown in figure 1). Diameter of anode is 12 mm. Hydrogen gas at 9 mbar of pressure was used in order to get maximum x-rays signal from the device. The experiment was performed with TLD-100 dosimeters array, which contained 21 dosimeters, in order to estimate the doses. Reason behind to use TLD-100 dosimeters for this study is that the material of these dosimeters have similar response to radiation as human body. The dosimeters array, as shown in figure 1, was kept on a specific holder which was specially designed for biological cell experiment. The holder was mounted outside the PF400J in the axial position. Three MCF-7 cells containing dishes are kept at the top of the holder before dosimeter array. The distance between the top of the anode and the bottom culture dish was 96 mm (95 mm from top of the anode to bottom of the holder +

1 mm thickness of holder). Height of each culture dish is about 13.0 mm so the distance between top of the anode and dosimeters array was about 135.00 mm. Two photomultiplier tubes (PMT), namely FM1, FM3 for hard x-rays detection were aligned in the axial and radial positions. The PMT which was in axial position was separated by 96 cm from top of the anode and radial PMT was at a distance about 131 cm from the center of the anode. In a first stage, the PMTs are used as referential devices. Later, the PMT signal will be used directly as doses measurements, considering the crossed calibration with the TLD dosimeters. The experiment was performed for different number of PF discharges, but in this work only the results for 300 discharges with x-rays are presented.

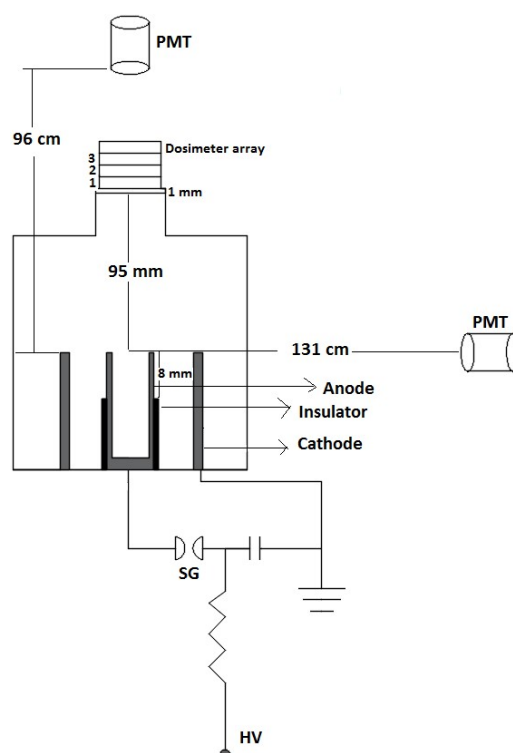


Figure 1. Schematic of PF-400J for cancer cell irradiation.

Figure 2 shows the electrical signals obtained during the experiments with plasma focus device PF400J. A dip in current derivative signal (obtained using Rogowski coil) is a signature of plasma column formation. In fact, during plasma column formation there is an increment in total impedance and hence reduction in current. We can clearly see the emission of pulse x-ray in figure 2. For this experiment maximum current was obtained about ~ 130 kA and the x-ray signal per shot, which is mean of area under curve of all the 300 x-ray signals, obtained using PMT in axial direction is about $(6.55 \pm 3.16) \times 10^{-8}$ V.s. Total accumulated signal of x-ray (sum of area under curve of all 300 x-ray signals) in PMT in axial direction was found about 2.00×10^{-5} V.s. These data were obtained for 300 discharges with x-rays signal. The total accumulated doses for 300 x-rays signal were found about tens of mSv. The dose per pulse was obtained about tens of μ Sv. The average x-ray pulse duration was ~ 10 ns.

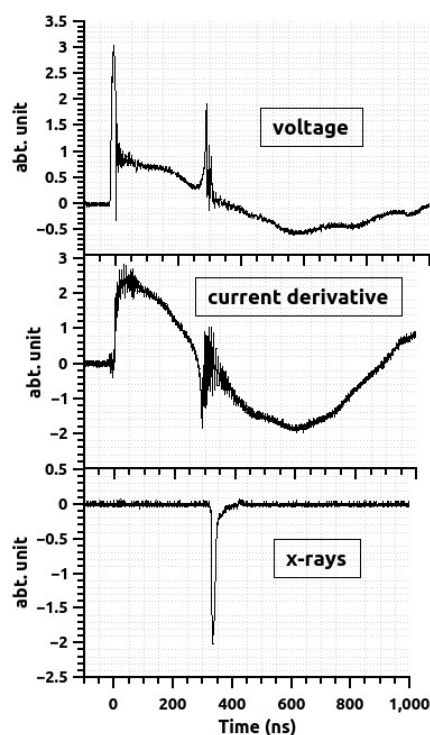


Figure 2. Various electrical signals obtained during the experiment with plasma focus device PF-400J.

2b. Cell culture preparation

Breast adenocarcinoma derived cells, MCF7, were maintained in Dulbecco's modified medium (DMEM) supplemented with 10% bovine fetal serum, in an atmosphere of 5 % CO₂ at 37 °C. The day before irradiation, cells were cultured in five 35mm dishes: one control dish was kept in the incubator, one control was mock irradiated and three plates were irradiated. After irradiation, every cell culture was seeded in 96-well plates, at a density of 2×10^3 cell per well in 100 μ l complete medium.

2c. Cell Proliferation assay (MTS)

Cell proliferation was assessed at 24, 48 and 72 hours after irradiation by using a MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) assay. 20 μ l MTS solution was added to each well of the 96 well plates and incubated at 37 °C. Live cells interact with MTS solution to produce formazan, which absorb light at 570 nm. Proliferation rate was estimated as the absorbance (abs) of every time point normalized by the abs at time 0.

3. Results and discussion

In figure 3, proliferation rate of breast cancer cells, MCF-7, exposed to 300 shots of pulsed x-ray is shown. Control incubator represent the MCF-7 cells that were not exposed to x-rays and were kept in control conditions. Mock control corresponds to cells that although were not irradiated, they had the same manipulation as irradiated cells. There were three cell culture dishes numbered 1, 2 and 3 as shown in figure 1. Proliferation rate for the cells kept first on the holder (at top of the anode) (culture1) and cells which were kept at last (culture 3) are shown. As it can be seen from figure 3, 48 hours after irradiation, the proliferation rate seems to be higher for the irradiated cells (cultures 1 and 3) than for control cells. While 72 hours after irradiation, the effect was reversed for culture 3, which seems to show a decrease in proliferation rate. However, important is to notice that the present study

is limited to only one experiment and biological samples, especially cell lines, have high intrinsic variance, therefore, more experiments are required to state confident conclusions. With this preliminary study the dose per shot was found about tens of μSv in ~ 10 ns pulse duration time, which is about mSv for total 300 shots. There is a possibility to enhance the emission of x-rays from PF-400J either by pre-ionizing mechanism [24] or by inserting another material (lead/copper) in hollow anode [25].

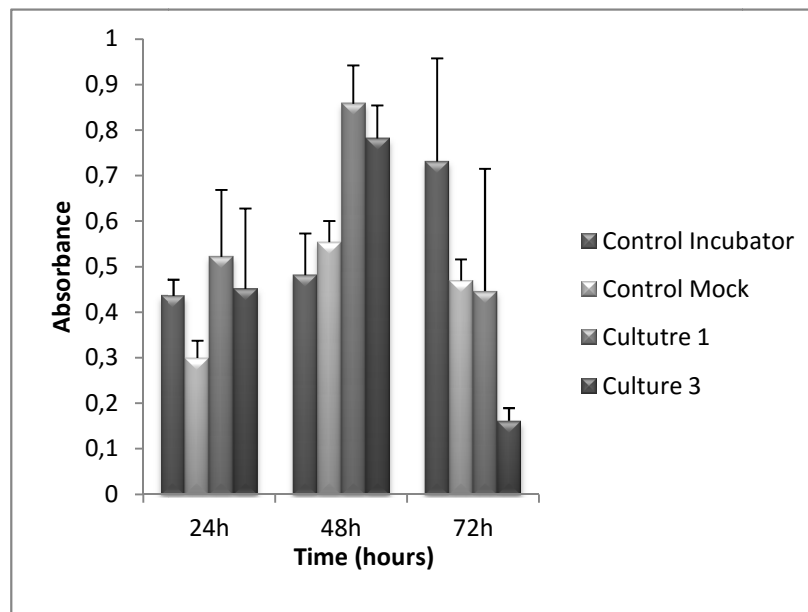


Figure 3. Proliferation rate of cancer cell line MCF-7 at 24, 48 and 72 hours after irradiation. The cells were exposed to 300 shots of x-ray pulses.

4. Conclusion

Preliminary experiments with plasma focus device PF-400J has been carried out in order to irradiate the breast cancer cells MCF-7, by pulsed x-rays. Based on the obtained results it can be concluded that the x-rays radiation emitted from plasma focus device affect the cancer cells. However in the present work the studies performed on cancerous cells are limited only for one experiment with 300 x-ray pulses. In order to make a trustable conclusion a repetitive behavior of both the studies-emission of radiation (x-rays, neutrons) from PF400J and response of cancerous cells to the irradiation should appear with some standard deviation. Due to this reason further studies by keeping in mind the statistical approach will be carried out.

Acknowledgement

The work is supported by grant ACT-1115, CONICYT, Chile.

References

- [1] Soto L, 2005 *Plasma Phys. and Control. Fusion* **47**, A361
- [2] L. Soto, C. Pavez, A. Tarifeño, J. Moreno and F. Veloso, 2010 *Plasma Sources Sci. and Technol.* **19**, 055017
- [3] Bernard A, Bruzzone H, Choi P, Chuaqui H, Gribkov V, Herrera J, Hirano K, Krejci A, Lee S, Luo C, Mezzetti F, Sadowski M, Schmidt H, Ware K, Wong C S, Zoita V 1998 *J. Moscow Phys. Soc.* **8** 93
- [4] Pouzo J O and Milanese M M 2003 *IEEE Trans. Plasma Sci.* **31**, 1237

- [5] Pavez C, Pedreros J, Tarifeño-Saldivia A and Soto L, 2015 *Physics of Plasmas* **22**, 040705
- [6] Dubrovsky V, Gazaryan I G, Gribkov V A, Ivanov Yu P, Kost O A, Orlova M A, and Troshina N N, 2003 *Journal of Russian Laser Research* **24**, 289
- [7] Orlova M A, Kost O A, Gribkov V A, Gazaryan I G, Dubrovsky A V, Egorov V A, and Troshina N N 2000 *Applied Biochemistry and Biotechnology* **88**243
- [8] Stevens C V 1988 *EIR Science and Technology* **15**, 22
- [9] Moreno C, Vénere M, Barbuzza R, Fresno M D, Ramos R, Bruzzone H, González F P J and Clausse A, 2002 *Braz. J. Phys.* **32**, 20
- [10] Hussein E and Waller E, 1998 *Radiat. Meas.* **29**, 581.
- [11] Lee S, Kudryashov V, Lee P, Zhang G, Serban A, Liu M, Feng X, Springham S, Wong T and Selvam C, 1998 *ICPP and 25th EPS Conf. on Controlled Fusion and Plasma Physics* vol 22C, 2591.
- [12] Soto L, Pavez C, Moreno J, Inestrosa-Izurieta M J, Veloso F, Gutierrez G, Vergara J, Clausse A, Bruzzone H, Castillo Fand Delgado-Aparicio L F, 2014 *Physics of Plasmas* **21**, 122703
- [13] Inestrosa-Izurieta M J, Ramos-Moore E and Soto L, 2015 *Nuclear Fusion* **55**, 093011
- [14] Haines M G, 2011 *Plasma Phys. Control. Fusion* **53**, 093001
- [15] Kubes P, Klir D, Kravarik J, Rezac K, Kortanek J, Krauz V, Mitrofanov K, Paduch M, Scholz M, Pisarczyk T, Chodukowski T, Kalinowska Z, Karpinski L and Zielinska E, 2013 *Plasma Phys. Control. Fusion* **55**, 035011
- [16] Soto L, Pavez C, Castillo F, Veloso F, Moreno J, and Auluck S K H, 2014 *Physics of Plasmas* **21**, 072702
- [17] Kubes P, Paduch M, Cikhardt J, Kortanek J, Cikhardtova B, Rezac K, Klir D, Kravarik J and Zielinska E, 2014 *Phys. Plasmas* **21**, 122706
- [18] Pavez C, Pedreros J, Zambra M, Veloso F, Moreno J, Tarifeño-Saldivia A and Soto L, 2012 *Plasma Phys. and Control. Fusion* **54**, 105018
- [19] Rawat R S, 2013 *IEEE Trans. on Plasma Sci.* **41**, 701
- [20] http://en.wikipedia.org/wiki/Radiation_therapy
- [21] Litvyakov N V, Rostov V V, Bol'shakov M A, Buldakov M A, Afanas'ev K V, Astapenko A N, Kutenkov O P and Cherdyntseva N V, 2005 *Biophysics* **50**, S51
- [22] Barker Jr J L, Garden A S, Ang K K, O'Daniel J C, Wang H, Court L E, Morrison W H, Rosenthal D I, Clifford Chao K S, Tucker S L, Mohan R, Dong L, 2004 *International Journal of Radiation Oncology Biology Physics* **59**, 960
- [23] Silva P, Moreno J, Soto L, Birstein L, Mayer R, Kies W, 2003, *Applied Physics Letters* **83**, 3269
- [24] Ahmad S, Sadiq M, Shafiq M, Waheed A, Lee P and Zajaullah M, 2006 *Plasma Sources Sci. Technol.* **15**, 314
- [25] Hussain S, Shafiq M, Ahmad R, Waheed A and Zakaullah M, 2005 *Plasma Sources Sci. Technol.* **14**, 61