

The role of nanoparticles and high energy x-ray in increasing the sensitivity enhancement ratio(SER) for ovary malignant cells

Nihad A. Saleh¹, Talib A. Abdul Wahid^{2*}

¹Babylon university-science college- physics department, Iraq

²Kufa university-science college- physics department, Iraq

Abstract : This article aims to improve radiation therapy for patients with ovarian cancer with the aid of nano particles that possess high atomic number and high-energy X-rays. These nano particles are being added to the cancerous tumor. In this study we simulate insertion gold, gadolinium, silver and titanium nanoparticles as radio-sensitizing agent each type interacts with x-ray photons whose energy ranged from 2MeV to 20 MeV. The existence of nanoparticles is working to improve ovary cross section. High energy of X-ray causes to increase production of free radicals. In this article we get an enhancement in ovary radiotherapy this enhancement represented in increasing the number of destroyed cancer cells and reduce the number of surviving tumor cells. From these numbers we get sensitivity enhancement ratio (SER).The SER percentages were as follow 13.58% was SER for gold nano particles. 13.02%was SER for gadolinium nanoparticle.12.52%was SER for silvernano particles. 10.85%was SER for Titaniumnano particles.

Key words: ovary cancer, sensitivity enhancement ratio (SER), high energy x-ray, survival cancer cells, nanoparticles.

Introduction

The International Agency for Research on Cancer (IARC) and Global Cancer Statistics researches together concenter cancer as global disease spread among men and women lead death in late stage [1].Ovarian cancer in second order affects women after breast cancer [2].Ovarian cancer can be classified as solid tumor [3] so specialist can remove it easily by surgery then followed surgery with chemotherapy and radiation therapy. Radiation therapy is to give a radiation dose to the patient with range from 50 to 60 Cray. It takes a period of time from 5 to 7 weeks. This process called fractionation dose but during fractionation dose there missed dose due to organ movement during breathing, limitation of organ tolerance [4].To increase the organ tolerance for radiation dose absorption inside the tumor injected particles that have high radiation dose absorption inside tumor[5,6,7].

The choice of such material for several reasons, it is easy manufactured as nanomaterials, possess thermal stability, do not interact with organ tissue finally do not have a toxic effect [8].

The vascular inside tumor is larger than vascular inside healthy tissue surrounding the tumor. This lead to produce the concentration of the nanoparticles within the tumor is larger than the healthy tissue. In other words the absorption of radiation dose within the tumor is larger than the absorption of radiation in living tissue that surrounds the tumor [9, 10].

Products of ionizing radiation interaction with water inside cell are free radicals. The accumulation of free radicals leads to the formation of a toxic molecule. These toxic molecule works on the destruction of cancer cells. Since the production of free radicals within the tumor is larger than produced in the healthy tissue surrounds the tumor so the destruction inside tumor is large [11].

The importance of this research to improve the process of absorption dose by increasing SER and production maximum destruction in malignant cells with minimum damage to the healthy cells surrounding the tumor. This leads to reduce the duration of radiation therapy then reduce the side effects of radiation therapy.

Theoretical part:

High energy x-ray considered ionizing radiation which is used in radiotherapy. This ionizing either destroyed or shrinking cancer cells but it is cause damage to the surrounding health tissue therefore radiologist need arises to find a way to occur maximum destruction in malignant cells with minimum damage to the healthy cells surrounding the tumor [4]. The best way to perform this idea is the use of nanoparticles with high energy x-ray interaction. This interaction leads to ensure the production of electron and positron inside tumor, who are working to increase the ionization process inside tumor then lead to increase product of free radicals and toxic molecules and where the accumulation of reaction products leads to cancer cell death [12, 13, 14, 15,16].

Total cross section for ovary with presence nano-particles as contras agent inside ovary equal sum of tow cross sections [17]:

$$\sigma_{\text{total}} = \sigma_{\text{ovary}} + \sigma_{\text{agent}} \dots\dots\dots(1)$$

Where σ_{total} , total cross section, σ_{ovary} ovary cross section, σ_{agent} agent cross section.

Cross section (σ) and mass energy absorption coefficient ($\frac{\mu_{\text{en}}}{\rho}$) are related together in the following equation [18]

$$\frac{\mu_{\text{en}}}{\rho} = \frac{N_A \sigma}{A} \dots\dots\dots(2)$$

N_A : Avogadro's number, A : Mass number

Equation1 can be modified as follow:

$$(\mu_{\text{en}}/\rho)_{\text{total}} = (\mu_{\text{en}}/\rho)_{\text{ovary}} + (\mu_{\text{en}}/\rho)_{\text{nanoparticles}} \dots\dots\dots(3)$$

Where $(\mu_{\text{en}}/\rho)_{\text{total}}$: total mass energy absorption coefficient, $(\frac{\mu_{\text{en}}}{\rho})_{\text{ovary}}$: ovary mass energy absorption coefficient, $(\mu_{\text{en}}/\rho)_{\text{nanoparticles}}$: nanoparticles mass energy absorption coefficient.

The dose(d) for different medium can calculate from this equation [19]:

$$d(\text{Gy}) = 8.9 \times 10^{-3} \left(\frac{(\mu/\rho)_{\text{organ}}}{(\mu/\rho)_{\text{air}}} \right) * X \dots\dots\dots(4)$$

Where: $(\mu/\rho)_{\text{organ}}$ mass attenuation coefficient for organ, $(\mu/\rho)_{\text{air}}$:mass attenuation coefficient for air. $X(R)$: The exposure.

The dosage fractionation equation with nano material will be :

$$d(\text{Gy}) = 8.9 \times 10^{-3} \left(\frac{\left(\frac{\mu}{\rho} \right)_{\text{ovary}} + \left(\frac{\mu}{\rho} \right)_{\text{nano}}}{\left(\frac{\mu}{\rho} \right)_{\text{air}}} \right) * X \dots \dots \dots (5)$$

Where $\left(\frac{\mu}{\rho} \right)_{\text{ovary}}$ is mass attenuation coefficient of ovary. $\left(\frac{\mu}{\rho} \right)_{\text{nano}}$ is mass attenuation coefficient for nanoparticles.

Irradiation equation of dosage fractionation [20]

$$N_s = N_i * \text{Exp} \left(- \left(1 + \frac{d}{\alpha/\beta} \right) \right) \dots \dots \dots (6)$$

Where: N_s = survival cells number after irradiation. N_i = initial cells number before irradiation. α/β is a factor represent radio-sensitivity (for ovary 1.5) .

By substituting equation (5) in equation (6) we get the irradiation equation modification:

$$N_s = N_i e^{\left(- \left(1 + \frac{8.9 \times 10^{-3} \left(\frac{\left(\frac{\mu}{\rho} \right)_{\text{ovary}} + \left(\frac{\mu}{\rho} \right)_{\text{nano}}}{\left(\frac{\mu}{\rho} \right)_{\text{air}}} \right) * X}{\alpha/\beta} \right) \right)} \dots \dots \dots (7)$$

Results:

When irradiate ovary with and without gold nanoparticles by x ray ranged from 2 MeV to 20 MeV It is shows reduction in surviving cancer cells with gold nano particles less than irradiates without gold nano particles as shown in figure 1.

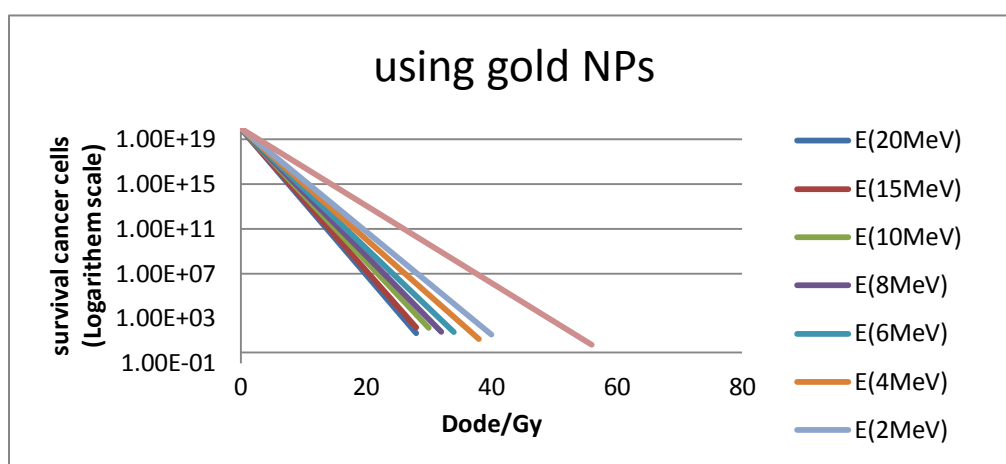


Figure 1: shows reduction of surviving cancer cells with and without gold nano particles irradiate by x ray (2-20) MeV.

When introduced gadolinium nano particles inside ovary then irradiated by x ray (2-20) MeV there was decreasing in survival cancer cells as shown in figure 2. But the decreasing in surviving cancer cells with gold nano particles was larger than with gadolinium nano particles.

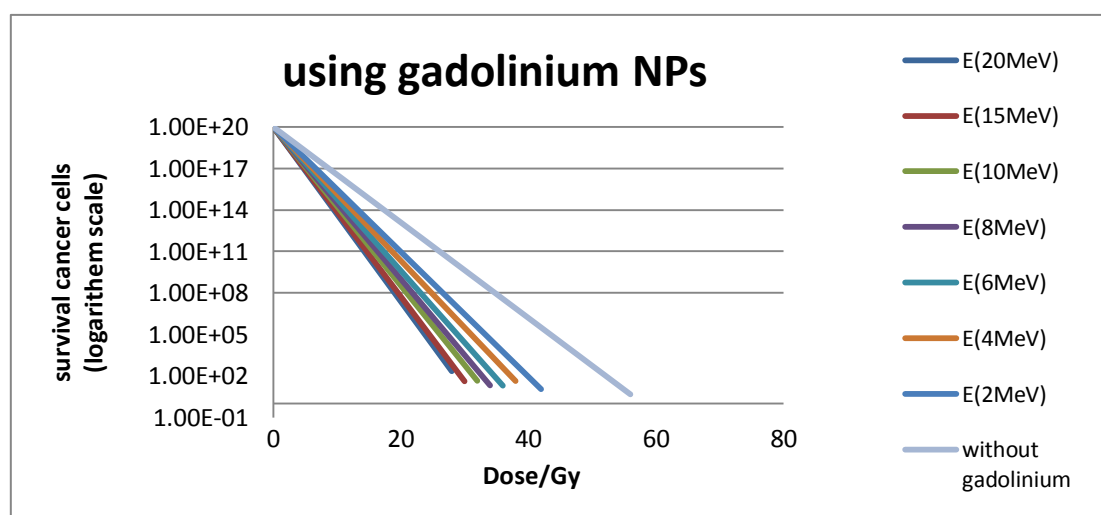


Figure 2: shows number of surviving cancer cells with and without gadolinium nano particles irradiate by x ray (2-20)MeV.

Existence of silver nano particles during x ray irradiation from 2 MeV to 20 MeV gives decreasing in number of surviving cancer cells as shown in figure 3 but with efficiency less than existence of gold nano particles and gadolinium nano particles respectively.

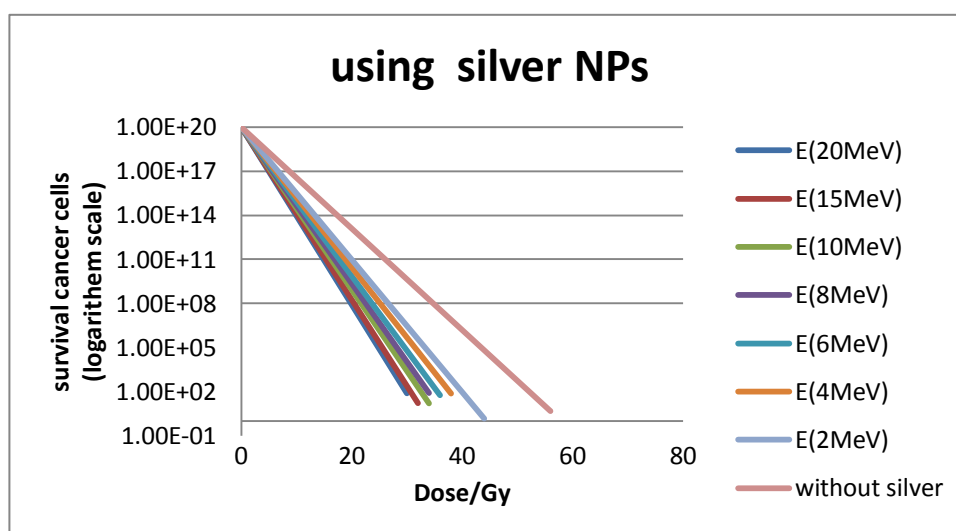


Figure 3 : shows number of surviving cancer cells with and without silver nano particles irradiate by x ray (2-20)MeV.

Finally irradiation ovary without and with titanium nano particles by high energy x ray ranged from 2 MeV to 20 MeV also shows decreasing in number of surviving cancer cell as shown in figure 4 . But efficiency with presence titanium NPs less than the efficiency with presence of gold NPs, gadolinium NPs and silver NPs respectively.

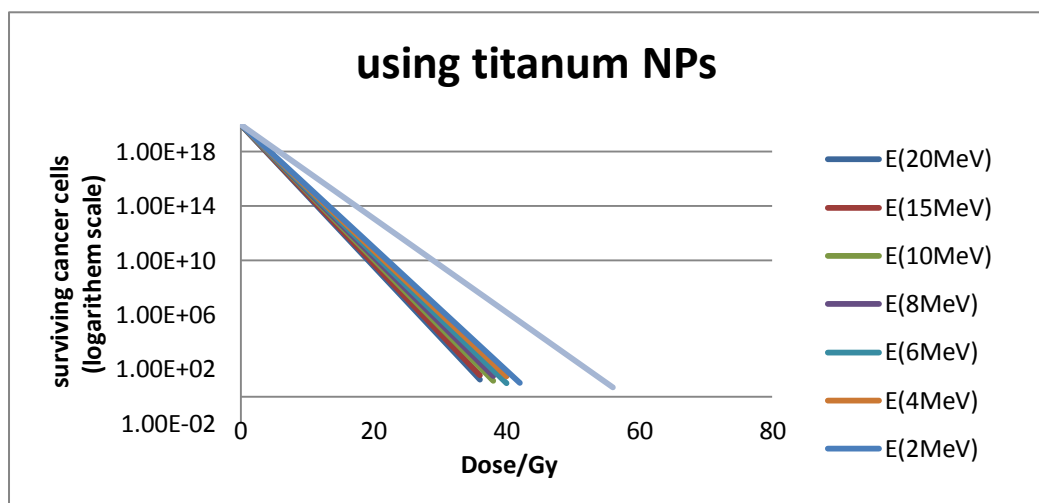


Figure 4: shows number of surviving cancer cells with and without titanium nano particles irradiate by x ray (2-20)MeV.

Discussion:

Gold($Z=79$), gadolinium(64), silver(47) and titanium(22) has a high cross-section because it contains a high atomic number so these elements working to enhance (SER) of ovary. Depending on the atomic number the probabilities of interaction are as follows gold, gadolinium, silver and titanium. These elements are concentrated inside tumor larger than outside tumor because tumor vasculature larger than surrounding healthy tissue[18-20]. Therefore, the interaction of X-rays will be concentrated into the tumor without the healthy tissue that surrounds the tumor. This means the absorption of the radiation dose will be concentrated into the tumor without the surrounding healthy tissue. From this produces an increase in the number of destroyed cancer cells by depending on type of nano particles that added to tumor.

High energy x ray helps to increase free radicals that produce interaction of x ray with water molecules inside cells. And thus lead to an increase in the number of destructive cells and decreasing in the number of surviving cancer cells as shown in figures 1, 2, 3, 4.

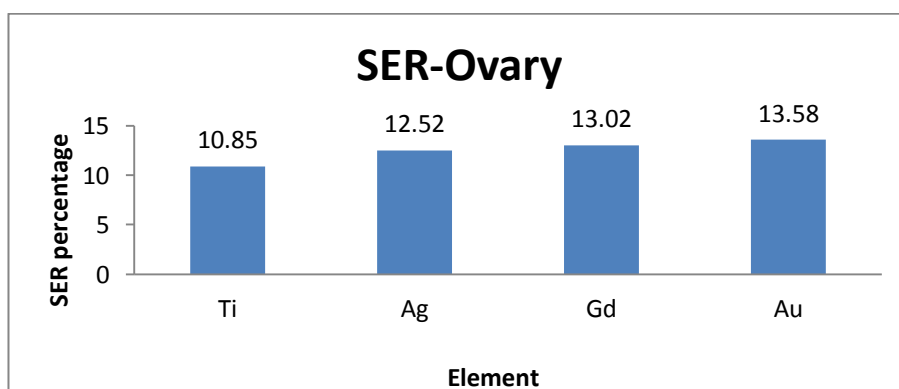


Figure 5: show improvement in sensitivity enhancement ratio (SER) for ovary with using gold NPs, gadolinium NPs, silver NPs and titanium NPs.

Conclusion:

From the results obtained we conclude that there is improving in SER percentage. This improvement in SER shows as follows 13.58 because of the presence of gold NPs ($Z=79$). Then gadolinium NPs ($Z=64$) has SER percentage 13.02. Silver NPs ($Z=47$) has SER percentage 12.52. Finally titanium ($Z=22$) has SER

percentage 10.85 . It's clear that SER percentage depend on atomic number as it illustrated in figure 5 in other words depend on cross section.

From previous results we conclude that the improvement in (SER) depends on the type of NPs that is added. Improvement in SER is directly proportional to the atomic number which has high mass energy absorption coefficient.

The x ray possesses high energy products large number of the destructive cancer cells. The large number of destructive cancer cells means reducing the time period for radiation therapy and reduce the side effects.

Acknowledgements:

The authors acknowledge the help of the middle Euphrates Center to cancer in the Najaf city, Iraq specially Dr. Hyder N. Rebeea and Dr.Imad Kareem Alsaabery, kufa University –Faculty science – members of physics department to complete this research.

References:

1. World Health Organization, the International Agency for Research on Cancer (2013).
2. Torre L. A., Bray F., Siegel R.L., Ferlay J., Lortet-Tieulent J., Jemal A. "Global Cancer Statistics" . Cancer Journal Clinical 65 (2015): 87–108.
3. Torre, F.Bray, R.L. Siegel, J. Ferlay, J. L. Tieulent, A. Jemal, " Global Cancer Statistics", CA Cancer Journal Clinical (2015);65:87–108.
4. Jameson C.W. ,LunnR.M., Jeter S. and, Sabella A.," Report on Carcinogens Background Document for X Radiation & Gamma Radiation and Neutrons ", U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program, Research Triangle Park, NC 27709(2003).
5. Jain R. K. and Stylianopoulos T.," Delivering nanomedicine to solid tumors", clinical oncology, (2010),7,653-664.
6. Hansen E.K. and Roach M. ,"Handbook of Evidence-Based Radiation Oncology", ,2nd Edition, Springer Science+Business Media, LLC (2010).
7. Hainfeld J.F. Slatkin D.N. Smilowitz H.M. The use of gold nanoparticles to enhance radiotherapy in mice. Physics in Medicine & Biology (2004) 49(18):N309-N315.
8. Lechtman E, Chattopadhyay N, Cai Z, Mashouf S, Reilly R and Pignol J P, Implications on clinical scenario of gold nanoparticle radiosensitization in regards to photon energy, nanoparticle size, concentration and location; Physics in Medicine and Biology; Phys. Med. Biol. (2011) 56, 4631–4647.
9. Babaei M., Ganjalikhani M.," The potential effectiveness of nanoparticles as radio sensitizers for radiotherapy", BioImpacts (2014), 4(1), 15-20.
10. Su X., Liu P.D., Wu H. and Gu N.,"Enhancement of radiosensitization by metal-based nanoparticles in cancer radiation therapy", Cancer Biol Med. (2014) 11(2): 86–91.
11. Townley H.E., Kim J., Dobson P.J.,"In vivo demonstration of enhanced radiotherapy using rare earth doped titanium nanoparticles", Nanoscale (2012) 4,5043–5049
12. Robar J.L., Riccio S.A., Martin M.A.,"Tumour dose enhancement using modified megavoltage photon beams and contrast media", Phys Med Biol. (2002),47:2433–49.
13. Prezado Y., Fois G., Duc G. and Bravin A.," Gadolinium dose enhancement studies in microbeam radiation therapy", Med. Phys.(2009)36 3568–74.
14. Jain R.K. and Stylianopoulos T.," Delivering nanomedicine to solid tumors", clinical oncology(2010)7,653-664.
15. Rieger H. and Welter M.," Integrative models of vascular remodeling during tumor growth", WIREs Syst Biol Med (2015) 7:113–129.
16. Rieger H.,Fredrich T. and WelterM.,"Physics of the tumor vasculature",Eur. Phys. J. Plus (2016) 131: 31.
17. MaylesP.,Nahum A. and Croswald J.," Handbook of Radiation Physics", Taylor and Francis Group(2007).
18. Hubbell J., "Review of photon interaction cross section data in the medical and biological context ",Phy.Med.Bio.(1999)44,R1-R22.

19. Halperin E.C., Perez C.A., Brady L.W., " Perez and Brady's Principles and Practice of Radiation Oncology", 6th Edition, Lippincott Williams and Wilkins, 2013.
20. Chapman J. D. and Nahum A.E., " Radiotherapy Treatment Planning",by Taylor & Francis Group(2015).
