Effect of nanoparticles and x-ray(2-20)MeV on sensitivity enhancement ratio in brain malignant cells

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Abstract:

The importance of this research is to reduce the number of radiotherapy sessions that are given to patients with brain cancer then result in reducing the side effects of radiation therapy. This is done by increasing sensitivity enhancement ratio (SER). SER is the ratio of survival cells to initial cells for irradiation without and with nanoparticles. The direct injection of nanoparticles into brain tumor considered a perfect method to increase (SER). In this study gold, gadolinium, silver and titanium nanoparticles were used as radio-sensitizing agents to increase (SER). The contrast agent loaded to brain tumor interacts with x-ray photons whose energy ranged from 2MeV to 20 MeV This led to enhance brain radio-sensitivity by increasing the absorbed dose due to the presence of high absorption coefficient elements. In this research, we get a percentage of SER from 11.63 to 14.26 depending on the type of contrast agent.

Keywords: Brain cancer, sensitivity enhancement ratio (SER), nano particles, high energy x- ray.

تأثير الجسيمات النانوية واشعة اكس (2-20) ميكا الكترون فولت على معدل التحسس الاشعاعي لخلايا الدماغ الخبيثة

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الخلاصة:

تبرز اهمية هذا البحث في تقليل عدد جلسات العلاج الاشعاعي لمرضى سرطان الدماغ ومن هذا ينتج تقليل الاعراض الجانبية الناتجة عن العلاج الاشعاعي . وهذا يتم بواسطة تحسين العلاج الاشعاعية للدماغ بواسطة زيادة نسبة تحسن الحساسية (SER). نسبة تحسن الحساسية (SER) تعرف بانها نسبة عدد الخلايا الناجية الى عدد الخلايا الابتدائية للإشعاع بوجود وعدم وجود المادة النانوية .تعتبر تقنية الحقن المباشر للجسيمات النانوية لورم الدماغ طريقة مثلى لزيادة الحساسية الاشعاعية (SER). في هذا البحث تم استخدام جسيمات الذهب و لكادولينيوم والفضة والتيتانيوم النانوية كعامل لزيادة الحساسية الاشعاعية . ان العامل المقارن المحمل الى ورم الدماغ يتفاعل مع اشعة سينية ذات طاقة عالية تتراوح من 2 ميكا الكترون فولت الى 20 ميكا الكترون فولت وهذا بدوره يؤدي الى تحسين العلاج الاشعاعي للدماغ من خلال زيادة الجرعة الممتصة بسبب وجود المادة النانوية ذات معامل الامتصاص العالي. في هذا البحث حصلنا على نسبة تحسن الحساسية تتراوح من 11.63 الى 14.26 حسب طبيعة المادة الموجودة.

الكلمات المفتاحية: سرطان الدماغ, معدل تحسن الحساسية للإشعاع, جسيمات نانوية ,اشعة اكس ذات طاقة عالية.

1. Introduction

Radiation therapy together with chemotherapy post-surgery can be considered as the optimal or full treatment strategy for cancers [1,2]. The effective radiation therapy of tumor occurs when applying high-energy X-ray using fractionation technique [3]. However, radiotherapy does not always give the required efficiency for the treatment of cancer cells. This is attributed for several reasons, first the possibility of exit radiation required for target, this case exists especially in some regions such as the brain and lungs because the difficulty of treatment in that region and the limited tolerance dose of the member. Second the radiation sensitivity of cancer cells is limited. Therefore it appears it's necessary to increase the radiation concentration within the ionization region and increase the sensitivity enhancement ratio (SER) [4]. The effective dosage of radiation involves the use of high energy X-ray and focusing of ionizing radiation into the tumor within the fractionation dose scheduled and sometimes this way has limited effect on the treatment process [5].

The direct injection technique of nanoparticles of high atomic number, such as gold and silver into the cancerous tumor has several practical advantages. First, it works on focusing the radiation inside the required region and it helps in increase the absorbed dose in the tumor. Finally, to avoid surrounding healthy tissue from exposure to unnecessary radiation[6,7]. Hainfeld et al. (2004) they used nano-particles as radio sensitive agent in vivo study where they injected cancer cells of mice with gold nano particles then irradiated with x-ray, the result show small gold nanoparticles can deliver high levels of gold to tumors with specificity and thereby improve x-ray therapy [8].

Hainfeld J.F. at el(2008) loaded the tumor with gold nanoparticles then irradiated by x-ray , the study showed Radiotherapy dose enhancement with gold nanoparticles appears to be a promising approach for improved cancer treatment[6].McMahon et al (2008) used nano particles as a compare agents due to high atomic number (Z) compare with human tissue[9].

Xiang-Yu Su et al (2014) they studied enhancement of radio-sensitization by gold nanoparticles and silver nanoparticles in cancer radiation therapy , they concluded anomaterials have been widely used in the diagnosis and treatment for disease[10].

Hossain M (2015) deduce adding nanoparticles efforts are underway to minimize toxicity of nanoparticles, improve targeting and combine radiation therapy with other therapeutic modalities in order to improve the efficacy of the method for in vivo applications [11] .This research aims to enhance brain radiotherapy by increasing SER then reduce the number dose fractions of radiotherapy therefore the side effect of radiotherapy will reduce.

2. Experiment

The human brain is composed of light elements. Each element has percentage by mass as follow H 10.7, C 14.5, N2.2 ,O71.2, Na 0.2, P 0.4, S 0.2 , Cl 0.3, K0.3[12] .So it has small cross section. To increase brain cross section element with high atomic number like gold, gadolinium, silver and titanium should be injected [6,7]. The final cross section is given as follow [12]:

$$\sigma_{total} = \sigma_{brain} + \sigma_{agent} \quad \ldots\ldots\ldots(1)$$

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

Cross section (σ) and mass energy absorption coefficient (μ_{en}/ρ) are related together in the following equation [13]

$$\mu_{en}/\rho = \frac{N_A \sigma}{A} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(2).$$

N_A: Avogadro's number, A: Mass number

From equation (1) and equation (2) we can find the total mass energy absorption coefficient μ_{en}/ρ of brain with nano-agent as follow :

$$(\mu_{en}/\rho)_{total} = (\mu_{en}/\rho)_{brain} + (\mu_{en}/\rho)_{nanoparticles} \quad \ldots\ldots\ldots(3)$$

The dose(d) for different medium can calculate from this equation [14]:

$$d(Gy) = 8.9*10^{-3}\left(\frac{\left(\mu/\rho_{media}\right)}{\mu/\rho_{air}}\right) * X \quad \ldots(4)$$

Where: $\left(\mu/\rho\right)_{Med}$ mass attenuation coefficient for medium, $\left(\mu/\rho\right)_{air}$:mass attenuation coefficient for air. X(R) : The exposure.

Then the dosage fractionation equation with nano material will be as follow:

$$d(Gy) = 8.9*10^{-3}\left(\frac{\left(\mu/\rho_{brain}\right)+\left(\mu/\rho_{nano}\right)}{\mu/\rho_{air}}\right) * X \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(5)$$

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

Irradiation equation of dosage fractionation [15-17]

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

Where: N_s= survival cells No. after irradiation. N_i= initial cells No. befor irradiation. α/ β is a factor represent radio-sensitivity (for CNS 2) .

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

$$N_s = N_i e^{\left(-\left(1+\frac{8.9*10^{-3}\left(\frac{\left(\mu/\rho_{brain}\right)+\left(\mu/\rho_{nano}\right)}{\mu/\rho_{air}}\right)*X}{\alpha/\beta}\right)\right)} \quad \ldots(7)$$

3. Result and Discussion:

By appling the irradiation equation (equation 7) on brain without and with using gold nano particles with x-ray photons whose energy range from 2MeV to 20 MeV we get figure shows a decrease in the number of surviving cancer cells due to presence of gold nanoparticles and increasing energy X-rays as showen in figure 1.

Then when applying the equation 7 on brain tumor with presence of gadolinum nanoparticles and high energy X-ray. We noticed there is also a decrease in the number of surviving cancer cells, but by less than the presence of gold nanoparticles.This is illustrated in Figure 2.

The brain without and with silver nano particles gives figure 3. From figure 3 we noticed there is a decrease in the number of surviving tumor cells. It means there is an increase in the number of destroyed cancer cells but by less than the presence of both gold and gadolinium nanoparticles.

At last when we applied the irradiation equation 7 without and with titanium nano particles we get a decrease in the number of surviving tumor cells but by less than the presence of gold, gadolinium and silver nanoparticles as shown in figure 4.

According to the number of surviving cancer cells without nanoparticles elements and the number of surviving cancer cells with presence of nanoparticles elements. we can find SER percentage as shown in Figure 5.

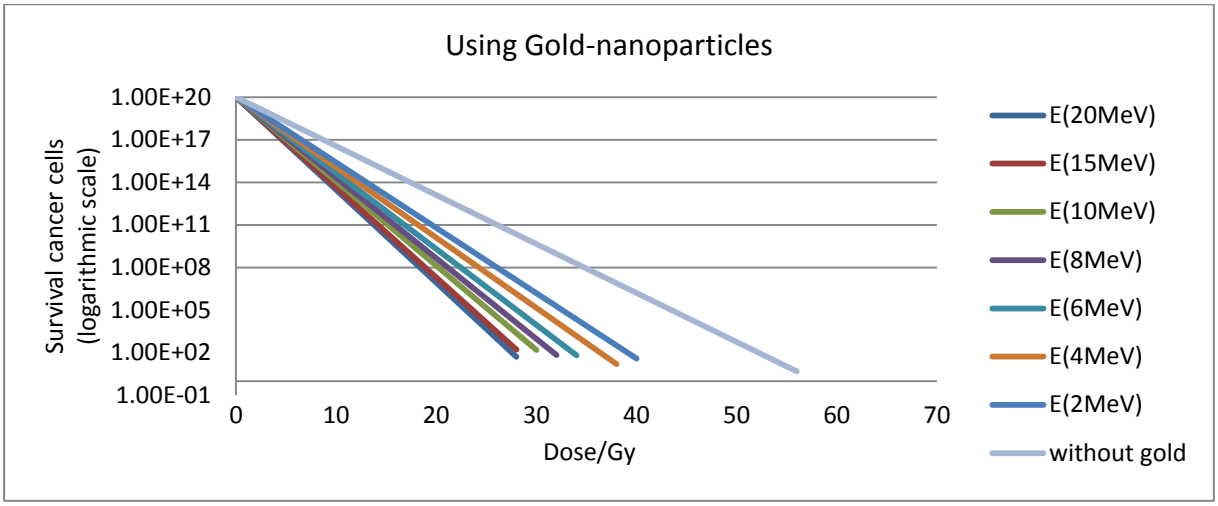

figure (1): Decreasing in the number of surviving cancer cells with increasing energy X-rays with the aid of gold nano particles.

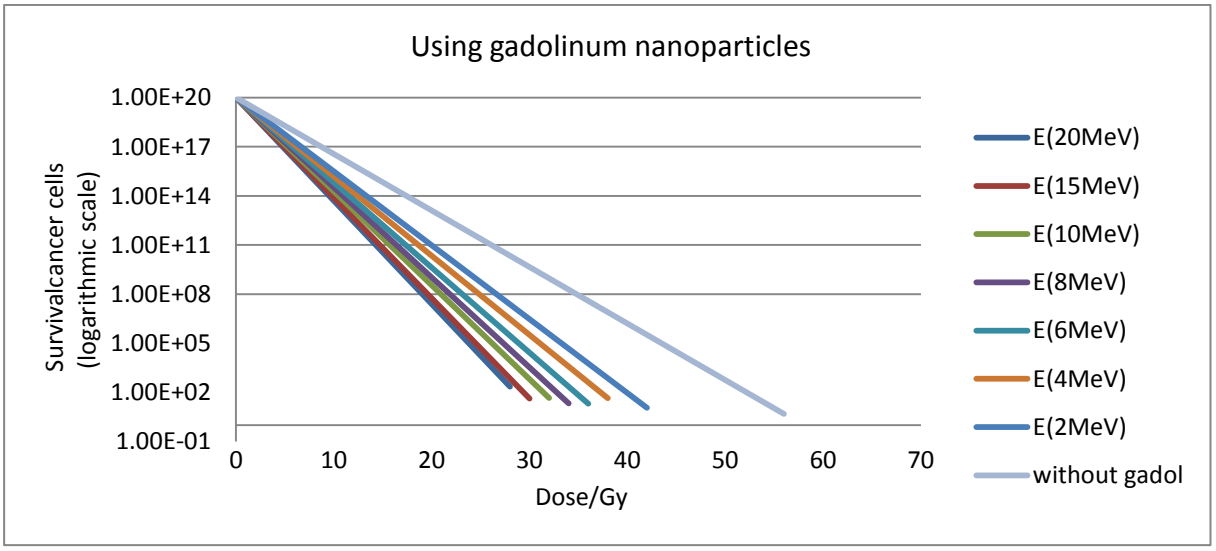

Figure (2): Decreasing in the number of surviving cancer cells with increasing energy X-rays with the aid of gadolinium nano particles

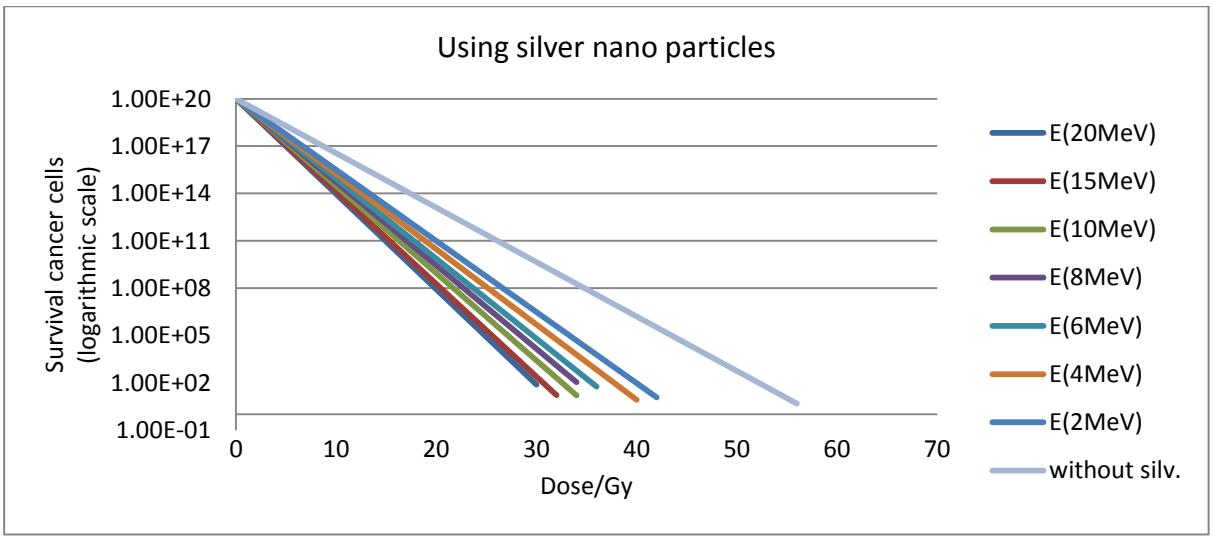

Figure (3): Decreasing in the number of surviving cancer cells with increasing energy X-rays with the aid of silver nano particles

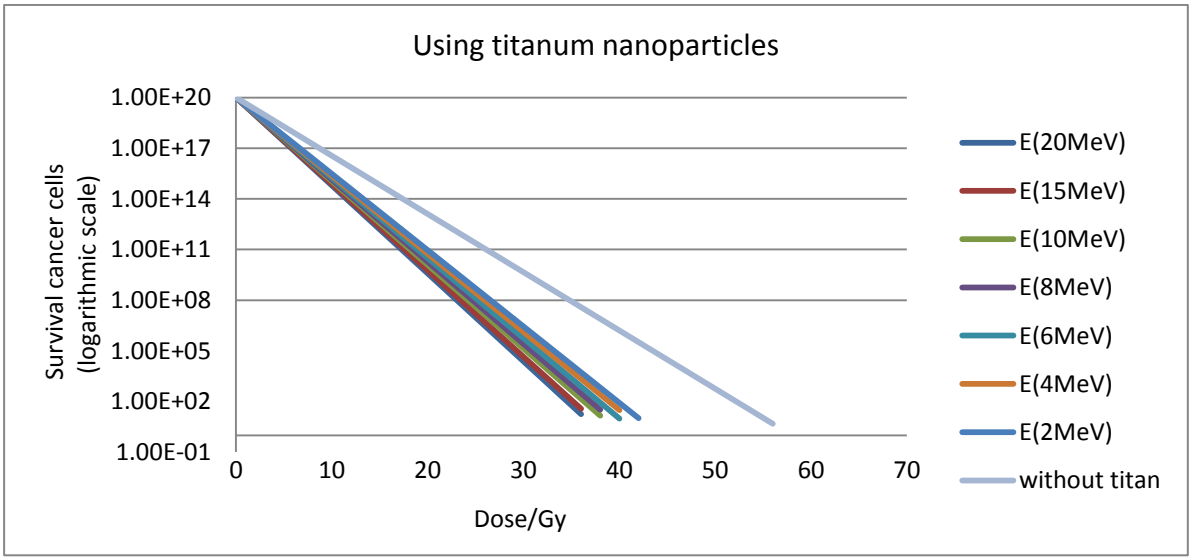

Figure (4): Decreasing in the number of surviving cancer cells with increasing energy X-rays with the aid of silver nano particles

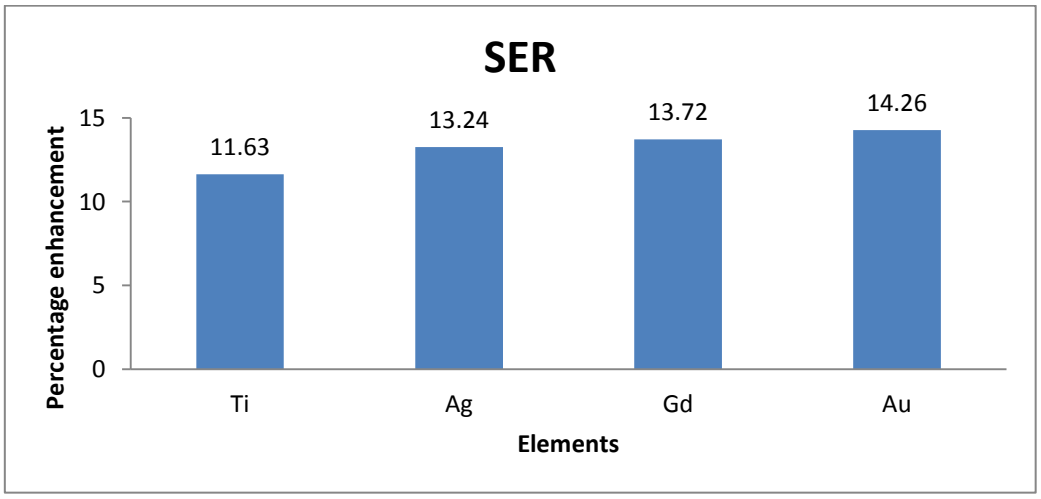

Figure 5: show the sensitivity enhancement ratio(SER) in brain malignant when using gold nanoparticles,gadolinium nano-particles , silver nanoparticles and titanium nanoparticles

4. Discussion

The element of high atomic number such as gold, gadolinium, silver and titanium are working on identifying the target accurately (ionization region) . This is because the cancer cells vasculature is large compared to normal tissue so nano particles concentrate inside cancer cells[18-20]. Also it works to increase the dose absorbed into the tumor exclusively zone because ionization region injected with nanoparticles materials with a high mass energy absorption coefficient [21]. Then, this can increase the number of destroyed malignant cell compared with the same area without nano particles material [22].

High energy X-ray is another factor which helps to enhance radio-sensitivity. To illustrate the interaction of high energy X-ray with high atomic number (nano material) loaded inside the brain cancerous cells working to increase free radical production. Free radical products of water interaction with X-ray [23,24].where increasing in free radical lead to increase destroying in cancer cells and decrease survival cancer cells as illustrated in figures 1,2,3,4. In this research we get SER percentage 14.26 with gold nano particles due to the gold has high atomic number79. Then it has high mass energy absorption coefficient. In the second order comes a gadolinium nanoparticle with atomic number64, SER percentage 13.72. The third order to silver nano particles has atomic number 47, SER percentage 13.24. Titanium (22) comes in the last order, SER percentage 11.63. It's clear that SER percentage depend on atomic number as it illustrated in figure 5 in other words depend on cross section.

5. Conclusions

The insertion of nanomaterial such as gold, gadolinium, silver and titanium into the brain tumor and using high energy X-ray are working together to increase the sensitivity enhancement ratio (SER). Because of concentrated nanoparticles within the tumor greater than healthy tissue, then healthy tissue can avoid the risk of ionizing radiation.

Figure 5 shows the sensitivity enhancement ratio(SER) 14.26% for gold nanoparticles, 13.72% for gadolinium nanoparticles, 13.24% for silver nanoparticles and 11.63%for titanium nanoparticles respectively.

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