Using gold nanoparticles with high energy gamma photons (6MeV)to treat ovary cancer

استعمال جسيمات الذهب النانوية مع فوتونات كاما ذات طاقة عالية(6MeV) لمعالجة سرطان المبيض

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Abstract:

Gold nanoparticles (GNPs) are good choice in medical application because it characterized by ability of synthesis as colloidal solution, did not interact with healthy tissue , less toxicity, ease of detection and thermal stability. The present project focuses on treatment of the ovary cancer by high energy photons of gamma ray (6MeV) and gold nanoparticles while preserving the ovary and prevents the risk of recurrence of ovary cancer. This occur in a minimum dose given for patient i.e. enhancing the radiotherapy that is used in ovary cancer treatment by depending on pair production phenomena . The obtained results showed that gold nano-particles (GNPs) with high energy of gamma photons (6MeV) significantly enhancing the radiotherapy for ovary cancer treatment .

Key Word: gold nanoparticles, gamma photons, Ovary cancer, pair production.

الخلاصة :

اختيار جسيمات الذهب النانوية في التطبيقات الطبية هو اختيار جيد بسبب القدرة على تصنيعها كمحلول غروي , لا يتفاعل مع النسيج الحيوي, لا يتأكسد فلا ينتج آثار سمية في النسيج الحي ومستقرة حراريا أيضا من مميزاته انه عنصر ثقيل نسبة إلى عناصر النسيج الحيوي لذا سهولة الكشف عنه داخل النسيج الحيوي وضمان حدوث ظاهرة إنتاج الزوج الالكتروني عند تفاعل الذهب مع فوتونات كاما ذات الطاقة العالية 6 ميكاالكترون فولت. في هذا البحث سنركز على كيفية علاج سرطان المبيض بواسطة فوتونات أشعة كاما ذات الطاقة العالية (6ميكاالكترون فولت) عند تفاعلها مع جسيمات الذهب النانوية مع البقاء على شكل المبيض دون استئصاله , أيضا منع خطورة إعادة المرض بعد العلاج يتم هذا بأقل جرعة من الإشعاع تعطى للمريض . بعبارة أخرى تحسين العلاج بالإشعاع المستخدم في علاج سرطان المبيض بالاعتماد على ظاهرة إنتاج الزوج الالكتروني . النتائج التي تم الحصول عليها أظهرت ان تفاعل جسيمات الذهب النانوية مع فوتونات اشعة كاما ذات طاقة عالية (6MeV) ينتج عنها تحسن ملحوظ لعلاج سرطان المبيض بواسطة الإشعاع .

كلمات مفتاحيه : جسيمات الذهب النانوية , فوتونات كاما ,سرطان المبيض , إنتاج الزوج .

1-Introduction:

Ovarian cancer is one of the most treatable solid tumors ,but it is represents the most common cause of death among women who develop cancers. Ovary cancer account for 4% of the total cancers in women in the world, ranked behind cancer of the lung, breast, colon and uterus[1]. Ovarian cancer in the first degree is a disease of women, with only 10% to 15% of all cases diagnosed in premenopausal women.The median age for diagnosis of women with epithelial ovarian cancer, the most common type, ranges between 60 and 65 years. Less than 1% of epithelial ovarian cancers are found in women younger , and most ovarian cancer in these younger patients are germ cell tumors (GCTs). Currently, patients with ovarian cancer are treated with surgical operation followed by radiotherapy and chemotherapy[2].Gold nanoparticles (AuNPs) are used in therapeutics because their unique properties of small size,high reactivity to the living cells, stability over high temperatures and translocation into the cells[3]. GNPs are the colloidal suspension of gold particles of nanometer sizes[4] .The size of GNPs is determined mainly by the gold salt concentration, temperature and rate of addition of reactants resulting in size range of 10–25 nm. However, the size range of 1–100 nm or more can also be achieved by varying the gold salt concentration and temperature [5].Therapy combined with metallic nanoparticles is a new way to treat cancer, in which gold nanoparticles (GNPs) are injected and bound to tumor sites. When an external photon-ray source hits these nanoparticles, particles can subsequently generate free radicals that damage cancer cells and induce cell apoptosis. Results have shown improvement in the treatment effects on ovary cancer cells with little or no increase in harm to normal surrounding tissues . In a translation study, GNPs were used to enhance ovary cancer apoptosis by radiotherapy[6].

3-Theoretical Models:

3-A:Equation derivation

Photons may undergo various possible interactions with atoms of an attenuator (photo electric effect, Compton scattering and pair production); the probability (cross-section) for each interaction depends on the energy hν of the incident photon and on the atomic number Z of the matter(attenuator) . When the energy of photon 6MeV and the attenuator is the gold (Z=79) the pair production(electron and positron) process is prevailing these electrons and positrons generate free radicals then cause damage to DNA of cancer cells[7].

The linear attenuation coefficient (μ) relate with probability for pair production interaction (cross section σ) by the following relation[8]:

$\mu = N_A \sigma w / A$ …….. (1)

Where μ: linear attenuation coefficient (cm^{-1}), N_A is Avogadro's number ($6.022\ 1367 * 10^{23}$ atoms/mol), σ: the microscopic cross section for reaction (cm^2) and A is mass No., w: is the weight (gram)[9].

Dividing both sides by ρ (density g/cm^3)

$\mu/\rho = N_A \sigma w/ \rho A$ …… (2)

μ/ ρ: mass attenuation coeff. (cm^2/g)

From eq.2 we can write the cross section as follow :

$$\sigma = \frac{(\mu/\rho)\,\rho A}{N A\ w} \text{……. (3)}$$

For photons of high energy (6MeV.) and the attenuator is the gold (Z=79) the pair production(electron and positron) process is prevailing . The equation of irradiation is given by

$N_d = \phi\ t\ N_i\ \sigma$ ……. (4)

N_d: The number of cells destryed cancer cells after irradiation,ϕ: is the flux of particles (particle/ cm^2.sec.), t: is the time of exposure to radiation(second),Ni: is the number of cells cancer per unit volume (cell/cm^3)[10].

By substitute eq.3 in eq.4 we get the final eq. for irradiation

$$Nd = \phi\, t\, Ni \frac{(\mu/\rho)\,\rho A}{NA\ w} \quad \text{..... (5)}$$

3-B: Theoretical Calculation and results :

The mass attenuation coefficient for gold and ovary can be calculated through the photon energy and number of atoms. from the National Institute of Standards and Technology (NIST2004) [11] and The National Institute of Standards and Technology (NIST) [12] and encyclopedia of medical devices and instrumentation [13]. Fractionation was assumed to create a suitable therapeutic [14].

Computer simulation was developed in fortran program (power station 90) using equation of radiation eq. (5) for a ovary with Gold nanoparticles (GNPs) in weights of (0.001,0.002, 0.003, 0.004, 0.005, 0.01, 0.02, 0.03, 0.04, 0.05, 0.1, 0.2, 0.3, 0.4, 0.5) grams. The energy of incident photon was 6MeV. The flux was 10^{16} (photon/cm^2.s) and time of irradiation was 1200 sec.(20 min.). The results were in agreement with those of fractionation in radiotherapy [14] and we find enhancement in radiotherapy and this result in agreement with literatures in the world[6][15][16][17][18][19].

Table-1(A) : Number of destroyed cancer cells by dose fractionation when photon energy 6MeV.,flux 10^{16} (photon/cm^2.sec.), irradiation time 1200 sec. concetration of gold nanoparticles(0.001-0.3)g.

Dose (Gy)	Cancer Cell Number	Number of destroyed cancer cells by dose fractionation at concentrations:								
		W=0.001g	W=0.002g	W=0.003g	W=0.004g.	W=0.005g	W=0.01g	W=0.02g	W=0.03g	W=0.04g
2	1,000,000,000	2114416557	1057210321	704808270	528607203	422886609	211445347	105724716	70484506	52864401
4	500,000,000	1071199349	535600709	357067843	267801389	214241540	107121805	53561937	35708648	26782003
6	250,000,000	542687788	271344418	180896635	135672733	108538404	54269726	27135387	18090607	13568218
8	125,000,000	274934853	137467692	91645308	68734111	54987399	27493965	13747248	9165009	6873889
10	62,500,000	139286667	69643468	46429070	34821868	27857550	13928909	6964589	4643149	3482429
12	31,250,000	70564992	35282564	23521755	17641350	14113108	7056622	3528379	2352298	1764257
14	15,625,000	35749423	17874746	11916521	8937407	7149940	3575004	1787536	1191714	893803
16	7,823,500	18111265	9055650	6037112	4527842	3622281	1811158	905596	603742	452815
18	3,906,250	9175474	4587746	3058503	2293881	1835109	917563	458790	305866	229404
20	1,953,125	4648451	2324230	1549489	1162119	929697	464853	232431	154957	116220
22	976,562	2354984	1177494	784997	588749	471000	235502	117753	78503	58879
24	488,281	1193075	596538	397693	298270	238616	119309	59655	39771	29829
26	244,140	604432	302216	201478	151108	120887	60444	30222	20148	15111
28	122,070	306215	153108	102072	76554	61243	30622	15311	10207	7655
30	61,035	155134	77567	51711	38783	31027	15513	7756	5171	3878
32	30,517	78593	39296	26197	19648	15718	7859	3929	2619	1964
34	15,258	39816	19908	13272	9954	7963	3981	1990	1327	995

Dose (Gy)	Cancer Cell Number	Number of destroyed cancer cells by dose fractionation at concentrations:								
		W=0.001g	W=0.002g	W=0.003g	W=0.004g.	W=0.005g	W=0.01g	W=0.02g	W=0.03g	W=0.04g
36	7,629	20171	10085	6723	5042	4034	2017	1008	672	504
38	3,814	10219	5109	3406	2554	2043	1021	510	340	255
40	1,907	5177	2588	1725	1294	1035	517	258	172	129
42	953	2622	1311	874	655	524	262	131	87	65
44	476	1328	664	442	332	265	132	66	44	33
46	238	673	336	224	168	134	76	33	22	16
48	119	341	170	113	85	68	34	17	11	8
50	59	172	86	57	43	34	17	8	5	4
52	29	87	43	29	21	17	8	4	3	2
54	15	44	22	14	11	8	4	2	1	1
56	7	22	11	7.4	5.6	4	2	1	0.7	0.5
58	4	11	5	3.7	2.8	2	1	0.5	0.3	0.3
60	2	5	2	1.9	1.4	1	0.5	0.3	0.2	0.1
62	1	2	1	0.9	0.7	0.5	0.2	0.1	0.09	0.07
		S.Sh.	S.Sh.	F	F	F	F	F	F	F

Note:1- W: represent the concentration of gold nanoparticles in gram. 2- S.Sh. : Single shot, F.:Fractionation

Table-1(B) : number of destroyed cancer cells by dose fractionation when photon energy 6MeV. ,flux 10^{18} (photon/cm^2.sec.), irradiation time 1200 sec. concetrations of gold nanoparticles(0.004-5)g.

Dose(Gy)	Cancer Cell Number	Number of destroyed cancer cells by dose fractionation at concentrations:					
		W=0.05g	W=0.1g	W=0.2g	W=0.3g	W=0.4g	W=0.5g
2	1,000,000,000	42292336	21148211	10576148	7052127	5290117	4232911
4	500,000,000	21426016	10714043	5358056	3572727	2680063	2144464
6	250,000,000	10854783	5427916	2714482	1810004	1357765	1086422
8	125,000,000	5499217	2749874	1375202	916979	687867	550399
10	62,500,000	2785997	1393133	696701	464557	348485	278841
12	31,250,000	1411433	705784	352960	235352	176548	141266
14	15,625,000	715056	357562	178815	119233	89442	71567
16	7,823,500	362259	181147	90591	60405	45313	36257
18	3,906,250	183526	91772	45895	30602	22956	18368
20	1,953,125	92977	46493	23251	15503	11630	9305
22	976,562	47104	23554	11779	7854	5892	4714
24	488,281	23863	11933	5967	3979	2984	2388
26	244,140	12089	6045	3023	2015	1512	1210
28	122,070	6124	3062	1531	1021	766	613
30	61,035	3102	1551	775	517	388	310
32	30,517	1572	786	393	262	196	157
34	15,258	796	398	199	132	99	79

Dose(Gy)	Cancer Cell Number	Number of destroyed cancer cells by dose fractionation at concentrations:					
		W=0.05g	W=0.1g	W=0.2g	W=0.3g	W=0.4g	W=0.5g
36	7,629	403	201	100	67	50	40
38	3,814	204	102	51	34	25	20
40	1,907	103	51	25	17	12	10
42	953	52	26	13	8	6	5
44	476	26	13	6	4	3	2
46	238	13	6	3	2	1	1
48	119	6	3	1	1	0.8	0.6
50	59	3	1	0.8	0.5	0.4	0.3
52	29	1	0.8	0.4	0.2	0.2	0.1
54	15	0.8	0.4	0.2	0.1	0.1	0.08
56	7	0.4	0.2	0.1	0.07	0.05	0.04
58	4	0.2	0.1	0.05	0.03	0.02	0.02
60	2	0.1	0.05	0.02	0.01	0.01	0.01
62	1	0.05	0.02	0.01	0.009	0.007	0.005
		F	F	F	F	F	F

Note:1- W: represent the concentration of gold nanoparticles in gram. 2- S.Sh. : Single shot, F.:Fractionation

4-Discussion

From the results in table 1 A and B we note that when we apply equation 5 with gold nanoparticles by Fortran program(power station 90) and input the parameters the number of ovary cancer cells, the flux of incident photons equal 10^{16} (photon/cm^2.sec.) and time of irradiation 1200 second there were increasing in number of distroyed cancer cells this result due to existence of gold nano-particles in cancer cells with high concentration .Gold nanoparticles (GNPs) have biocompatibility and ability to increase dose deposited because of their high mass energy absorption coefficient. which in turn caused breaks in DNA by generating free radicals that damage cancer cells . Results have shown improvement in the treatment effects on cancer cells.

Maximum damage noted in weights (0.001; 0.002) grams respectively because these nanoparticles formed in size to become capable to enter inside the cancer cells and make maximum damage in single shot (S.Sh.).

5-Conclusions

We have developed a method for enhancing the treatment of ovary cancer by using gold nano-particles as a colloidal to achieve targeted delivery at the ovary cancer cells. Our results showed that gold nano-particles (GNPs) with photons of high energy (6MeV.) significantly enhancing the radiotherapy . Where we note increase in number of destroyed cancer cells i.e. destroy large number from cancer cells in minimum dose that given to patient our results can be arranged in two benefits from using gold nano- particles with high energy photons :

1) GNPs can be enhanced the treatment by radiation. Thus, lower doses of radiation can be used, avoiding the risk of side effects.
2) Local damage to normal tissue surrounding the cancer is decreased because the concentrations of gold nanoparticles increase in cancer cells.

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