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Breast cancer treatment using Gold nanoparticles and gamma-ray photons With energy 12 Mev.

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Abstract

Gold nanoparticles are characterised by their small size to volume ratio and extensive thermal stability. Gold nanoparticles (AuNPs) are an obvious choice in medical application due to their amenability of synthesis and functionalization, less toxicity and ease of detection. The present paper focuses on treatment of the breast cancer by high energy photons of gamma ray (12MeV.) and gold nanoparticles while preserving the shape of the breast and prevents the risk of recurrence of breast cancer. This of course in a minimum dose given for patient i.e. enhancing the radiotherapy that is used in breast cancer treatment due to pair production phenomena.

علاج سرطان الثدي باستخدام جسيمات متناهية الصغر (نانوية) من الذهب و فوتونات اشعة كاما ذات طاقة ١٢ ميكا الكترون فولت

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الخلاصة

جسيمات الذهب النانوية تتميز بالقياس الصغير نسبة إلى الحجم ومستقرة حراريا.إن اختيار جسيمات الذهب النانوية في التطبيقات الطبية هو اختيار جيد بسبب القدرة على تصنيعها ، لا يتفاعل مع النسيج الحيوي، لا يتأكسد فلا ينتج آثار سمية في النسيج الحي 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 ١٢ ميكاالكترون فولت. في هذا البحث سنركز على كيفية علاج سرطان الثدي بواسطة فوتونات أشعة كاما ذات الطاقة العالية (12ميكاالكترون فولت) عند تفاعلها مع جسيمات الذهب النانوية مع البقاء على شكل الثدي دون استئصاله ، أيضا منع خطورة إعادة المرض بعد العلاج هذا بالطبع بأقل جرعة من الإشعاع تعطى للمريض . بعبارة أخرى تحسين العلاج بالإشعاع المستخدم في علاج سرطان الثدي بالاعتماد على ظاهرة إنتاج الزوج الالكتروني .

1-Introduction

Breast cancer is the most common type of cancer among women worldwide. “Global Breast Cancer Statistics” has reported that breast cancer is the most common form of cancer for women[1]. Breast cancer is the most frequently diagnosed cancer and the second most common cancer following only lung cancer cause of death for women[2]. Breast cancer is a malignant tumor that starts from cells of the breast. A malignant tumor is a group of cancer cells that may grow into (invade) surrounding tissues or spread (metastasize) to distant areas of the body. The disease occurs almost entirely in women, but men can get it, too.Female

breast cancer is a major medical problem with significant public health, Major advances have been made in the past 40 years in understanding the biologic and clinical nature of the disease[3]. Gold nanoparticles (AuNPs) are used in therapeutics due to their unique properties of small size, large surface area to volume ratio, high reactivity to the living cells, stability over high temperatures and translocation into the cells, etc[4]. GNPs are the colloidal suspension of gold particles of nanometer sizes[5] .The size of GNPs is determined mainly by the 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 salt concentration and temperature [6]. 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 radicals that damage cancer cells and induce cell apoptosis. Results have shown improvement in the treatment effects on cancer cells with little or no increase in harm to normal surrounding tissues in mice models. In a translation study, GNPs were used to enhance cancer apoptosis by radiotherapy[7].

2-Theoretical Models

2-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 of the photon and on the atomic number Z of the matter(attenuator) . When the energy of photon 12MeV. 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 [8]. The linear attenuation coefficient (μ) relate with probability for pair production interaction (cross section σ .in unit cm2 or barn, 1barn=10-24 cm2) by the following relation:[8]

$\mu = NA\ \sigma /A$ …….. (1)

μ: linear attenuation coefficient (cm-1), NA is Avogadro's number, σ: the microscopic cross section for reaction (cm2) and A is weight Number [9].

Equation (1) for one gram and for several grams eq.(1) becomes

$\mu = NA\ \sigma\ w /A$ ……..….. (2)

w: is the mass (gram).

Dividing both sides by ρ (g/cm3)

$\mu/\rho = NA\ \sigma\ w/\rho\ A$ …… (3)

μ/ ρ: mass attenuation coeff. (cm2/g)

From eq.(3) we get

$\sigma = \frac{(\mu/\rho)\,\rho A}{NA\ w}$…….. (4)

the equation of irradiation by photons is given by

$N = \phi\ t\ No\ \sigma t$ ……..…. (5)

N: The number of cells remains after irradiation , ϕ: is the flux of particles (photon/ cm2.sec.) the number of particles per unit time per unit solid angle, t: is the time of exposure to radiation (second) ,No: is the number of cells cancer per unit volume (cell/cm3), σt: total cross section of interaction (photoelectric effect, Compton scattering and pair production) [10], [11].

For photons of high energy (12MeV.) and the attenuator is the gold (Z=79) the pair production(electron and positron) process is prevailing therefore the equation of irradiation becomes:

$N = \phi\ t\ No\ \sigma p.p.$ ……..……(6)

Where σp.p. is cross section of pair production only. By substitute eq.4 in eq.6 we get the final eq. for irradiation

$N = \phi\ t\ No \frac{(\mu/\rho)\,\rho A}{NA\ w}$……..… (7)

Equation (7) is represent the irradiation equation as a function of photon energy and concentration of gold nanoparticles.

2-B: Theoretical Calculation and results

The mass attenuation coefficient for gold and breast can be calculated through the photon energy and number of atoms. From the National Institute of Standards and Technology (NIST2004) [12] and The National Institute of Standards and Technology (NIST1998), **[13] and** encyclopedia of medical devices and instrumentation, [14]. Fractionation was assumed to create a favorable therapeutic ratio because the tolerance of normal tissues increased relative to that of tumors and because malignant cells had a greater reproductive capacity and were, therefore, more likely to be in a radiosensitive phase [15]. Computer simulation was developed in Fortran (power station 90) using equation (7) for a breast without Gold nanoparticles (GNPs). The energy of incident photon was 12MeV. The flux was 1018 (photon/cm2.s) and time of irradiation was 1200 sec.(20 min.). The results were in agreement with those of fractionation in radiotherapy[15].

Table 1: Radiotherapy for breast cancer irradiated by 12MeV gamma photons without gold nanoparticles.

Dose (Gy)	NO. of cancer cells	NO. of destroyed cells	NO. of cells remaining
2	1013233977	333548	1012900429
4	513321546	168981	513152565
6	260057416	85608	259971807
8	131749505	43370	131706134
10	66746537	21972	66724565
12	33814929	11131	33803798
14	17131217	5639	17125578
16	8678966	2857	8676109
18	4396911	1447	4395464
20	2227550	733	2226816
22	1128514	371	1128143
24	571724	188	571536
26	289645	95	289550
28	146739	48	146691
30	74340	24	74316
32	37662	12	37649
34	19080	6	19074
36	9666	3	9663
38	4897	1.6	4895
40	2480	0.8167	2480
42	1256	0.4138	256
44	636	0.2096	636
46	322	0.1062	322
48	163	0.0538	163
50	82	0.0273	82
52	41	0.0138	41
54	21	0.0070	21
56	10	0.0035	10
58	5	0.0018	5
60	2	0.0009	2
62	1.4	0.0005	1

The results in table (1) were in agreement in dose fractionation with the dose fractionation of radiotherapy. [16]And agreement in result with world results where The 44-62 Gy dose of irradiation gives low damage in nucleus of cancer cells [16].When we applied the same equation (7) with gold nano-particles in weights of (0.001;,0.01;0.1;0.002;0.02;0.2;0.003;0.03;0.3;0.004;0.04;0.4;0.005,0.05;0.5) grams , the energy of incident photon 12MeV. , the flux is 10^{18}, and the time of irradiation 1200 sec. By using Fortran program then we find enhancement in radiotherapy and this result in agreement with literatures in the world [7][17][18][19][20][21].

Table-2(A) : Number of destroyed cancer cells by dose fractionation when photon energy 12MeV.,flux 10^{18} (photon/cm^2.sec.), irradiation time 1200 sec. ; gold density 19.32 g/cm^3 ,photon energy ; mass number of gold 196.97 ; breast average atomic weigh (A) 9.673, breast density 0.960 g/cm^3,cocentration of gold nanoparticles(0.001-0.04)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	232746161981	116373231812	77582258100	58186766728	46549476962	23274889303	11637595473	7758497530	5818948558
4	500,000,000	117913159724	58956656271	39304489978	29478404544	23582755846	11791454332	5895803575	3930586656	2947978196
6	250,000,000	59736809912	29868443666	19912322356	14934260543	11947424753	5973751086	2986914253	1991301975	1493495836
8	125,000,000	30263682754	15131860988	10087920791	7565950105	6052768351	3026403787	1513221504	1008827410	756630363
10	62,500,000	15332095825	7666057848	5110712053	3833038859	3066435275	1533227573	766623722	511089104	383321796
12	31,250,000	7767500218	3883755142	2589173551	1941882604	1553508205	776759136	388384601	258926423	194197334
14	15,625,000	3935147570	1967576335	1311719307	983790717	787033649	393519374	196762237	131176524	98383668
16	7,823,500	1993612612	996807598	664539285	498405090	398724617	199363600	99683092	66456256	49842837
18	3,906,250	1009998018	504999663	336666891	252500486	202000664	101000986	50501147	33667868	25251228
20	1,953,125	511682154	255841408	170561166	127921036	102336968	51168815	25584739	17056714	12792701
22	976,562	259226872	129613604	86409184	64806970	51845646	25922991	12961663	8641221	6480999
24	488,281	131328737	65664453	43776361	32832312	26265885	13133027	6566599	4377789	3283384
26	244,140	66533369	33266727	22177848	16633407	13306743	6653415	3326750	2217862	1663418
28	122,070	33706935	16853489	11235674	8426766	6741422	3370733	1685388	1123606	842716
30	61,035	17076506	8538264	5692183	4269143	3415319	1707670	853846	569238	426934
32	30,517	8651248	4325629	2883756	2172820	1730258	865134	432573	288385	216292

Dose (Gy)		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
34	15,258	4382869	2191437	1460960	1095721	876578	438292	219148	146101	109577
36	7,629	2220436	1110219	740147	555111	444089	222046	111024	74017	55513
38	3,814	1124910	562456	374971	281228	224983	112492	56246	37498	28124
40	1,907	569898	284949	189966	142475	113980	56990	28495	18997	14248
42	953	288720	144360	96240	72180	57744	28872	14436	9624	7218
44	476	146270	73135	48757	36567	29254	14627	7313	4875	3656
46	238	74103	37051	24701	18525	14820	7410	3705	2470	1852
48	119	37541	18770	12514	9385	7508	3754	1877	1251	938
50	59	19019	9509	6339	4754	3803	1901	950	634	475
52	29	9635	4817	3211	2408	1927	963	481	321	240
54	15	4881	2440	1627	1220	976	488	244	162	122
56	7	2473	1236	824	618	494	247	123	82	61
58	4	1252	626	417	313	250	125	62	41	31
60	2	634	317	211	158	126	63	31	21	15
62	1	321	160	107	80	64	32	16	10	8
		S.Sh.	S.Sh.	S.Sh.	S.Sh.	S.Sh.	S.Sh.	S.Sh.	S.Sh.	S.Sh.

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

Table-2(B) : Number of destroyed cancer cells by dose fractionation when photon energy 12 MeV.,flux 10^{18} (photon/cm^2.sec.), irradiation time 1200 sec. ; gold density 19.32 g/cm^3 ,photon energy ; mass number of gold 196.97 ; breast average atomic weigh(A) 9.673, breast density 0.960 g/cm^3,cocentration of gold nanoparticles(0.05-5)g.

Dose(Gy)	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	W=1g	W=2g	W=3g	W=4g	W=5g
2	4655219002	2327760323	1164030983	776121184	582166313	465793386	233047515	116674579	77883601	58488111	46850818
4	2358413032	1179282925	589717871	393196177	294935344	235978842	118065830	59109324	39457155	29631071	23735420
6	1194812108	597444764	298761092	199199863	149419256	119550890	59814155	29945787	19989665	15011604	12024767
8	605312112	302675667	151357444	100918034	75698333	60566512	30302867	15171044	10127104	7605133	6091951
10	306661399	153340635	76680252	51126790	38350061	30684024	15351947	7685909	5130562	3852889	3086286
12	155359874	77684970	38847518	25901700	19428792	15545047	7777557	3893812	2599230	1951939	1563564
14	78707952	39356526	19680813	13122241	9842956	7875385	3940242	1972671	1316814	988885	792128
16	39874785	19938684	9970634	6647950	4986608	3989804	1996193	999388	667120	500986	401305
18	20201243	10101276	5051292	3367964	2526300	2021302	1011305	506307	337974	253808	203308
20	10234293	5117478	2559070	1706268	1279866	1024026	512344	256503	171223	128583	102999
22	5184866	1591601	1296468	864424	648402	518789	259562	129949	86744	65142	52181
24	2626741	1313455	656813	437932	328491	262827	131498	56834	43946	33002	26435
26	1330751	665419	332752	221863	166419	133152	66619	33352	22263	16719	13392
28	674181	337112	168578	112399	84310	67457	33750	16897	11279	8470	6785
30	341551	170786	85404	56943	42713	34175	17098	8560	5714	4291	3437
32	173035	86523	43267	28848	21639	17313	8662	4336	2894	2174	1741

Dose(Gy)	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	W=1g	W=2g	W=3	W=4	W=5
34	87662	43834	21919	14615	10962	8771	4388	2197	1466	1101	882
36	44411	22207	11105	7404	5553	4443	2223	1113	743	557	446
38	22499	11250	5626	3751	2813	2251	1126	563	376	282	226
40	11398	5699	2850	1900	1425	1140	570	285	190	143	114
42	5774	2887	1443	962	722	577	289	144	96	72	58
44	2925	1462	731	487	365	292	146	73	48	36	29
46	1482	741	370	247	185	148	74	37	24	18	14
48	750	375	187	125	93	75	37	18	12	9	7
50	380	190	95	63	47	38	19	9	6	4	3
52	192	96	48	32	24	19	9	4	3	2	2
54	97	48	24	16	12	9	4	2	2	1	1
56	49	24	12	8	6	5	2	1	0.8	0.6	0.4
58	25	12	6	4	3	2	1	0.6	0.4	0.3	0.2
60	12	6	3	2	2	1	0.6	0.3	0.2	0.1	0.1
62	6	3	1	1	1	0.6	0.3	0.1	0.1	0.08	0.06
	S.Sh.	S.Sh.	S.Sh.	F	F	F	F	F	F	F	F

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

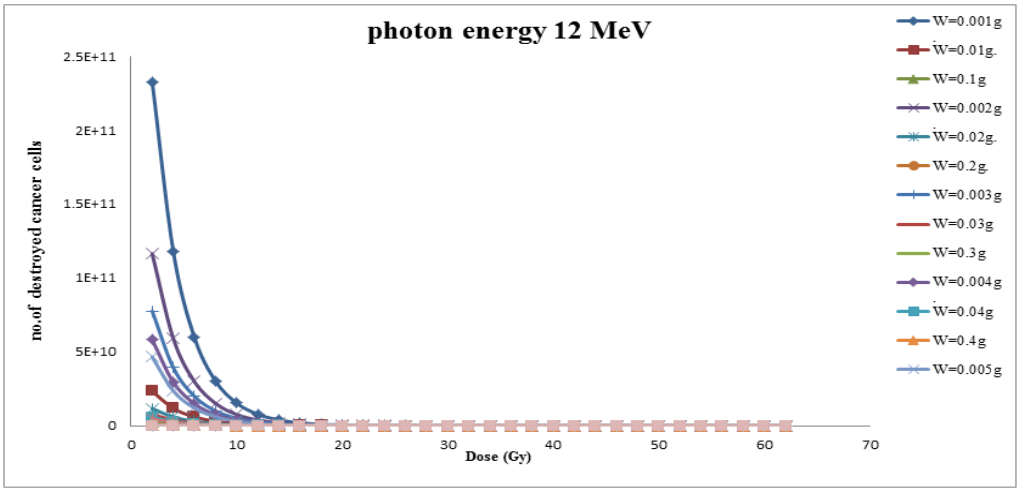

Fig.1: Number of destroyed cancer cells by dose fractionation when photon energy 12MeV and gold nanoparticles concentrations (0.001-5) g.

4-Discussion

From the results in table 2(A and B) we note that when we apply equation 7 with gold nanoparticles by Fortran program(power station 90) and input the parameters the number of breast cancer cells, the flux of incident photons equal 10^{18} (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[22]. Gold nanoparticles (GNPs) have biocompatibility and ability to increase dose deposited because of their high mass energy absorption coefficient[23] , 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; 0.003; 0.004; 0.005) 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 breast cancer by using gold nanoparticles as a colloidal to achieve targeted delivery at the breast cancer cells. Our results showed that gold nano-particles (GNPs) with high energy photons (12 MeV.) significantly enhancing the radiotherapy . Where we note increase in number of distroyed cancer cells i.e. destroy large number from cancer cells in minimum dose that given to patient our results can be arranged in three benefits from using gold nano particles with high energy photons :

1) Compared to GNPs, localized delivery a higher local concentration of GNPs in breast cancer cells.

2) GNPs can increase absorption of the radiation. Thus, lower doses of radiation can be used, avoiding the risk of side effects.

3) Local damage to normal tissue surrounding the cancer is decreased because the concentrations of gold nanoparticles increase in cancer cells.

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