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The enhancement of prostate cancer treatment using gold nanoparticles and high energy photons

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Abstract

Gold nanoparticles (AuNPs) are widely used for medical applications, because it ability to convert as colloidal solution, have no interaction with biotic tissue, low toxicity, easy in the detection, and thermally stabile. This study focuses on the treatment of prostate cancer by interaction the gamma ray (6 MeV) with Gold nanoparticles, without the extirpation of prostate. This method occurs in a minimum dose given for the patient for the improvement of radiotherapy that is used in prostate cancer treatment by depended on pair production phenomenon.

Keywords: gold nanoparticles(AuNPs), gamma photons, prostate cancer, pair production.

1. Introduction

The prostate gland sits in the pelvis, surrounded by the rectum, the bladder, and it is fixed to the bladder floor, the urethra communicates between the bladder and the prostate into the penis (Kantarjian *et al.* 2007). Prostate cancer is the most common cancer in men and the second after lung cancer leading cause of cancer death among men in the world (Jemal *et al.* 2010). In most men, the cancer grows slowly, many men with the disease will never know they had the condition. Early prostate cancer is confined to the prostate gland itself and the majority of patients can live for years with no problems (Christopher *et al.* 2010). This cancer is characterized by both grade and stage. The size and extent of the tumor determine its stage. The physician can be divided the treatment options according to risk (Christopher *et al.* 2010). Local treatment is composed of surgery and radiotherapy (External beam radiotherapy: EBRT or Brach therapy: BT). Systemic treatment is hormonal therapy (LHRH agonist or anti androgen) or systemic chemotherapy (Barrett *et al.* 2009). Radiotherapy consists of external beam radiotherapy (EBRT) and brachytherapy (BT). These treatments can be used as mono therapy or combined with each other. Radiotherapy can be used as radical treatment (EBRT or BT or both of them), adjuvant treatment after radical prostatectomy (EBRT) and palliative treatment (EBRT). Radiotherapy has been developed for a long time in giving the dose directly to the target lesion (prostate gland, seminal vesicles, and lymph nodes) (Bentzen *et al.* 2008). To increase the absorbed dose in cancer tumor inserting a material with a high atomic number (gold Z=79) locally in the region of the malignant cells (Hainfeld *et al.* 2008). In vivo this would be achieved by injecting gold nanoparticles. The injection of gold nanoparticles to enhance dose has already been proven to be viable using an animal model together with high energy photon beams (Hainfeld *et al.* 2004). 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 (Pooja *et al.* 2011). AuNPs are the colloidal suspension of gold particles of nanometer sizes (Roa *et al.* 2009) .The size of AuNPs is determined by the gold salt concentration, temperature, and rate of addition of reactants resulting in size range of 10 nm to 25 nm (Grzelczak *et al.* 2008). Therapy combined with metallic nanoparticles is a new way to treat cancer, in which gold nanoparticles (AuNPs) 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, AuNPs were used to enhance prostate cancer apoptosis by radiotherapy with little or no increase in harm to normal surrounding tissues (Liu *et al.* 2010).

2. Theoretical Calculations and Results

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 incident photon and on the atomic number Z of the matter. When the energy of photon 6 MeV and the attenuator

is the gold (Z=79) the pair production is prevailing these electrons and positrons generate free radicals then cause damage to DNA of cancer cells (Powsner and Powsner 2006).

The linear attenuation coefficient (μ) relate with probability for pair production interaction (cross section σ) by (Henke *et al.* 1993):

$$\mu = N_A \sigma w / A \quad (1)$$

where μ= linear attenuation coefficient (cm^{-1}), N_A= Avogadro's number, σ= the microscopic cross section for reaction (cm^2), A= mass number, and w= the mass (g).
Dividing both sides by ρ (g cm^{-3})

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

μ/ρ= mass attenuation coefficient (cm^2 g^{-1}), from equation 2 the cross section equal:

$$\sigma = \frac{(\mu/\rho)\rho A}{NA\ w} \quad (3)$$

The equation of irradiation is given by (Proh *et al.* 2004)

$$N_d = \phi\ t\ N_i\ \sigma \quad (4)$$

N_d= the number of cells destroyed cancer cells after irradiation, ϕ= the flux of particles (photon cm^{-2} sec^{-1}), t= the time of exposure t (s), and Ni= the number of cancer cells per unit volume (cell cm^{-3}).

By substitute equation 3 in equation 4 result the equation of irradiation can be applied in simulation program

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

The mass attenuation coefficient for the gold and prostate can get it from National Institute of Standards and Technology (NIST2004) (Hubbell and Seltzer 1996), the composition of prostate tissue can get from references (Wood and White 1986), and the fractionation was assumed to create a suitable therapeutic (Halperin *et al.* 2008). Computer program was developed in a simulation program using (5) for a prostate with Gold nanoparticles (AuNPs) in concentrations (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, and 0.5 g). The energy of incident photon was 6 MeV, the flux was 10^{16} (photon cm^{-2} s^{-1}), and time of irradiation was 1200 s. The results are tabulated in Table 1 and Table 2.

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

Dose (Gy)	Cancer Cell No.	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	33911845839	17005653538	11370256541	8552557387	6861938629	3480699933	1790080585	1226540802	944770911
4	500,000,000	17180317221	8615352987	5760365130	4332870869	3476374685	1763381719	906885235	621386408	478636994
6	250,000,000	8703840576	4364684187	2918298836	2195105992	1761190474	893359136	459443467	314804910	242485632
8	125,000,000	4409513503	2211223159	1478459768	1112077987	892249015	452590915	232761865	159485515	122847341
10	62,500,000	2233934452	1120243218	749012836	563397601	452028509	229290246	117921115	80798071	62236549
12	31,250,000	1131749145	567534246	379462627	285426796	229005322	116162334	59740840	40933675	31530093
14	15,625,000	573363344	287522490	192242213	144602064	116017986	58849812	30265724	20737695	15973681
16	7,823,500	290475610	145663778	97393171	73257862	58776683	29814314	15333130	10506068	8092538
18	3,906,250	147159879	73795744	49341035	37113677	29777266	15104438	7768024	5322552	4099817
20	1,953,125	74553694	37386178	24997006	18802419	15085668	7652165	3935413	2696495	2077037
22	976,562	37770168	18940472	12663908	9525625	7642656	3876716	1993747	1366090	1052262
24	488,281	19135008	9595565	6415751	4825843	3871899	1964010	1010066	692084	533093
26	244,140	9694120	4861276	3250328	2444854	1961570	995001	511716	350621	270074
28	122,070	4911206	2462805	1646671	1238604	993764	504084	259244	177630	136824
30	61,035	2488100	1247698	834231	627498	503458	255377	131337	89990	69317
32	30,517	1260513	632105	422636	317901	255060	129378	66537	45590	35117
34	15,258	638597	320235	214114	161054	129217	65545	33709	23097	17791
Dose (Gy)	Cancer Cell No.	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	323524	162236	108474	81592	65464	33206	17077	11701	9013

38	3,814	163903	82191	54954	41336	33165	16822	8651	5928	4566
40	1,907	83036	41639	27841	20941	16802	8522	4383	3003	2313
42	953	42067	21095	14104	10609	8512	4317	2220	1521	1171
44	476	21312	10687	7145	5374	4312	2187	1124	770	593
46	238	10797	5414	3620	2723	2184	1108	569	390	300
48	119	5469	2743	1834	1379	1106	561	288	197	152
50	59	2771	1389	929	698	560	284	146	100	77
52	29	1403	704	470	354	284	144	74	50	39
54	15	711	356	238	179	143	73	37	25	19
56	7	360	180	120	90	72	36	19	13	10
58	4	182	91	61	46	36	18	9	6	5
60	2	92	46	31	23	18	9	4	3	2
62	1	46	23	15	11	9	4	2	1	1
		S	S	S	S	S	S	S	S	F

W= represent the concentration of gold nanoparticles (g), S= single shot, F= fractionation

Table 2. Number of destroyed cancer cells by dose fractionation when photon energy 6 MeV, flux 10^{15} (photon $cm^{-2}s^{-1}$), irradiation time 1200 s. concentrations of gold nanoparticles (0.004g to 5 g).

Dose(Gy)	Cancer Cell No.	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	775708951	437585094	268523165	212169186	183992201	167086009
4	500,000,000	392987333	221688042	136038397	107488514	93213575	84648611
6	250,000,000	199094059	112310928	68919363	54455507	47223580	42884424
8	125,000,000	100864432	56898624	34915720	27588085	23924268	21725977
10	62,500,000	51099635	28825809	17688897	13976592	12120440	11006749
12	31,250,000	25887943	14603644	8961495	7080779	6140421	5576206
14	15,625,000	13115271	7398454	4540046	3587243	3110841	2825000
16	7,823,500	6644419	3748182	2300064	1817358	1576005	1431193
18	3,906,250	3366175	1898893	1165251	920704	798431	725066
20	1,953,125	1705361	962011	590336	466444	404498	367331
22	976,562	863965	487371	299074	236308	204925	186096
24	488,281	437699	246910	151516	119718	103818	94279
26	244,140	221745	125089	76760	60651	52596	47763
28	122,070	112340	63372	38888	30726	26646	24197
30	61,035	56913	32105	19701	15566	13499	12259
32	30,517	28833	16265	9981	7886	6839	6210
34	15,258	14607	8240	5056	3995	3464	3146
Dose(Gy)	Cancer Cell No.	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	7400	4174	2561	2024	1755	1594
38	3,814	3749	2114	1297	1025	889	807
40	1,907	1899	1071	657	519	450	409
42	953	962	542	333	263	228	207
44	476	487	275	168	133	115	105
46	238	246	139	85	67	58	53
48	119	125	70	43	34	29	26
50	59	63	35	21	17	15	13
52	29	32	18	11	8	7	6
54	15	16	9	5	4	3	3
56	7	8	4	2	2	1	1
58	4	4	2	1	1	0.9	0.8
60	2	2	1	0.7	0.5	0.5	0.4
62	1	1	0.6	0.3	0.2	0.2	0.2
	F	F	F	F	F	F	F

3. Discussion

The results were showed increasing in number of destroyed cancer cells due to existence of gold nanoparticles in cancer cells with high concentration. These results were agreement with literatures (Halperin *et al.* 2008; Butterworth *et al.* 2010, Heuvel *et al.* 2010; Pissuwan *et al.* 2008). Gold nanoparticles (AuNPs) have biocompatibility and ability to increase dose deposited in tissue because of their high mass energy absorption coefficient, which caused breaks in DNA (Conde *et al.* 2012; McMahon *et al.* 2011). Results have improvement in the treatment effects on cancer cells. Maximum damage noted in concentrations (0.001, 0.002, 0.003, 0.004, 0.005) and then (0.01, 0.02, 0.03, 0.04, 0.05) as shown in Figures (1, 2, and 3), because nanoparticles formed in size to become capable to enter the cancer cells and make maximum damage inside the prostate cancer cells by single shot.

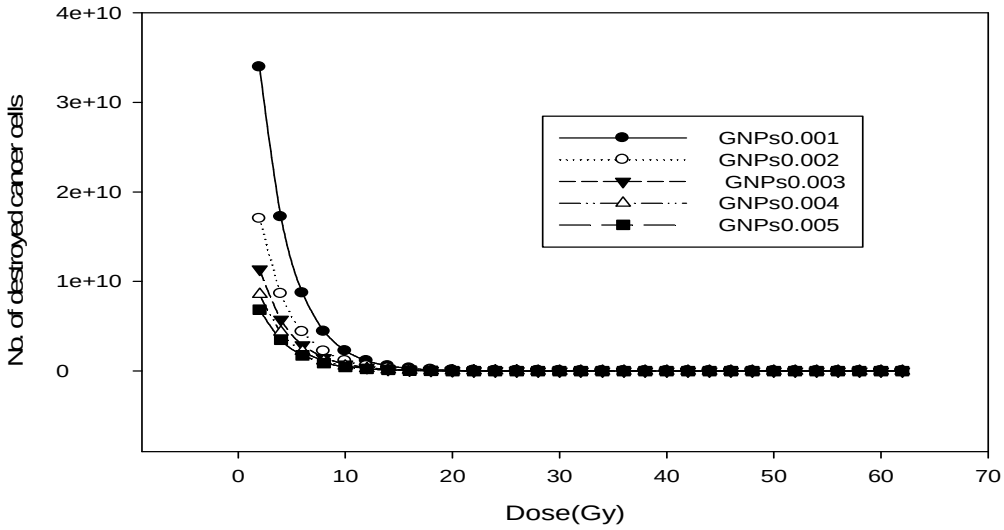

Figure 1. Number of destroyed cancer cells by dose fractionation when photon energy 6 MeV and gold nanoparticles concentrations (0.001 g to 0.005 g).

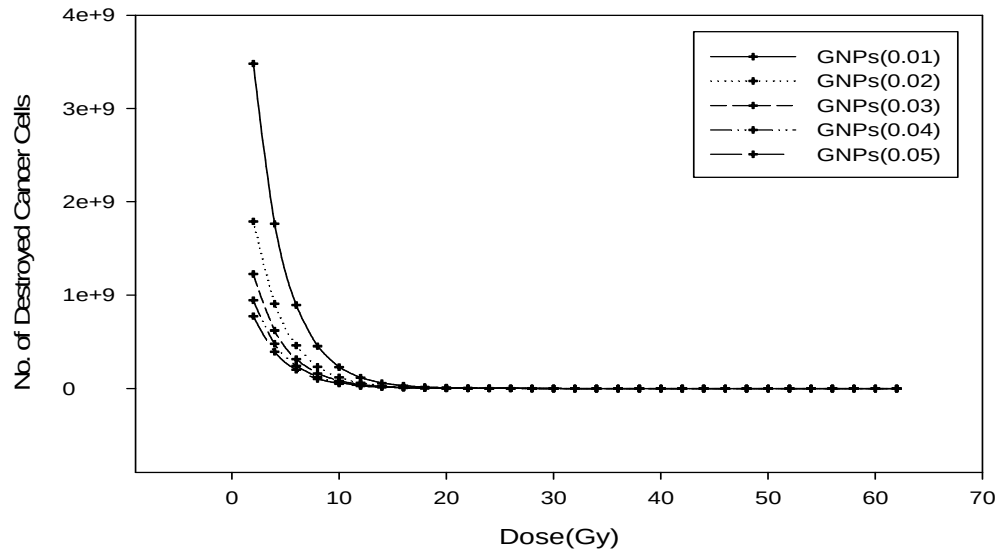

Figure 2. Number of destroyed cancer cells by dose fractionation when photon energy 6 MeV and gold nanoparticles concentrations (0.01 g to 0.05 g).

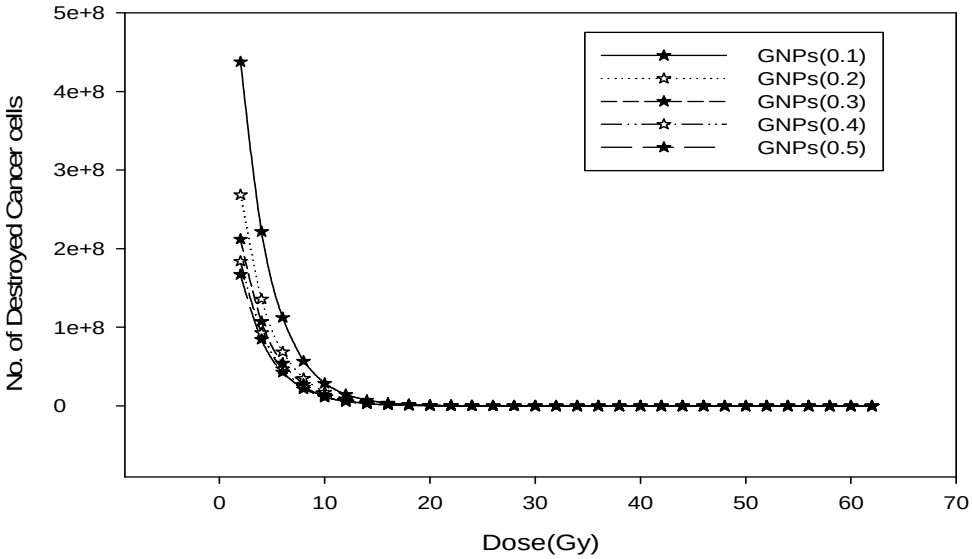

Figure 3. Number of destroyed cancer cells by dose fractionation when photon energy 6 MeV and gold nanoparticles concentrations (0.1 g to 0.5 g).

4. Conclusions

This work developed a method for enhancing the treatment of prostate cancer by using gold nanoparticles with gamma photons. The results showed that gold nanoparticles (AuNPs) with high energy photons enhanced the radiotherapy, where increase the number of destroyed cancer cells (destroy large number from cancer cells in minimum dose that given for patient), the results can be arranged in three benefits using gold nano particles with high energy photons:

a. Compared to AuNPs localized a higher concentration of AuNPs in prostate cancer cells.
b. AuNPs increase the absorption of radiation in tissue. Thus, lower doses of radiation can be used, avoiding the risk of side effects.
c. Damage to the tissue, which it surrounding of the cancer is decreased because the concentrations of gold nanoparticles increase in cancer cells.

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