# Treatment of breast cancer by 6 MeV gamma photons with Gold nanoparticles

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**1-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 (6MeV.) 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.

## معالجة سرطان الثدي بفوتونات كاما ذات طاقة 6 ميكاالكترون فولت مع جسيمات الذهب النانوية

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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 6 ميكاالكترون فولت. في هذا البحث سنركز على كيفية علاج سرطان الثدي بواسطة فوتونات أشعة كاما ذات الطاقة العالية (6ميكاالكترون 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 .

## 2-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]

## 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 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. [8]

The linear attenuation coefficient (μ) relate with probability for pair production interaction ( cross section σ ,in unit $cm^2$ or barn ,1barn=$10^{-24}$ $cm^2$) by the following relation:[9]

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

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 weight No.[10]

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

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

w: is the weight (gram).

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

$$\mu/\rho = N_A \sigma w/\rho A \quad \ldots\ldots\ldots\ldots (3)$$

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

From eq.3 we get

$$\sigma = \frac{(\mu/\rho)\,\rho A}{N A\ w} \quad \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

the equation of irradiation by photons is given by

$$\mathbf{N = \phi\, t\, No\, \sigma} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (5)$$

N: The number of cells remains after irradiation.

$\phi$: is the flux of particles (particle/ $cm^2$.sec.) the number of particles per unit time per unit solid angle.

t: is the time of exposure to radiation(second ).

$N_o$: is the number of cells cancer per unit volume (cell/$cm^3$). [8], [11], [12]

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

$$\mathbf{N = \phi\, t\ N_o\ \sigma} \quad \ldots\ldots\ldots\ldots\ldots\ldots (6)$$

By substitute eq.4 in eq.6 we get the final eq. for irradiation

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

**3-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) [13] and The National Institute of Standards and Technology (NIST1998), [14] and encyclopedia of medical devices and instrumentation, [15].

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. [16]

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 6MeV. The flux was $10^{18}$ (photon/$cm^2$.s) and time of irradiation was 1200 sec.(20 min.). The results were in agreement with those of fractionation in radiotherapy.[16]

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. [17]

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 6MeV. , 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][18][19][20][21][22][23]

Table 1: Radiotherapy for breast cancer irradiatedby 6MeV 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 | 4895.4 |
| 40 | 2480 | 0.8167 | 2480.1731 |
| 42 | 1256 | 0.4138 | 256.4978 |
| 44 | 636 | 0.2096 | 636.5631 |
| 46 | 322 | 0.1062 | 322.4937 |
| 48 | 163 | 0.0538 | 163.3808 |
| 50 | 82 | 0.0273 | 82.7715 |
| 52 | 41 | 0.0138 | 41.9334 |
| 54 | 21 | 0.0070 | 21.2442 |
| 56 | 10 | 0.0035 | 10.7627 |
| 58 | 5 | 0.0018 | 5.4526 |
| 60 | 2 | 0.0009 | 2.7624 |
| 62 | 1.4 | 0.0005 | 1.3995 |

Table-2(A) : Number of destroyed cancer cells by dose fractionation when photon energy 6MeV.,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/$cm^3$,concetration of gold nanoparticles(0.001-0.3)g. where W: represent the concentration of gold nanoparticles in gram. , S.Sh. : Mean Single shot, F.: mean Fractionation

| Dose (Gy) | W=0.001g. | W=0.01g. | W=0.1g | W=0.002g. | W=0.02g. | W=0.2g. | W=0.003g | W=0.03g | W=0.3g |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 211441621505 | 21144508745 | 2114795913 | 105721002485 | 10572446105 | 1057589689 | 70480798880 | 7048425224 | 705187596 |
| 4 | 107119917581 | 10712167349 | 1071391537 | 53560055925 | 5356180809 | 535792903 | 35706770092 | 3570851962 | 357260016 |
| 6 | 54268770079 | 5426965965 | 542785154 | 27134434249 | 2713532192 | 271441787 | 18089656342 | 1809054268 | 180993993 |
| 8 | 27493480880 | 2749393155 | 274984180 | 13746765370 | 1374721508 | 137517020 | 9164527223 | 916497626 | 91694632 |
| 10 | 13928664493 | 1392889281 | 139311657 | 6964344877 | 696457270 | 69668459 | 4642905185 | 464313267 | 46454058 |
| 12 | 7056498062 | 705661373 | 70577652 | 3528255430 | 352837085 | 35295224 | 2352174643 | 235228989 | 23534415 |
| 14 | 3574941799 | 357500040 | 35755837 | 1787474141 | 178753261 | 17881160 | 1191651635 | 119171002 | 11922934 |
| 16 | 1811126249 | 181115593 | 18114514 | 905564767 | 90559439 | 9058899 | 603710963 | 60374054 | 6040361 |
| 18 | 917547326 | 91756236 | 9177120 | 458774495 | 45878950 | 4589392 | 305850230 | 30586521 | 3060149 |
| 20 | 464845063 | 46485268 | 4649285 | 232422953 | 23243055 | 2325064 | 154948922 | 15495651 | 1550323 |
| 22 | 235498406 | 23550226 | 2355406 | 117749416 | 11775326 | 1177917 | 78499756. | 7850360 | 785420 |
| 24 | 119307493 | 11930944 | 1193289 | 59653854 | 5965580 | 596752 | 39769310 | 3977125 | 397907 |
| 26 | 60443203 | 6044419 | 604540 | 30221656 | 3022264 | 302325 | 20147808 | 2014879 | 201586 |
| 28 | 30621553 | 3062205 | 306270 | 15310804 | 1531130 | 153163 | 10207221 | 1020772 | 102127 |
| 30 | 15513399 | 1551365 | 155161 | 7756713 | 775696 | 77594 | 5171152 | 517140 | 51739 |
| 32 | 7859351 | 785948 | 78607 | 3929682 | 392981 | 39310 | 2619793 | 261992 | 26212 |
| 34 | 3981681 | 398174 | 39823 | 1990844 | 199090 | 19915 | 1327231 | 132729 | 13279 |
| 36 | 2017187 | 201722 | 20175 | 1008595 | 100862 | 10089 | 672398 | 67243 | 6727 |
| 38 | 1021941 | 102195 | 10221 | 510971 | 51098 | 5111 | 340648 | 34066 | 3408 |
| 40 | 517732 | 51774 | 5178 | 258866 | 25887 | 2589 | 172578 | 17258 | 1726 |
| 42 | 262292 | 26229 | 2623 | 131146 | 13115 | 1311 | 87431 | 8743 | 874 |
| 44 | 132881 | 13288 | 1329 | 66440 | 6644 | 664 | 44294 | 4429 | 443 |
| 46 | 67320 | 6732 | 673 | 33660 | 3366 | 336 | 22440 | 2244 | 224 |
| 48 | 34105 | 3410 | 341` | 17052 | 1705 | 170 | 11368 | 1136 | 113 |

| Dose (Gy) | W=0.001g. | W=0.01g. | W=0.1g | W=0.002g. | W=0.02g. | W=0.2g. | W=0.003g | W=0.03g | W=0.3g |
|---|---|---|---|---|---|---|---|---|---|
| 50 | 17278 | 1727 | 172 | 8639 | 863 | 86 | 5759 | 575 | 57 |
| 52 | 8753 | 875 | 87 | 4376 | 437 | 43 | 2917 | 291 | 29 |
| 54 | 4434 | 443 | 44 | 2217 | 221 | 22 | 1478 | 147 | 14 |
| 56 | 2246 | 224 | 22 | 1123 | 112 | 11 | 748 | 74 | 7 |
| 58 | 1138 | 113 | 11 | 569 | 56 | 5 | 379 | 37 | 3 |
| 60 | 576 | 57 | 5 | 288 | 28 | 2 | 192 | 19 | 2 |
| 62 | 292 | 29 | 3 | 146 | 14 | 1 | 97 | 9 | 1 |
| | S.Sh. | S.Sh. | S.Sh. | S.Sh. | S.Sh. | S.Sh. | S.Sh. | S.Sh. | F |

Table-2(B) : number of destroyed cancer cells by dose fractionation when photon energy 6MeV. ,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/$cm^3$,concetrations of gold nanoparticles(0.004-5)g. W: represent the concentration of gold nanoparticles in gram. , S.Sh. : Mean Single shot, F.: mean Fractionation

| Dose (Gy) | W=0.004g. | W=0.04g | W=0.4g | W=0.005g | W=0.05g | W=0.5g | W=1g | W=2g | W=3 | W=4 | W=5 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | 52860692974 | 5286414784 | 528986576 | 42288634026 | 4229208363 | 423265960 | 211824712 | 106104088 | 70863880 | 53243776 | 42671714 |
| 4 | 26780125097 | 2678187539 | 267993586 | 21424140428 | 2142588805 | 214433726 | 107313998 | 53754133 | 35900845 | 26974201 | 21618215 |
| 6 | 13567266335 | 1356815306 | 135770103 | 10853833510 | 1085471888 | 108635768 | 54367094 | 27232757 | 18187978 | 13665588 | 10952155 |
| 8 | 6873407616 | 687385684 | 68783441 | 5498736449 | 549918499 | 55036726 | 27543293 | 13796577 | 9214338 | 6923219 | 5548547 |
| 10 | 3482185068 | 348241265 | 34846859 | 2785753301 | 278598054 | 27882540 | 13953900 | 6989580 | 4668140 | 3507420 | 2810988 |
| 12 | 1764134113 | 176424941 | 17654011 | 1411309949 | 141142507 | 14125768 | 7069283 | 3541040 | 2364959 | 1776918 | 1424094 |
| 14 | 893740312 | 89379872 | 8943821 | 714993596 | 71505192. | 7156354 | 3581418 | 1793951 | 1198128 | 900217 | 721470 |
| 16 | 452784025 | 45281361 | 4531092 | 362227902 | 36225745 | 3625530 | 1814407 | 908846 | 606992 | 456065 | 365509 |
| 18 | 229388079 | 22940307 | 2295528 | 183510809 | 18352577 | 1836755 | 919209 | 460436 | 307512 | 231050 | 185173 |
| 20 | 116211898 | 11621949 | 1162953 | 92969693 | 9297727 | 930531 | 465687 | 233265 | 155791 | 117054 | 93811 |

| Dose (Gy) | W=0.004g. | W=0.04g | W=0.4g | W=0.005g | W=0.05g | W=0.5g | W=1g | W=2g | W=3 | W=4 | W=5 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 22 | 58874921 | 5887876 | 589172 | 47100026 | 4710386 | 471423 | 235925 | 118176 | 78926 | 59301 | 47526 |
| 24 | 29827035 | 2982898 | 298484 | 23861673 | 2386361 | 238830 | 119523 | 59870 | 39985 | 30043 | 24077 |
| 26 | 15110882 | 1511187 | 151217 | 12088729 | 1208971 | 120995 | 60552 | 30331 | 20257 | 15220 | 12198 |
| 28 | 7655430 | 765593 | 76609 | 6124355 | 612485 | 61298 | 30677 | 15366 | 10262 | 7710 | 6179 |
| 30 | 3878370 | 387862 | 33811 | 3102702 | 310295 | 31054 | 15541 | 7784 | 5199 | 3906 | 3130 |
| 32 | 1964848 | 196497 | 19662 | 1571881 | 157201 | 15732 | 7873 | 3943 | 2634 | 1979 | 1586 |
| 34 | 995425 | 99549 | 9961 | 796342 | 79640 | 7970 | 3988 | 1998 | 1334 | 1002 | 803 |
| 36 | 504299 | 50433 | 5046 | 403440 | 40347 | 4038 | 2020 | 1012 | 676 | 507 | 407 |
| 38 | 255486 | 25550 | 2556 | 204389 | 20440 | 2045 | 1023 | 512 | 342 | 257 | 206 |
| 40 | 129433 | 12944 | 1295 | 103547 | 10355 | 1036 | 518 | 259 | 173 | 130 | 104 |
| 42 | 65573 | 6557 | 656 | 52458 | 5246 | 525 | 262 | 131 | 87 | 66 | 52 |
| 44 | 33220 | 3322 | 332 | 26576 | 2657 | 266 | 133 | 66 | 44 | 33 | 26 |
| 46 | 16830 | 1683 | 168 | 13464 | 1346 | 134 | 67 | 33 | 22 | 17 | 13 |
| 48 | 8526 | 852 | 85 | 6821 | 682 | 68 | 34 | 17 | 11 | 8 | 7 |
| 50 | 4319 | 431 | 43 | 3455 | 345 | 34 | 17 | 8 | 6 | 4 | 3 |
| 52 | 2188 | 218 | 21 | 1750 | 175 | 17 | 9 | 4 | 3 | 2.2 | 2 |
| 54 | 1108 | 110 | 11 | 886 | 88 | 9 | 4 | 2 | 1.4 | 1.1 | 0.8 |
| 56 | 561 | 56 | 6 | 449 | 44 | 4 | 2 | 1 | 0.7 | 0.6 | 0.4 |
| 58 | 284 | 28 | 3 | 227 | 22 | 2 | 1 | 0.5 | 0.4 | 0.3 | 0.2 |
| 60 | 144 | 14 | 2 | 115 | 11 | 1 | 0.5 | 0.2 | 0.19 | 0.15 | 0.1 |
| 62 | 73 | 7 | 1 | 58 | 5 | 0.5 | 0.2 | 0.1 | 0.09 | 0.07 | 0.05 |
| | S.Sh. | S.Sh. | F | S.Sh. | S.Sh. | F | F | F | F | F | F |

Note: 1- the numbers inside table cells represent numbers of destroyed cancer cells.

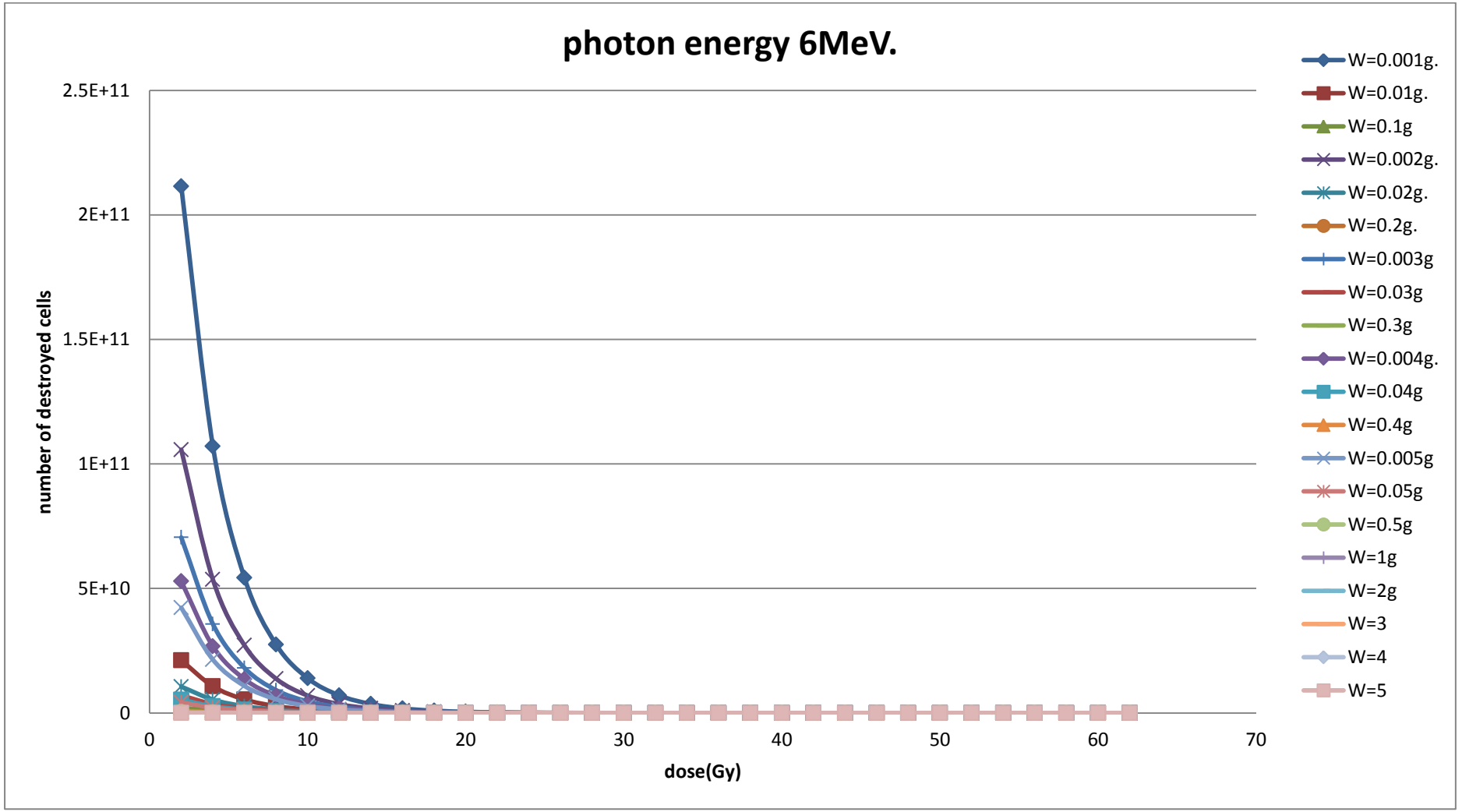


Fig.1: number of destroyed cancer cells by dose fractionation when photon energy 6MeV and gold nanoparticles concentrations (0.001-5) g.

## 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[24] .Gold nanoparticles (GNPs) have biocompatibility and ability to increase dose deposited because of their high mass energy absorption coefficient.[25] , 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 photons of high energy (6MeV.) 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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