Investigation of Gold Nanoparticles Effects in Radiation Therapy of Cancer: A Systematic Review

Hossein Khosravi[1] iD, Amin Doosti-Irani[2] iD, Hamid Bouraghi[3] iD, Safoora Nikzad[4*] iD

1. Dept. of Radiology, Faculty of Allied Medical Sciences, Hamadan University of Medical Sciences, Hamadan, Iran
2. Dept. of Epidemiology, Hamadan University of Medical Sciences, Iran
3. Dept. of Health Information Technology, Faculty of Allied Medical Sciences, Hamadan University of Medical Sciences, Hamadan, Iran
4. Dept. of Medical Physics, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

Article Info

Corresponding Information:
Safoora, Nikzad,
Dept. of Medical Physics, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
E-Mail: s.nikzad@umsha.ac.ir

ABSTRACT

Background & Objective: In recent years, the use of nanoparticles (NPs), especially gold nanoparticles (GNPs) in radiotherapy, has been repeatedly studied by in-vitro, in-vivo experiments, and Monte Carlo simulation. Some studies declare that specific absorption of GNPs (with a higher atomic number) by cancerous cells increases radiations' lethal effect compared to normal cells. This review article aimed to investigate the radiosensitizing effect of GNPs in cancer radiotherapy.

Materials & Methods: Research databases such as Web of Science, PubMed, and Scopus were examined from December 2019. All Gold Nanoparticles Radiation Therapy (GNRT) articles that studied the radiosensitization of gold nanoparticles in radiotherapy were involved in the assessment. Among 706 chosen articles, 52 documents were included in this investigation.

Results: The results of all these studies indicate that an increase in tumor mortality happens due to higher radiation absorption by nanoparticles entering the tumor; however, the relationship between the interaction of radiant energy and the size of gold nanoparticles is controversial.

Conclusion: This review article will discuss recent advances in the development of gold-based NPs to improve radiotherapy.

Keywords: Gold Nanoparticle, Radiotherapy, Radio sensitization, Cancer

Introduction

Nanoparticles are particles with a dimension of 1 to 100 nm (1, 2). Medications that can better penetrate the cells have been proposed for diagnosis and targeted treatment of cancer by nanomedicine. The distribution of nanoparticles is affected by various parameters, including their size and ability to inactivate cancer cells (3, 4). In radiation therapy, ionizing radiation such as high-energy photons and particles are widely used to treat cancerous tumors in solid form. Unfortunately, ionizing radiation cannot distinguish cancer cells from healthy cells (5, 6); therefore, normal tissues are damaged by radiation therapy used to eradicate cancer cells. The main purpose of using nanoparticles in cancer treatment is to enhance the outcome of radiotherapy by increasing the lethality of radiation in tumors and reducing it for healthy cells due to the accumulation of nanoparticles in the tumor compared to healthy tissues (7, 8). Among the various nanoparticles, most preclinical studies have been performed on gold nanoparticles with distinctive specifications such as tiny size, desirable biological adaptability and little toxicity (9, 10). These characteristics establish gold nanoparticles for use in various medical applications such as biosensors, drug delivery, chemotherapy, and radiation therapy (11, 12).

Hainfeld et al. (13) investigated the toxicity of GNP on breast cancer cells in mice in experimental training. The first group received GNP before irradiation of 250 kVp photon. The second group received sole radiation, and the last group received merely GNP. Results show that the one-year survival rate was 86%, 20%, and 0% in the first, second and third groups, respectively (13).

In another study by Chithrani et al., the accumulation of GNP in cancer cells and transplanted tumors of mice were studied, and the treatment ratio after 25MeV of 6MeV electron beam was investigated. Results showed that the amount of GNP accumulated in cells significantly affected mortality due to radiation (with a value of P = 0.02). This rate was less than 0.05 in mouse tumors (P<0.05). However, Chang et al. Obtained a more significant effect using GNP with a mean dimensional of 13 nm compared to the former study (14, 15).

Recent progress in synthesizing and creating multifunctional nanoparticle platforms has prepared great opportunities and benefits for targeted gene delivery. Using bioinformatics methods in cancer therapy, such as evaluating the molecular interactions of plant-derived inhibitors in contrast to E6AP, p53, and c-Myc has improved the usage of nanoparticles in cancer treatment **(3, 4)**.

Several studies have been published regarding using gold nanoparticles in radiation therapy. The controversial results concerning GNP radiosensitization could be emanated from the differences in GNP shape, scale, origin and type of cell lines, energy and type of radiation. Therefore, the purpose of this review article was to consider the gold nanoparticles' radiosensitization in cancer radiation therapy.

Materials and Methods

A current systematic review was done according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (16). All GNRT studies that investigated the radiosensitization of gold nanoparticles in radiotherapy were included in the article. Moreover, review articles, editorials, and letters to the editor were excluded.

Eligibility Criteria

Original peer-reviewed articles published in the English language on the application of GNPs in cancer (as well as in-vitro, cell, cancer, radiation therapy, radiosensitization, and neoplasms) were evaluated. Articles that used NPs without any gold component were omitted. The last finding was assessed in the case of numerous studies derived from the same institution.

Data Origin and Examination

A wide literature search was performed up to December 2019 using Web of Science, PubMed and Scopus databases. The MeSH search terms used were "gold nano*" and "*radiosensitization*" or "*radiation therapy*" or "radiotherapy" and "cancer" and "neoplasms" and "*invitro."*

Article and Data Assortment Process

In the first step, the title and abstract of chosen articles were independently scanned by two authors (HK, SN). In the case of disagreement between authors in selecting the articles, the problem was resolved using the third author's judgment (ADI). The next step was considering the chosen articles based on the eligibility criteria. Finally, data such as: **(1)** the name of the first Authors, **(2)** date of Publication, **(3)** Site of Study, **(4)** Type of Study, **(5)** used NP Size, **(6)** NP size in intervention group, **(7)** NP size in the control group and the **(8)** Effect of NP Size extracted from the chosen articles by two authors (HK, SN). There was a suitable agreement between the two authors, and minor disagreements were discussed between all authors until a full consensus was reached on the studies included in the study.

Data Items

Microsoft Excel software was used to extract and manage the data of the chosen studies. Other data extracted from the studies: Type of Study, Sample size (Sample size in intervention and control group), type of GNP, shape, average size, Effect size (Radiosensitivity, Dose Enhancement Factor, rate of mortality and percentage of remaining cells).

Results

OFT results

Initial examines by of the mentioned MeSH terms discovered 706 articles. At first, the titles of the articles were reviewed to reach higher quality and appropriate articles. Duplicate articles and articles whose titles were not related to the dimensions of research effectiveness were removed. After checking the eligibility criteria, 52 articles regarding the radiosensitization of gold nanoparticles in radiotherapy were included in the review (Figure 1).

GNPs used as cancer radiation sensitizers often included a combination of conjugated GNPs with silica, PEG, chitosan and iron core. Although different shapes of NPs have been used, rods and sphere shapes were more common. The identifiable characteristics of GNPs used in articles are presented in Tables 1, 2, and 3.

Table 1 represents the rate of increase in radiation sensitization using gold nanoparticles in recent research. The mean value of rising in radiosensitivity for these studies was SER = 1.59 ± 0.30.

Table 2 shows the rate of increase in the absorption dose factor in the studies conducted using gold nanoparticles in recent years. The mean value of the increase in absorption dose factor for these studies was DEF[1] = 1.45 ± 0.39.

Table 3 indicates the mortality rate and percentage of cells remaining due to radiation using gold nanoparticles in recent years. The mean mortality for these studies was 42.67 ± 24.78. It should be noted that this table examines the various parameters related to the tumor, but the differences in the results in some studies are very large.
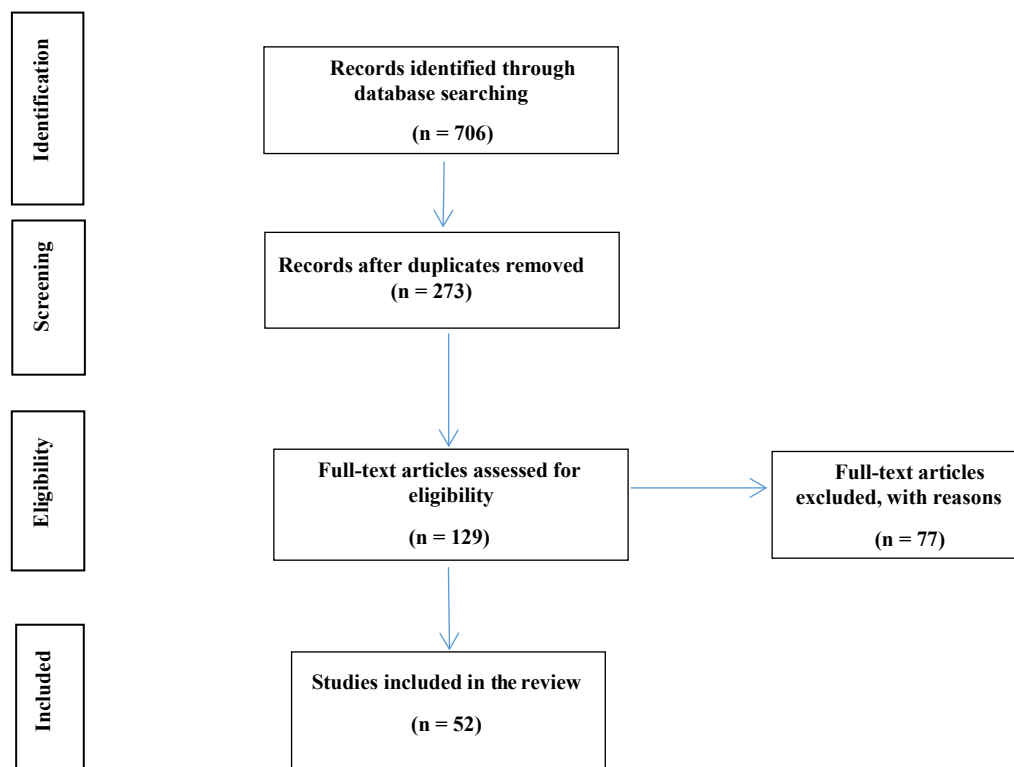
---

[1]Dose Enhancement Factor

Figure 1. PRISMA Flowchart: Flowchart using syntax appropriate search and identification step to include in the Review

Table 1. The rate of increase in radiosensitivity in research using gold nanoparticles

ID	Author	Study	Shape	Average Size (nm)	Sample Size	Sample size in intervention group	Sample size in control group	Effect size
1	Zhu, C. D. (17)	E	Sp	20	3000 cell/well	3000 cell/well	3000 cell/well	SER =1.96
2	Zhu, C. (18)	E	Sp	20	3000 cell/well	3000 cell/well	3000 cell/well	SER=2
3	Zheng Q. (19)	E	Sp	100	4000 cell/well	4000 cell/well	4000 cell/well	SER=1.769
4	Zhao, N. (20)	E	Rod	20	5000 cell/well	5000 cell/well	5000 cell/well	SER=1.52
5	Zhang, Y. (21)	E	Sp	32	mice	mice	mice	SER=1.73
6	Zhang, X. (22)	E	Sp	4.8-46.6	1000000 cell/well	1000000 cell/well	1000000 cell/well	SER=2.07(For GNP: 46.6 nm)
7	Zhang, X. (23)	E	Sp	6.3	1000000 cell/well	1000000 cell/well	1000000 cell/well	SER=1.59
8	Zabihzadeh, M. (24)	E	Sp	24	1000000 cell/well	1000000 cell/well	1000000 cell/well	SER=1.25
9	Wang, C. (25)	E	Sp	16 & 49	4000 cell/well	4000 cell/well	4000 cell/well	SER=1.86 (For GNP: 49nm) SER=1.49 (FOR GNP:16nm)
10	Sung, W. (26)	S	Sp	2,15,20 & 5	--			SER=1.2(For GNP: 50nm)
11	Shi, M. (27)	E	Sp	4.8	cell	cell	cell	SER=1.48 (For Dose=1 Gy) SER=1.69 (For Dose=4 Gy)
12	Nicol, J. R. (28)	E	Sp	13	30000 cell/well	30000 cell/well	30000 cell/well	SER=1.25 (NPs alone) SER=3.19 (For NPs+RT)
13	Mehrnia, S. S. (29)	E	Sp	10	Cell	Cell	Cell	SER=1.43 AND 1.40 (FOR TWO CELL LINES)
14	McMahon, S. J. (30)	S	Sp	2				SER = 1.29 and 1.16 (For E=6 MeV and 15 MeV)
15	Ma, N. N. (31)	E	Sp & Rod	20	cell	cell	cell	SER: 1.62, 1.37, and 1.21 (For different shapes of gold nanoparticles)
16	Ma, N. (32)	E	Sp & Rod	50	cell	cell	cell	SER=2.30
17	Ab Rashid, R. (33)	E	Sp	1.9	2000 cells (HeLa)	1000 cells per well	1000 cells per well	SER=1.78
18	Al Zaki, A. (34)	E	Sp	1.9	16 mice	8 mice	8 mice	SER=1.7
19	Enferadi, M. (35)	E	Sp	1.8	10000 ALTS1C1, AML12, and RAW cells	5000	5000	SER =1.66
20	Jain, S. (36)	E	Sp	1.9	150000 MDA-MB-231 breast cancer cells	75000	75000	SER=1.41

E: Experimental – **S**: Simulation - Sp: Spherical

Table 2. The dose enhancement factor in research using gold nanoparticles

ID	Author	Shape	Average Size (nm)	Study	Sample Size	Sample size in intervention group	Sample size in control group	Effect size
1	Taggart, L.E. (37)	Spherical	1.9 nm	Experimental	100000 cell/well	100000 cell/well	100000 cell/well	DEF=1.52
2	Khosravi,H. (38)	Spherical	15, 50, and 100 nm	Simulation		-		DEF=2.66 (For E=50 keV) DEF=1.10 (For E=6 MeV)
3	Rezaee, Z. (39)	Spherical	15 nm	Experimental	cell	cell	cell	DEF=1.17-2.89 (For various times)
4	Rahman, W. N. (40)	Spherical	1.9 nm	Experimental	50000cell	50000cell	50000cell	DEF=1.14-1.74 (For different energies)
5	Rahman, W. N. (41)	Spherical	1.9 nm	Experimental	10000 cell/well	10000 cell/well	10000 cell/well	DEF=4 (FOR E=6 MeV)
6	Mousavi, M. (42)	Spherical	24.7±3.6 nm	Experimental	Cell	Cell	Cell	DEF=1.22
7	Cui, L. (43)	Spherical	5.81 ± 1.53 nm	Experimental	2000000 MDA-MB-231 breast cancer cells	1000000	1000000	DEF=1.39
8	Amato, E. (44)	Spherical	50 μm	Simulation		-		DEF=1.6- 6.5
9	Cui, L. (45)	Spherical	2.7 nm	Experimental	2000000 MDA-MB-231 breast cancer cells	1000000	1000000	DEF = 1.39
10	Khosravi,H. (46)	Spherical	15 nm	Experimental/ Simulation	MAGIC-f polymer gel	gel+gnp	gel	DEF=1.12
11	Her, S. (47)	Spherical	15 nm	Experimental	2000000 Human breast carcinoma cells	1000000	1000000	DEF=1.55
12	Smith, C. L. (48)	Spherical	5 nm	Experimental	cell	cell	cell	DEF= 10%
13	Roeske, J. C. (49)	Spherical	1.9 nm	Simulation	Simulation		-	DEF=1.01
14	Chithrani, D. B. (50)	Spherical	14–74 nm	Experimental	2000000 HeLa cells	1000000	1000000	DEF=1.43
15	Geng, F. (51)	Spherical	14.37 ± 2.49 nm	Experimental	4000 SK-OV-3 cell	2000	2000	DEF=30.48
16	Brivio, D. (52)	Spherical	20 nm	Simulation		-		DEF=1.97
17	Gadoue, S. M. (53)	Spherical	100 nm	Simulation		-		DEF=%64
18	Ghorbani, M. (54)	Spherical	50 nm	Simulation		-		DEF=1.79
19	Koger, B. (55)	Spherical	10, 20, and 50 nm	Simulation		-		DEF=34% (FOR GNP:50 nm)

Table 3. Mortality rate and percentage of cells remaining due to radiation using gold nanoparticles

ID	Author	Shape	Average Size (nm)	Study	Sample Size	Sample size in intervention group	Sample size in control group	Effect size
1	Zhang, X. (56)	Spherical	15 nm	Experimental	3000 cell/well	300 cell/well	300 cell/well	Death=45.97%
2	Zhang, A. (57)	Spherical	58.14 ± 4 nm	Experimental	5000 cell/well	5000 cell/well	5000 cell/well	Death in Control=9.9% Death in Treated =10.85%
3	Hainfeld, J. F. (58)	Spherical	1.9 nm	Experimental	2000000 EMT-6 mouse	1000000	1000000	Some 86% long-term (>1 year) cures of EMT-6 mouse mammary
4	Zhang, Z. (59)	Spherical	10 nm	Experimental	5000 cell/well	5000 cell/well	5000 cell/well	Viability=4%
5	Vieira, L. (60)	Spherical	18±4 nm	Experimental	100000 cell/well	100000 cell/well	100000 cell/well	Cell Viability=62%
6	Tentor, F. R. (61)	Spherical	20 nm	Experimental	250000 cell/well	250000 cell/well	250000 cell/well	Viability in Control=94% Viability in Treated Group=67%
7	Roa, W. (62)	Spherical	15 nm	Experimental	cell	cell	cell	Cell Survival = 36%
8	Movahedi, M. M. (63)	Spherical	58 nm	Experimental	10000cell/well	10000cell/well	10000cell/well	Cell Viability in Control Group =86% Cell Viability in Treated RT+NP=69%
9	Zavidij, O. (64)	Not mentioned	Not mentioned	Experimental	mice	mice	mice	SF= 30% In Treated SF = 0% In Control
10	Miladi, I. (65)	Spherical	Not mentioned	Experimental	mice	mice	mice	Survival in Control Group =28 day Survival by RT + NPs=117 day (Improvement: 50%)
11	Atkinson, R. L. (66)	nanoshell	-	Experimental	10 million cells/ml	5 million cells/ml	5 million cells/ml	Survival Fraction=1/3
12	Chattopadhyay, N. (67)	Spherical	30 nm	Experimental	100000 MDA-MB-361 human breast cancer cells	500000	500000	Death=46%
13	Liu, C. J. (68)	Spherical	6.1 ± 1.9	Experimental	(B16) cell lines	5000	5000	Death≅45%

Discussion

This study investigated the sensitizing effect of gold nanoparticles in cancer radiotherapy around three main axes: the rate of radiation sensitivity, the rate of absorption dose factor, the rate of mortality, and the percentage of remaining cells.

Using gold nanoparticles as a radiation sensitizer in irradiation of cancer cells led to an increase in therapeutic efficiency up to 59% at low photon energies by using orthovoltage sources. The results of using these nanoparticles showed that reducing the prescribed dose by about 60% could have a similar lethal effect in cancer cells. The cause of radiation sensitization of gold nanoparticles is the high atomic number of gold relative to the atomic number of biological elements present in the tissue or cells. Many studies confirm the irradiative sensitivity of gold nanoparticles. As the study conditions vary greatly from study to study, the sensitivities reported in such studies are different (17-36, 69-72).

With the use of gold nanoparticles, the radiation absorption dose was increased by an average of 45%. In general, the difference in the rate of increase in absorbed dose in various studies can be attributed to differences in the concentration of GNPs, the type of coat of GNPs, and the type of investigated cell line or a combination of these factors. It is clear that by increasing the concentration of GNPs, a higher dose coefficient can be achieved. In using larger NPs to increase the dose, a compromise must be made between entering and accumulating more NPs inside the cells (37-55, 69).

The mortality rate and percentage of cancerous cells remaining after radiotherapy using GNPs have been studied in various experimental studies over the past years. The average rate of mortality in these studies was about 42%. Results of studies, which have investigated the toxicity of GNPS, show that these NPs can reduce viability and cancerous cell growth. However, the toxicity of GNPs depends on the concentration, size and shape of NPs, the incubation period, and the investigated cell line type. In addition, comparisons were made between different beams at a given incubation time. Results showed that the X-ray peak at 180 kV could be more effective than the other energies, although this variation was not statistically significant. The theoretical fact can explain this increase in the absorption dose coefficient of 180 kV X-ray that photons with energies about 50 kV have a higher mass-energy absorption coefficient in gold than water or water equivalent (56-69).

Also, recent studies have concluded that gold nanoparticles in combination with chemotherapy medicines such as Bleomycin (70) or immunomodulation (71) can enhance the treatment results and increase the Plasmid DNA damages due to MV radiations (71).

Conclusion

The results of all studies in this field confirm the increase in the absorbed dose of the tumor in radiation therapy due to the replacement of gold nanoparticles in the tumor. However, the results of the interaction of photon energy with the magnitude of GNPs are still controversial. Monte Carlo simulation studies have investigated GNPs with 10 to 100 nm dimensions, while biological studies have studied dimensions up to 1.9 nm. Results of simulations show that the most effective parameters of NPs are larger dimensions, high molar concentrations, and low-energy X-ray or gamma photons that allow for higher dose escalation. This article aimed to answer some of the questions in this field. More and more extensive research in this regard is necessary to reach a global consensus and clinical application.

Conflict of Interest

None declared.

References

1. Dorsey JF, Sun L, Joh DY, et al. Gold nanoparticles in radiation research: potential applications for imaging and radiosensitization. Translat Cancer Res. 2013;2(4):280.

2. Hainfeld JF, Dilmanian FA, Zhong Z, Slatkin DN, Kalef-Ezra JA, Smilowitz HM. Gold nanoparticles enhance the radiation therapy of a murine squamous cell carcinoma. Physics Med Biol. 2010;55(11):3045. [DOI:10.1088/0031-9155/55/11/004] [PMID]

3. Gharbavi M, Johari B, Rismani E, Mousazadeh N, Taromchi AH, Sharafi A. NANOG decoy oligodeoxynucleotide-encapsulated niosomes nnanocarriers: A promising approach to suppress the metastatic properties of U87 human glioblastoma multiforme cells. ACS Chem Neurosci. 2020;11(24):4499-515. [DOI:10.1021/acschemneuro.0c00699] [PMID]

4. Moradi M, Abdolhosseini M, Zarrabi A. A review on application of nano-structures and nano-objects with high potential for managing different aspects

of bone malignances. Nano-Struct Nano-Object. 2019;19:100348.
[DOI:10.1016/j.nanoso.2019.100348]

5. Kim JK, Seo SJ, Kim HT, et al. Enhanced proton treatment in mouse tumors through proton irradiated nanoradiator effects on metallic nanoparticles. Physic Med Biol. 2012;57(24): 8309. [DOI:10.1088/0031-9155/57/24/8309] [PMID]

6. Kirkby C, Ghasroddashti E. Targeting mitochondria in cancer cells using gold nanoparticle-enhanced radiotherapy: A Monte Carlo study. Med Physic. 2015;42(2):1119-28. [DOI:10.1118/1.4906192] [PMID]

7. Misra R, Acharya S, Sahoo SK. Cancer nanotechnology: application of nanotechnology in cancer therapy. Drug Discover Today. 2010;15 (19-20):842-50. [DOI:10.1016/j.drudis.2010.08.006] [PMID]

8. Su XY, Liu PD, Wu H, Gu N. Enhancement of radiosensitization by metal-based nanoparticles in cancer radiation therapy. Cancer Biol Med. 2014;11(2):86.

9. Brun E, Sanche L, Sicard-Roselli C. Parameters governing gold nanoparticle X-ray radiosensitization of DNA in solution. Colloids Surf B Biointerfaces. 2009;72(1):128-34. [DOI:10.1016/j.colsurfb.2009.03.025] [PMID]

10. Huang YC, Yang YC, Yang KC, et al. Pegylated gold nanoparticles induce apoptosis in human chronic myeloid leukemia cells. BioMed Res Int. 2014;2014: 182353. [DOI:10.1155/2014/182353] [PMID] [PMCID]

11. King RB, McMahon SJ, Hyland WB, et al. An overview of current practice in external beam radiation oncology with consideration to potential benefits and challenges for nanotechnology. Cancer Nanotechnol. 2017;8(1):1-12. [PMCID] [DOI:10.1186/s12645-017-0027-z] [PMID]

12. Singh N. Nano-particulate technology: a promising technology in the field of cancer treatment therapies in recent scenario. Int J Recent Sci Res.2018; 9(3): 25078-82.

13. Hainfeld JF, Slatkin DN, Smilowitz HM. The use of gold nanoparticles to enhance radiotherapy in mice. Physic Med Biol. 2004;49(18):N309. [DOI:10.1088/0031-9155/49/18/N03] [PMID]

14. Chang MY, Shiau AL, Chen YH, Chang CJ, Chen HHW, Wu CL. Increased apoptotic potential and dose-enhancing effect of gold nanoparticles in combination with single-dose clinical electron beams on tumor-bearing mice. Cancer Sci. 2008;99(7):1479-84. [DOI:10.1111/j.1349-7006.2008.00827.x] [PMID]

15. Chithrani BD, Ghazani AA, Chan WC. Determining the size and shape dependence of gold nanoparticle uptake into mammalian cells. Nano Lett. 2006;6(4):662-8. [DOI:10.1021/nl052396o] [PMID]

16. McInnes MD, Moher D, Thombs BD, et al. Preferred reporting items for a systematic review and meta-analysis of diagnostic test accuracy studies: the PRISMA-DTA statement. JAMA. 2018;319(4):388-96. [DOI:10.1001/jama.2017.19163] [PMID]

17. Zhu CD, Zheng Q, Wang LX, et al. Synthesis of novel galactose functionalized gold nanoparticles and its radiosensitizing mechanism. J Nanobiotechnol. 2015;13:67. [PMCID] [DOI:10.1186/s12951-015-0129-x] [PMID]

18. Zhu C, Wang L, Cai Y, et al. Enhanced radiation effect on SMCC7721 cells through endoplasmic reticulum stress induced by C225-GNPs in vitro and in vivo. Oncol Lett. 2018;15(4):4221-8. [DOI:10.3892/ol.2018.7864] [PMID] [PMCID]

19. Zheng Q, Yang H, Wei J, Tong JL, Shu YQ. The role and mechanisms of nanoparticles to enhance radiosensitity in hepatocellular cell. Biomed Pharmacother. 2013;67(7):569-75. [DOI:10.1016/j.biopha.2013.04.003] [PMID]

20. Zhao N, Yang ZR, Li BX, et al. RGD-conjugated mesoporous silica-encapsulated gold nanorods enhance the sensitization of triple-negative breast cancer to megavoltage radiation therapy. Int J Nanomed. 2016;11:5595-610. [DOI:10.2147/IJN.S104034] [PMID] [PMCID]

21. Zhang Y, Huang F, Ren C, et al. Enhanced radiosensitization by gold nanoparticles with acid-triggered aggregation in cancer radiotherapy. Adv Sci. 2019;6(8):1801806. [DOI:10.1002/advs.201801806] [PMCID]

22. Zhang XD, Wu D, Shen X, et al. Size-dependent radiosensitization of PEG-coated gold nanoparticles for cancer radiation therapy. Biomaterials. 2012;33(27):6408-19. [DOI:10.1016/j.biomaterials.2012.05.047] [PMID]

23. Zhang X, Wang H, Coulter JA, Yang R. Octaarginine-modified gold nanoparticles enhance the radiosensitity of human colorectal cancer cell line LS180 to megavoltage radiation. Int J Nanomed. 2018;13:3541-52. [DOI:10.2147/IJN.S161157] [PMID] [PMCID]

24. Zabihzadeh M, Hoseini-Ghahfarokhi M, Bayati V, et al. Enhancement of radio-sensitivity of colorectal cancer cells by gold nanoparticles at 18 MV energy. Nanomed J. 2018;5(2):111-20.

25. Wang C, Jiang Y, Li X, Hu L. Thioglucose-bound gold nanoparticles increase the radiosensitivity of a triple-negative breast cancer cell line (MDA-

MB-231). Breast Cancer (Tokyo, Japan). 2015;22(4):413-20. [DOI:10.1007/s12282-013-0496-9] [PMID]

26. Sung W, Ye SJ, McNamara AL, et al. Dependence of gold nanoparticle radiosensitization on cell geometry. Nanoscale. 2017;9(18):5843-53. [DOI:10.1039/C7NR01024A] [PMID] [PMCID]

27. Shi M, Paquette B, Thippayamontri T, Gendron L, Guerin B, Sanche L. Increased radiosensitivity of colorectal tumors with intra-tumoral injection of low dose of gold nanoparticles. Int J Nanomed. 2016;11:5323-33. [DOI:10.2147/IJN.S97541] [PMID] [PMCID]

28. Nicol JR, Harrison E, O'Neill SM, Dixon D, McCarthy HO, Coulter JA. Unraveling the cell-type dependent radiosensitizing effects of gold through the development of a multifunctional gold nanoparticle. Nanomed-Nanotechnol Biol Med. 2018;14(2):439-49. [DOI:10.1016/j.nano.2017.11.019] [PMID]

29. Mehrnia SS, Hashemi B, Mowla SJ, Arbabi A. Enhancing the effect of 4MeV electron beam using gold nanoparticles in breast cancer cells. Phys Med. 2017;35:18-24. [DOI:10.1016/j.ejmp.2017.02.014] [PMID]

30. McMahon SJ, Hyland WB, Muir MF, et al. Nanodosimetric effects of gold nanoparticles in megavoltage radiation therapy. J Europ Soc Ther Radiol Oncol. 2011;100(3):412-6. [DOI:10.1016/j.radonc.2011.08.026] [PMID]

31. Ma NN, Jiang YW, Zhang XD, et al. Enhanced radiosensitization of gold nanospikes via hyperthermia in combined cancer radiation and photothermal therapy. Acs Appl Mater Interfaces. 2016;8(42):28480-94. [DOI:10.1021/acsami.6b10132] [PMID]

32. Ma NN, Wu FG, Zhang XD, et al. Shape-dependent radiosensitization effect of gold nanostructures in cancer radiotherapy: comparison of gold nanoparticles, nanospikes, and nanorods. Acs Appl Mater Interfaces. 2017;9(15):13037-48. [DOI:10.1021/acsami.7b01112] [PMID]

33. Ab Rashid R, Razak KA, Geso M, Abdullah R, Dollah N, Rahman WN. Radiobiological characterization of the radiosensitization effects by gold nanoparticles for megavoltage clinical radiotherapy beams. Bionanosci. 2018;8(3):713-22. [DOI:10.1007/s12668-018-0524-5]

34. Al Zaki A, Joh D, Cheng ZL, et al. Gold-loaded polymeric micelles for computed tomography-guided radiation therapy treatment and radiosensitization. Acs Nano. 2014;8(1):104-12. [DOI:10.1021/nn405701q] [PMID] [PMCID]

35. Enferadi M, Fu SY, Hong JH, Tung CJ, et al. Radiosensitization of ultrasmall GNP-PEG-cRGDfK in ALTS1C1 exposed to therapeutic

36. Jain S, Coulter JA, Hounsell AR, et al. Cell-specific radiosensitization by gold nanoparticles at megavoltage radiation energies. Int J Radiat Oncol, Biol, Physic. 2011;79(2):531-9. [PMCID] [DOI:10.1016/j.ijrobp.2010.08.044] [PMID]

37. Taggart LE, McMahon SJ, Butterworth KT, Currell FJ, Schettino G, Prise KM. Protein disulphide isomerase as a target for nanoparticle-mediated sensitisation of cancer cells to radiation. Nanotechnol. 2016;27(21):215101. [DOI:10.1088/0957-4484/27/21/215101] [PMID]

38. Khosravi H, Hashemi B, Mahdavi SR, Hejazi P. Target dose enhancement factor alterations related to interaction between the photon beam energy and gold nanoparticles' size in external radiotherapy: using Monte Carlo method. Koomesh. 2015:255-61.

39. Rezaee Z, Yadollahpour A, Bayati V, Dehbashi FN. Gold nanoparticles and electroporation impose both separate and synergistic radiosensitizing effects in HT-29 tumor cells: An in vitro study. Int J Nanomed. 2017;12:1431-9. [DOI:10.2147/IJN.S128996] [PMID] [PMCID]

40. Rahman WN, Corde S, Yagi N, Abdul Aziz SA, Annabell N, Geso M. Optimal energy for cell radiosensitivity enhancement by gold nanoparticles using synchrotron-based monoenergetic photon beams. Int J Nanomed. 2014;9(1):2459-67. [DOI:10.2147/IJN.S59471] [PMID] [PMCID]

41. Rahman WN, Bishara N, Ackerly T, et al. Enhancement of radiation effects by gold nanoparticles for superficial radiation therapy. Nanomedicine. 2009;5(2):136-42. [DOI:10.1016/j.nano.2009.01.014] [PMID]

42. Mousavi M, Nedaei HA, Khoei S, et al. Enhancement of radiosensitivity of melanoma cells by pegylated gold nanoparticles under irradiation of megavoltage electrons. Int J Radiat Biol. 2017;93(2):214-21. [DOI:10.1080/09553002.2017.1231944] [PMID]

43. Cui L, Her S, Dunne M, et al. Significant radiation enhancement effects by gold nanoparticles in combination with cisplatin in triple negative breast cancer cells and tumor xenografts. Radiat Res. 2017;187(2):147-60. [DOI:10.1667/RR14578.1] [PMID]

44. Amato E, Italiano A, Leotta S, Pergolizzi S, Torrisi L. Monte Carlo study of the dose enhancement effect of gold nanoparticles during X-ray therapies and evaluation of the anti-angiogenic effect on tumour capillary vessels. J X-ray Sci Technol.

2013;21(2):237-47. [DOI:10.3233/XST-130374] [PMID]

45. Cui L, Tse K, Zahedi P, et al. Hypoxia and cellular localization influence the radiosensitizing effect of gold nanoparticles (AuNPs) in breast cancer cells. Radiat Res. 2014;182(5):475-88. [DOI:10.1667/RR13642.1] [PMID]

46. Khosravi H, Ghazikhanlousani K, Rahimi A. Use of gold nanoparticles in MAGIC-f gels to 18 MeV photon enhancement. Nanomed J. 2019;6(1):67-73.

47. Her S, Cui L, Bristow RG, Allen C. Dual action enhancement of gold nanoparticle radiosensitization by pentamidine in triple negative breast cancer. Radiat Res. 2016;185 (5):549-62. [DOI:10.1667/RR14315.1] [PMID]

48. Smith CL, Ackerly T, Best SP, et al. Determination of dose enhancement caused by gold-nanoparticles irradiated with proton, X-rays (kV and MV) and electron beams, using alanine/EPR dosimeters. Radiat Measur. 2015;82: 122-8. [DOI:10.1016/j.radmeas.2015.09.008]

49. Roeske JC, Nunez L, Hoggarth M, Labay E, Weichselbaum RR. Characterization of the theorectical radiation dose enhancement from nanoparticles. Technol Cancer Res & Treat. 2007;6(5):395-401. [DOI:10.1177/153303460700600504] [PMID]

50. Chithrani DB, Jelveh S, Jalali F, et al. Gold nanoparticles as radiation sensitizers in cancer therapy. Radiation Res. 2010;173(6):719-28. [DOI:10.1667/RR1984.1] [PMID]

51. Geng F, Song K, Xing JZ, et al. Thio-glucose bound gold nanoparticles enhance radio-cytotoxic targeting of ovarian cancer. Nanotechnol. 2011;22(28):285101. [DOI:10.1088/0957-4484/22/28/285101] [PMID]

52. Brivio D, Zygmanski P, Arnoldussen M, et al. Kilovoltage radiosurgery with gold nanoparticles for neovascular age-related macular degeneration (AMD): a Monte Carlo evaluation. Phys Med Biol. 2015;60(24):9203-13. [DOI:10.1088/0031-9155/60/24/9203] [PMID] [PMCID]

53. Gadoue SM, Toomeh D. Radio-sensitization efficacy of gold nanoparticles in inhalational nanomedicine and the adverse effect of nano-detachment due to coating inactivation. Phys Med. 2019;60:7-13. [DOI:10.1016/j.ejmp.2019.02.013] [PMID]

54. Ghorbani M, Bakhshabadi M, Golshan A, Knaup C. Dose enhancement by various nanoparticles in prostate brachytherapy. Australas Phys Eng Sci Med. 2013;36(4):431-40. [DOI:10.1007/s13246-013-0231-z] [PMID]

55. Koger B, Kirkby C. Dosimetric effects of polyethylene glycol surface coatings on gold nanoparticle radiosensitization. ACS Nano. 2017;62(21):8455-69. [DOI:10.1088/1361-6560/aa8e12] [PMID]

56. Zhang XJ, Xing JZ, Chen J, et al. Enhanced radiation sensitivity in prostate cancer by gold-nanoparticles. Clin Investiga Med. 2008;31 (3):E160-E7. [DOI:10.25011/cim.v31i3.3473] [PMID]

57. Zhang AW, Guo WH, Qi YF, Wang JZ, Ma XX, Yu DX. Synergistic effects of gold nanocages in hyperthermia and radiotherapy treatment. Nanoscale Res Lett. 2016;11(1):279. [PMCID] [DOI:10.1186/s11671-016-1501-y] [PMID]

58. Hainfeld JF, Dilmanian FA, Slatkin DN, Smilowitz HM. Radiotherapy enhancement with gold nanoparticles. J Pharmacy Pharmacol. 2008; 60(8):977-85. [DOI:10.1211/jpp.60.8.0005] [PMID]

59. Zhang Z, Niu N, Gao X, et al. A new drug carrier with oxygen generation function for modulating tumor hypoxia microenvironment in cancer chemotherapy. Colloids Surf B Biointerfaces. 2019;173:335-45. [DOI:10.1016/j.colsurfb.2018.10.008] [PMID]

60. Vieira L, Castilho ML, Ferreira I, Ferreira-Strixino J, Hewitt KC, Raniero L. Synthesis and characterization of gold nanostructured chorin e6 for photodynamic therapy. Photodiag Photodynam Ther. 2017;18:6-11. [DOI:10.1016/j.pdpdt.2016.12.012] [PMID]

61. Tentor FR, de Oliveira JH, Scariot DB, et al. Scaffolds based on chitosan/pectin thermosensitive hydrogels containing gold nanoparticles. Int J Biol Macromolec. 2017;102: 1186-94. [DOI:10.1016/j.ijbiomac.2017.04.106] [PMID]

62. Roa W, Zhang X, Guo L, et al. Gold nanoparticle sensitize radiotherapy of prostate cancer cells by regulation of the cell cycle. Nanotechnol. 2009;20(37):375101. [DOI:10.1088/0957-4484/20/37/375101] [PMID]

63. Movahedi MM, Mehdizadeh A, Koosha F, et al. Investigating the photo-thermo-radiosensitization effects of folate-conjugated gold nanorods on KB nasopharyngeal carcinoma cells. Photodiag Photodynam Ther. 2018;24:324-31. [DOI:10.1016/j.pdpdt.2018.10.016] [PMID]

64. S R Bhattarai , Derry P, Aziz K, et al. Gold nanotriangles: scale up and X-ray radiosensitization effects in mice. Nanoscale. 2017 ;9(16):5085-93. [DOI:10.1039/C6NR08172J] [PMID] [PMCID]

65. Miladi I, Alric C, Dufort S, et al. The in vivo radiosensitizing effect of gold nanoparticles based MRI contrast agents. Small. 2014;10(6):1116-24. [DOI:10.1002/smll.201302303]

66. Atkinson RL, Zhang M, Diagaradjane P, et al. Thermal enhancement with optically activated gold nanoshells sensitizes breast cancer stem cells to radiation therapy. Sci Translat Med. 2010;2(55). [DOI:10.1126/scitranslmed.3001447]   [PMID] [PMCID]

67. Chattopadhyay N, Cai Z, Kwon YL, Lechtman E, Pignol JP, Reilly RM. Molecularly targeted gold nanoparticles enhance the radiation response of breast cancer cells and tumor xenografts to X-radiation. Breast Cancer Res Treat. 2013;137 (1):81-91.   [DOI:10.1007/s10549-012-2338-4] [PMID]

68. Liu CJ, Wang CH, Chen ST, et al. Enhancement of cell radiation sensitivity by pegylated gold nanoparticles. Physic Med Biol. 2010;55(4):931-45. [DOI:10.1088/0031-9155/55/4/002] [PMID]

69. Vlastou E, Pantelis E, Efstathopoulos EP, Karaiskos P, Kouloulias V, Platoni K.

Quantification of nanoscale dose enhancement in gold nanoparticle-aided external photon beam radiotherapy. Cancers. 2022; 14(9):2167. [PMID] [DOI:10.3390/cancers14092167] [PMCID]

70. Han O, Bromma K, Palmerley N,et al. Nanotechnology driven cancer chemoradiation: exploiting the full potential of radiotherapy with a unique combination of gold nanoparticles and bleomycin. Pharmaceutics. 2022;14(2):233. [DOI:10.3390/pharmaceutics14020233]   [PMID] [PMCID]

71. Yogo K, Misawa M, Shimizu H, et al. Radiosensitization effect of gold nanoparticles on plasmid DNA damage induced by therapeutic MV X-rays. Nanomaterials (Basel). 2022;12(5):771. [DOI:10.3390/nano12050771] [PMID] [PMCID]

72. Janic B, Brown SL, Neff R, et al. Therapeutic enhancement of radiation and immunomodulation by gold nanoparticles in triple negative breast cancer. Cancer Biol Ther. 2021;22(2):124-135. [DOI:10.1080/15384047.2020.1861923] [PMID] [PMCID]

How to Cite This Article:

Khosravi H, Doosti-Irani A, Bouraghi H, Nikzad S. Investigation of Gold Nanoparticles Effects in Radiation Therapy of Cancer: A Systematic Review, J Adv Med Biomed Res. 2022; 30(142): 388-96.

Download citation:
BibTeX | RIS | EndNote | Medlars | ProCite | Reference Manager | RefWorks

Send citation to:
Mendeley   Zotero   RefWorks   RefWorks