ORIGINAL ARTICLE

Dose of radiation enhancement, using silver nanoparticles in a human tissue equivalent gel dosimeter

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Abstract

Objective: To quantify the radiation dose enhancement in a human tissue-equivalent polymer gel impregnated with silver nanoparticles.

Methods: The case-control study was conducted at the Bahawalpur Institute of Nuclear Medicine and Oncology, Bahawalpur, Pakistan, in January 2014. Silver nanoparticles used in this study were prepared by wet chemical method. Polymer gel was prepared by known quantity of gelatine, methacrylic acid, ascorbic acid, copper sulphate pentahydrate, hydroquinone and water. Different concentrations of silver nanoparticles were added to the gel during its cooling process. The gel was cooled in six plastic vials of 50ml each. Two vials were used as a control sample while four vials were impregnated with silver nanoparticles. After 22 hours, the vials were irradiated with gamma rays by aCobalt-60 unit. Radiation enhancement was assessed by taking magnetic resonance images of the vials. The images were analysed using Image J software.

Result: The dose enhancement factor was 24.17% and 40.49% for 5Gy and 10Gy dose respectively. The dose enhancement factor for the gel impregnated with 0.10mM silver nanoparticles was 32.88% and 51.98% for 5Gy and 10Gy dose respectively.

Conclusion: The impregnation of a tissue-equivalent gel with silver nanoparticles resulted in dose enhancement and this effect was magnified up to a certain level with the increase in concentration of silver nanoparticles.

Keywords: Radiation therapy, Radiation therapy enhancement, Silver nanoparticles, Gel dosimeter. (JPMA 66: 45; 2016)

Introduction

In radiation therapy we commonly use X-rays and gamma rays[1] for the therapeutic handling of numerous cancers.[2] The objective of radiation therapy has always been to maximise the chance of controlling the cancer and minimising normal tissue problems. The achievement of this objective is the key element driving the technological improvements.[3,4]

The objective can be achieved by increasing the dose to the tumour, increasing the sensitivity of tumour cells and targeting the cancer cells. Radiosensitive agents or radiation dose enhancers can boost the result of radiation to the tumour if they are selectively targeted to cancer cells.[5] Enhancing tumour radiosensitivity by increasing the cross-section of radiation interaction in the tissue using higher atomic number (Z) materials has been explored over the last 20 years, typically using iodinated contrast agents.[6] Development in the field of nanotechnology has potentially provided a choice to enhance the dose of radiation by using heavy metal nanoparticles (NPs).

NPs made of higher atomic number materials act as radiosensitisers in the target because the interaction of photons depend upon the density and atomic number. Gold NPs are used as radiation therapy agents most extensively, but they are very costly. Silver NPs (AgNPs) are an attractive option as a radiation dose enhancer due to their low cost compared to gold NPs and anti-tumour activity.[7,8]

Polymer gel dosimeters are a kind of radiation dosimeter used in medical radiation treatments that are capable of directly assessing the special effects of contrast agents or metallic radiation dose enhancers, such as iodine and AgNPs within the dosimeter. In gel dosimeter, contrast agents are able to be saturated within the dosimeter itself and so the special effects of these objects can be directly quantified.[9,10] A polymer gel dosimeter is Methacrylic Ascorbic in Gelatin Initiated by Copper with Agarose added (MAGICA).

The current study was planned to assess effectiveness of AgNPs for dose enhancement in a human tissue-equivalent MAGICA polymer gel impregnated with different concentrations of AgNPs and irradiated with different doses.

Materials and Methods

The case-control study was conducted at the Bahawalpur Institute of Nuclear Medicine and Oncology (BINO),

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Bahawalpur, Pakistan, in January 2014. AgNPs were synthesised by wet chemical method. The beakers, test tubes and magnetic stirrer were washed with sulphuric acid and the quantity of chemicals was carefully weighed by digital weight balance. Silver nitrate (AgNO3) solution of 0.0844 g/50ml was used as a precursor. A predetermined quantity 0.05 g/50ml of polyvinylpyrrolidone (PVP) was added to the AgNO3 solution. Then 0.18g/50ml D-Glucose was added as reducing agent. Molar concentrations were made and kept constant during the reaction. The pH of the reaction solution was kept between 8.5 and 9.0 throughout their action using sodium hydroxide (NaOH) (0.02 g/50ml) andsodium carbonate (Na2CO3) (0.0265 g/50 ml). The reaction mixture was heated in a water bath at 55°C to 60°C for 1hr with vigorous agitation by magnetic stirrer. After one hour, the brownish colour and absorption peak around 410nm confirmed the formation of AgNPs.[11]

The MAGICA polymer gel was selected because it can be prepared easily and quickly in the normal room atmosphere than the other gel types. The normoxic MAGICA gel was prepared by the method described in literature.[12] It shows significant potential as radiation dosimeter. Ideally, X-ray attenuation, optical and mechanical properties of the gel are needed to be tested to closely match the target tissue characteristics. The dose response can be varied by altering the precise composition of the gel. For one litre batch of 9% MAGICA gel, the process began by placing 700ml of water and a magnetic stir-bar in a glass flask and then adding 80g of gelatin. After the gelatin was swelled from soaking, the flask was heated to ~500C to ensure complete dissolution of gelatin. At this point 2.0g of hydroquinone in 48ml of high-pressure liquid chromatography (HPLC)-grade distilled water was added and the solution was allowed to cool. When the solution was allowed to cool to ~37°C, the appropriate amounts of ascorbic acid (0.352 g in 50ml of water), copper sulphatepenta-hydrate (CuSo4.5H2O) (0.2 g in 30 ml of water) and 90g of methacrylic acid were added to the flask. The solution was allowed to stir until the mixture was homogeneously dissolved. The MAGICA polymer gel was cooled for 22 hours at room temperature in eight plastic vials each of volume 50ml, with different concentrations (0.05mM, 0.10mM) of AgNPs.[9] Finally, two vials were used as the control sample, while four vials were impregnated with AgNPs.

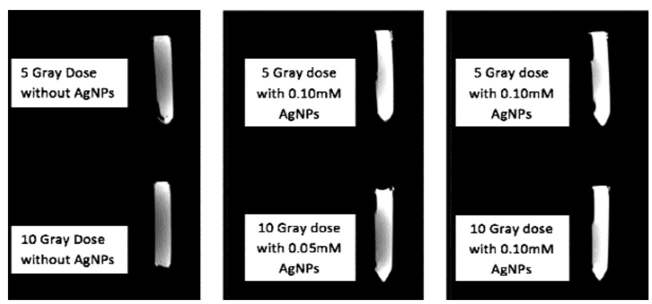
The dose enhancement factor (DEF) was calculated as.

DEF = (M (AgNPs-MAGICA) - M(MAGICA)) ÷ M(MAGICA)

This gave the increase in gray (Gy) values, and also told about whether the dose enhancement was occurring or not by impregnating a tissue-equivalent gel with the AgNPs. The DEF was calculated by the ratio of difference of the mean Gy value of pure gel (control gel) and gel impregnated with AgNPs to the pure gel (control sample).

The ImageJ software established at the National Institute of Health (NIH) was used as a tool to visualize the images and to get numerical analysis of different regions of interest (ROI). The software is very beneficial to analyze the medical images. Image examination functions can be applied to particular ROI for plotting profile and calculation of image intensity. The user has option to select ROI in polygonal, rectangular, line or round shape.[13,14]

Results



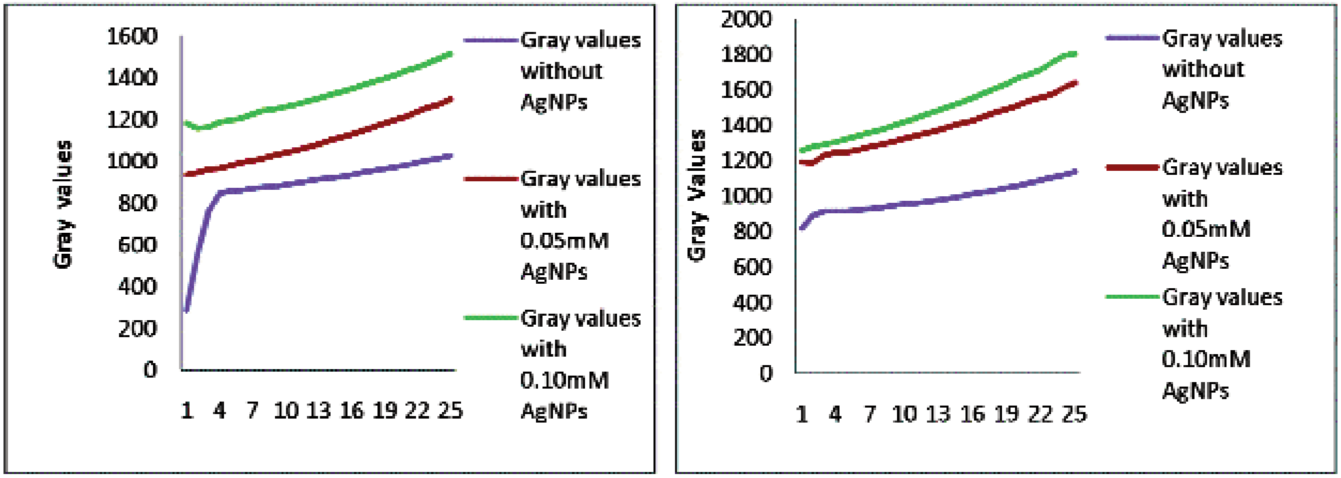
MAGICA: Methacrylic Ascorbic in Gelatin Initiated by Copper with Agarose added. AgNPs: Silver nanoparticles.

Figure-1: Magnetic resonance images of MAGICA gel samples with different concentrations (without AgNPs, with 0.05mM AgNPs and with 0.10mM AgNPs) after irradiation by Co-60 unit for 5 and 10 Gy dose.

Table: Percentage increase in Gray values of MAGICA gel samples without AgNPs, with 0.05mMAgNPs and with 0.10mMAgNPs after irradiating it for 5 Gy and 10 Gy dose.

Dose increase (Gy)	Concentration of NPs	Mean Gray values of sample without NPs M(MAGICA)	Standard deviation of Gray values of sample without NPs S.D (σ)	Mean Gray values of sample with NPs M(AgNPs-MAGICA)	Standard deviation of Gray values of sample with NPs S.D (σ)	Percentage in Gray values DEF
5 Gy	0.05mM	881.3876	155.503	1094.443	110.191	24.17%
	0.10mM	881.3876	155.503	1313.104	109.249	32.88%
10Gy	0.05mM	988.328	79.427	1388.459	133.173	40.49%
	0.10mM	988.328	79.427	1502.045	169.362	51.98%

MAGICA: Methacrylic Ascorbic in Gelatin Initiated by Copper with Agarose added. AgNPs: Silver nanoparticles. DEF: Dose enhancement factor.



(a) (b)

MAGICA: Methacrylic Ascorbic in Gelatin Initiated by Copper with Agarose added. AgNPs: Silver nanoparticles.

Figure-2: Graph between Gray values of MAGICA gel samples without AgNPs, with 0.05mM AgNPs and with 0.10mM AgNPs after irradiating with the Co-60 unit. Graph (a) for 5 Gray dose and (b) for 10 Gray dose.

Magnetic resonance images (MRIs) of control samples and samples having different concentrations of AgNPs (0.05mMAgNPs and with 0.10mMAgNPs), irradiated by 5 Gy and 10 GY dose, were noted (Figures-1 and 2).

Discussion

The study used different concentrations of AgNPs in tissue-equivalent MAGICA gel and showed the enhancement of dose radiation. These have the potential to be used as an alternative agent for human cancer therapy.[7,8]

Most of the work on enhancement of dose radiation is done by gold nanoparticles (AuNPs) and dose enhancement is higher for low-energy beams compared to beams in mega-voltage range. There are very few studies about the use of AgNPs as radiation dose enhancer.

A study on the dose enhancement effect of gold nanoparticles on MAGICA polymer gel showed that dose enhancement occurred with the increase in AuNPs concentration. The dose enhancement process was nonlinear by AuNPs.[15] A study on the enhancement of breast cancer radiation therapy used AgNPs with 6 MeV Gamma Photons. However, it did not give the quantitative relation for radiation therapy enhancement.16Another study used Monte Carlo N-Particle eXtended (MCNPX) code for brachy therapy source and found the DEF to be 1.15 for AgNPs with concentrations 30 mg/ml.[17]

The AgNPs were synthesised by wet chemical method and it was found that the stability of AgNPs was about one week. They decomposed after one week because they did not resist to oxidation. From this fact it is obvious that AgNPs should be used within one week.

The prepared MAGICA gel should be used within three days, because it will liquify after three days and will not preserve the path of radiation.

In this work, the dose enhancement was directly related to the Gray (Gy) value; higher the Gyvalue, the greater was the intensity of radiation, and more was the dose enhancement. The enhancement in the dose was significant as the concentration of AgNPs increased (Figure-2). The increase in Gy values with the increase in concentration of AgNPs showed that the dose was enhanced. The DEF for a human tissue-equivalent gel impregnated with 0.05mM AgNPs was 24.17% and 40.49% for 5Gy and 10Gy dose respectively (Table). The DEF for a human tissue-equivalent gel impregnated with 0.10mM AgNPs was 32.88%and 51.98% for 5Gy and 10Gy dose respectively.

Conclusion

Results suggest that AgNPs might be a potential alternative to AuNPs for radiation therapy enhancement. However, further in vivo studies might be considered necessary to check the cumulative toxicity of AgNPs.

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