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by Eko Hidayanto

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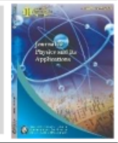

Dose Distribution 6 MV of X-Ray Photon Beam over Cerium Oxide Nanoparticles Solution

Iis Nurhasanah[1*], Hella Arofah[1], Agus Subagio[1], Eko Hidayanto[1], Tri Windarti[2]

[1]*Department of Physics, Faculty of Science and Mathematics, Universitas Diponegoro, Semarang. Indonesia*
[2]*Department of Chemistry, Faculty of Science and Mathematics, Universitas Diponegoro, Semarang. Indonesia*

[*)]*Corresponding author: Nurhasanah@fisika.fsm.undip.ac.id*

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ABSTRACT

CeO_2 nanoparticles are biomaterial that demonstrate potential as antioxidant and radioprotector for medical application. In this study, the radioprotector properties of CeO_2 nanoparticles was evaluated by measuring absorbed dose of X-ray radiation. CeO_2 nanoparticles were synthesized by precipitation and characterized using UV-Vis and FTIR spectrometers. CeO_2 nanoparticle solution was prepared with various concentrations from 0.005 mg/mL to 0.06 mg/mL. The solution was exposed to 6 MV X-ray photon beam from medical linear acceleration with a source-to-surface distance of 100 cm and radiation dose of 2 Gy. The absorbed dose of X-ray by CeO_2 nanoparticle solution was measured by an ion chamber detector. The absorbance peak at 301 nm observed in UV-Vis spectrum and absorbance peak at 854 and 492 cm^{-1} in the FTIR spectrum confirmed the formation of CeO_2 nanoparticles. Radiation dose measurement exhibited dose reduction of CeO_2 nanoparticles solution depend on concentration. CeO_2 nanoparticle solution with concentration higher than 0.04 mg/mL showed potential application for radioprotector 6 MV of X-ray photon beam.

1. Introduction

To date, ionizing radiation such as X-rays is considered the most adequate method for cancer therapy. Cancer cells can be killed easily by ionizing radiation but this technique can also damage healthy tissues [1,2]. In high doses, healthy tissues are more difficulty in repairing themselves as opposed to abnormal tissues. Therefore, the challenge in cancer therapy is optimizing cancer cell killing and minimizing healthy cell damage surrounding cancer tissues. To overcome these problems, radiosensitizers have been developed to enhance cancer cell killing, whereas radioprotectors have been developed to protect healthy tissue and reduce radiation damage.

Cell damage due to ionizing radiation with low LET (photon or electron) is mainly ascribed to the effect of free radical generation [3]. Therefore, the material that can scavenge free radicals is beneficial as a radioprotector. Suitable antioxidant treatment in radiotherapy appears to inhibit or reduce harmful effect of free radical, thereby protecting against radiation. The toxicity, antioxidant activity and radioprotective effect of CeO_2 nanoparticles have been extensively investigated. The most attractive potential of CeO_2 nanoparticles is its possible application for anti-cancer treatment. CeO_2 nanoparticles are toxic to cancer cell, but exhibit low toxicity to healthy cells around the cancer tissue and tend to protect such cells [4-8]. Given the antioxidant properties of CeO_2 nanoparticles, they are a good radioprotector of healthy tissue in radiotherapy. Antioxidant properties of CeO_2 nanoparticles attributed to the reversible transformation of oxidation state between Ce^{3+} and Ce^{4+} [4-9].

In our previous study, we reported that the antioxidant activity of CeO_2 nanoparticles depends on the preparation synthesis. CeO_2 nanoparticles were synthesized by precipitation at various calcination temperatures. As-calcined CeO_2 nanoparticles at 500°C with concentrations of 0.02-0.06 mg/mL exhibited a protective effect on Escherichia coli damage induced by X-rays radiation [9]. When the CeO_2 nanoparticle solution was irradiated by 6 MV of X-rays photon beam, the X-rays interacted directly with the water molecules causing radiolysis and generating ROS. At the same time X-rays also interacted with CeO_2 nanoparticles causing the pair production effect [8, 10, 11]. In the present study, the radioprotective effect of CeO_2 nanoparticles were analyzed by investigating the dose distribution of X-rays radiation over CeO_2 nanoparticle solution with various concentrations. Furthermore, dose enhancement factor (DEF) of CeO_2 nanoparticles solutions was calculated to evaluate the role of CeO_2 nanoparticles in radiotherapy. Nanoparticles can act as radioprotector when DEF < 1.0 [8, 10, 11].

2. Experimental method

Synthesis and Characterization of CeO_2 Nanoparticles

CeO_2 nanoparticles were synthesized by precipitation with a solvent mixture of demineralized water and isopropanol with the volume ratio of 1:6. Precipitation was conducted by dripping ammonium hydroxide into cerium (III) nitrate hexahydrate solution until pH 10 was obtained. The product precipitate was dried at 60ºC for 1 h and calcined at 500ºC for 2 h [9].

Characterization was performed to identify the formation of CeO_2 nanoparticles. The optical properties and functional groups of CeO_2 nanoparticles were characterized using a UV-Vis and Fourier transform infrared (FTIR) spectrometer. The absorbance spectrum was then analyzed to determine the band gap, and the functional group of CeO_2 nanoparticles was identified by FTIR spectroscopy.

Measurement of Radiation Dose

CeO_2 nanoparticle solution was prepared by dissolving a certain amount of CeO_2 nanoparticles into 0.9% NaCl solution to obtain concentrations of 0.005, 0.01, 0.02, 0.04 and 0.06 mg/mL. Pure NaCl solution and CeO_2 nanoparticle solution were placed in a Petri dish with a diameter of 8.5 cm. Each solution was exposed to 6 MV X-ray photon beam from a medical linear accelerator. The radiation experiment was carried out with the source to surface distance of 100 cm, field width of 10 cm x 10 cm, and radiation dose of 2 Gy. The scheme of the setup for dose measurement is shown in Fig. 1. The radiation dose at given coordinate points was measured by an ion chamber detector. The data were then used to calculate the dose enhancement factor (DEF) using Eq. (1). DEF is defined as the ratio of absorbed dose with CeO_2 nanoparticles present to absorbed dose without CeO_2 nanoparticles [8, 10, 11].

$$\mathrm{DEF} = \frac{Dose\ in\ the\ sample\ with\ CeO2}{Dose\ in\ the\ sample\ without\ CeO2} \qquad (1)$$

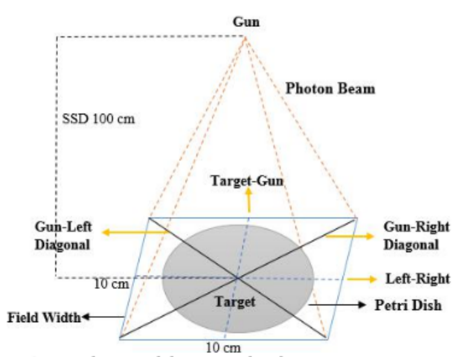


Fig 1: Scheme of the setup for dose measurement.

3. Results and discussion

Characteristic of CeO_2 nanoparticles

Nanoparticles were obtained in the form of a fine yellow powder suggesting the formation of CeO_2. This can be confirmed based on the absorbance spectrum analysis. The absorbance spectrum in Fig. 2 shows the strong absorption properties of CeO_2 nanoparticles in the wavelength range between 200 and 350 nm. The figure also shows the absorption peak at 301 nm which was the peak characteristic of CeO_2 and correspond to the band gap of CeO_2 nanoparticles. The band gap was determined using Tauc's plot method.as shown in the insert Fig. 2. On the basis of the extrapolation of Tauc's plot, the band gap of CeO_2 nanoparticles in this study was 3.49 eV. This value was higher than the band gap of bulk CeO_2 (3,2 eV) [12]. The increase in band gap of CeO_2 nanoparticles compared with that of bulk CeO_2 was also observed in several studies, with value of 3.44 [13], 3.64-3.76 eV [14] and 3.46 eV [15]. In addition, the peak at 301 nm revealed the existency of Ce^{4+} on the sample that important role in the interaction with x-ray radiation as radioprotection [4-9].

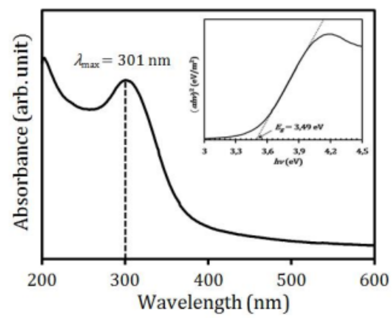


Fig. 2: An absorbance spectrum of CeO_2 nanoparticles.

Fig. 3 depicts the FTIR spectrum of the synthesized CeO_2 nanoparticles. The absorption peak at 2000-3400 cm-1 was observed for the OH stretching vibration of H_2O in the sample. The absorption bands at 1342 and 1542 cm^{-1} were related to the physically adsorbed water molecules. The absorption bands at 491 cm^{-1} corresponded to the stretching vibration characteristic of CeO_2. These results indicated the formation of CeO_2 nanoparticles [14-15].

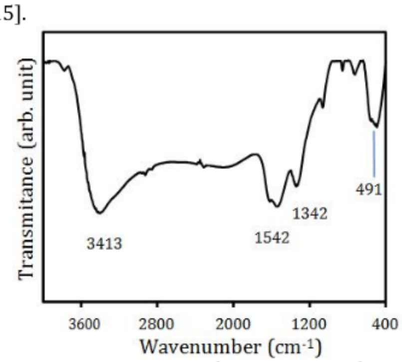
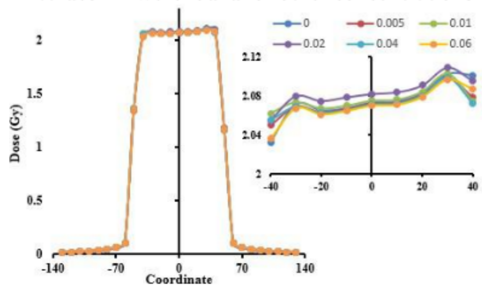


Fig. 3: FTIR spectrum of CeO_2 nanoparticles.

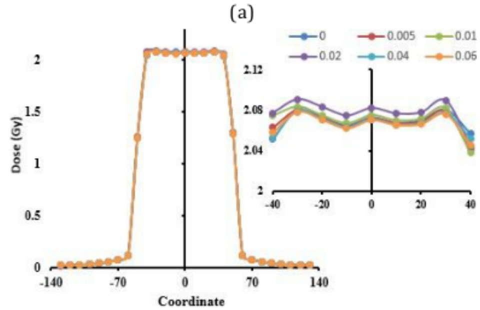
Dose Distribution of X-ray over CeO_2 Nanoparticles Solution

The role of nanoparticles as radioprotector in radiotherapy, can be determined by the ability of nanoparticles to absorb radiation and is characterized by DEF. The dose distribution of each coordinate position for various concentrations of CeO_2 nanoparticles is shown in Fig. 4. The coordinate points from -50 to 50 represent the value of absorbed dose measured on the radiation field, whereas the other coordinate points show exposure outside the radiation field, which was still captured by the detector. The insert in Fig. 4 shows the dose distribution over CeO_2 nanoparticle solutions differed for each concentration. The concentration of 0.02 mg/mL presented the highest absorbed dose value than the other concentrations, and it was higher than the absorbed dose for the solution without CeO_2 nanoparticles. Meanwhile, the absorbed dose of other concentrations was almost similar and close to the control. Thus, the ability of CeO_2 nanoparticles to absorb radiation was dependent on its concentration [8, 10, 11].

The potential role of CeO_2 nanoparticles in radiotherapy was then determined by calculating DEF. Nanoparticles can act as radioprotector when DEF < 1.0 [8, 10, 11]. Fig. 5 shows the DEF value of CeO2 nanoparticles solution with various concentrations. The DEF value >1 (1.001 and 1.004) were found for CeO_2 nanoparticle solutions with concentrations of 0.01 and 0.02 mg/mL, respectively. DEF values < 1 were found for other concentrations.



(a)



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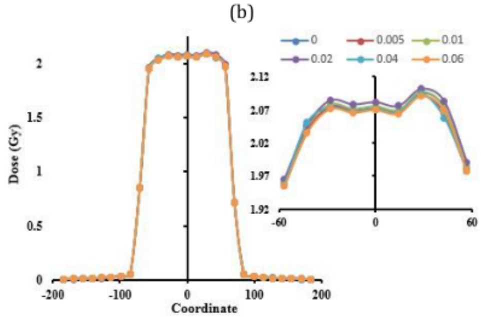

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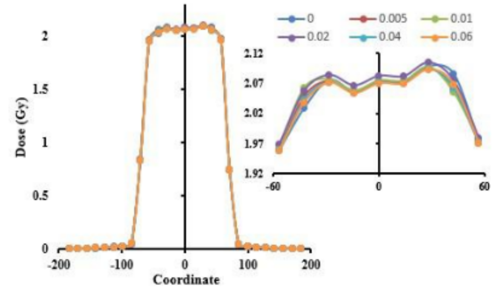

(d)

Fig. 4: Dose distribution in each position graph (a) target-gun, (b) left-right, (c) diagonal gun-right, and (d) diagonal gun-left, (the insert shows the dose distribution in a short range).

Theoretically, cross section probability of interaction between X-rays and CeO_2 nanoparticles solution would increase and X-rays radiation energy deposited in solution would also increase as increase in concentration [17-19]. Therefore, the absorbed dose increase and DEF decrease with increasing concentration of CeO_2 nanoparticles. However, DEF increased from 0.999 to 1.004 with increasing CeO_2 concentration from 0.005 to 0.02 mg/mL and then DEF decreased at concentration of CeO_2 nanoparticles 0.04 mg/mL. When the CeO_2 nanoparticle solution was irradiated by X-rays, the X-rays interacted directly with the water molecules causing radiolysis and generating ROS such as OH*, H_2O_2, OH•, O_2•, H_2O*, and H•. Two valence states Ce^{3+} and Ce^{4+} (co-exist) were present on the surface of CeO_2 nanoparticles. CeO_2 nanoparticles could reversibly oxidize from Ce^{3+} and Ce^{4+} through interaction with free radicals. This phenomenon led to a reduction in the absorbed dose [4-8]. In addition, the physical interaction between photons (with energy > 1.02 MeV) and the high-Z material like as Cerium (Z = 58) is predominantly based on the pair production effect [19]. The concentration of CeO_2 from 0.005 to 0.02 mg/mL did not provide an effective increase in the cross-section for the pair production, then DEF is increased. Meanwhile, the concentration of CeO_2 at 0.04 and 0.06 mg/mL provided more effective of cross section for the pair production lead to lower DEF.

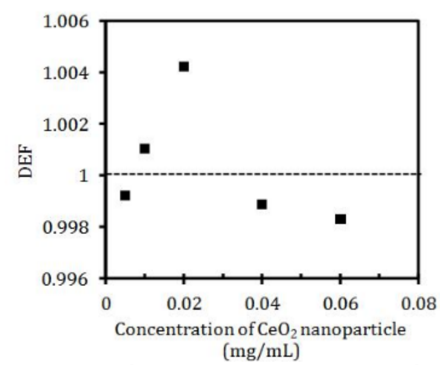

Fig. 3: DEF for various concentrations of CeO_2 nanoparticles solution.

The major component in biological systems such as human tissue is water molecules. Therefore, by injecting high-*Z* material, such as CeO_2 into tissue, the local radiation effect was enhanced and cell damage occurred. However, the obtaining DEF value is in the range of 0.998 to 1.004. These values are less than 1.01, so that CeO_2 nanoparticles could reduce the radiation dose and lead to a protective effect [8].

4. Conclusions

CeO_2 nanoparticles are biomaterials with potential application in radiotherapy. Cerium oxide nanoparticles were synthesized by precipitation. The peak in the observed absorbance spectrum at 301 nm wavelength and absorption bands at 491 cm^{-1} observed on the FTIR spectrum corresponded to characteristic of CeO_2 nanoparticles. The radiation dose of 6 MV X-ray photon beam was measured to investigate the absorbed dose over CeO_2 nanoparticle solutions. The radiation dose distribution of CeO_2 nanoparticles solution was depended on the concentration. The DEF of the CeO_2 nanoparticles solution was lower than 1.0 for the CeO_2 concentrations higher than 0.04 mg/mL. Therefore, CeO_2 nanoparticles were found to provide radioprotection effects.

Acknowledgment

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