Journal of Physics: Conference Series

OPEN ACCESS

Gel Dosimetry Analysis of Gold Nanoparticle Application in Kilovoltage Radiation Therapy

To cite this article: T Marques *et al* 2010 *J. Phys.: Conf. Ser.* **250** 012084

Journal of Physics: Conference Series **250** (2010) 012084 doi:10.1088/1742-6596/250/1/012084

Gel Dosimetry Analysis of Gold Nanoparticle Application in Kilovoltage Radiation Therapy

T. Marques[‡], M. Schwarcke[‡], C. Garrido[‡], V. Zucolotto[†], O. Baffa[‡], P. Nicolucci[‡]

[‡] Department of Physics and Mathematics - University of Sao Paulo.
Av. Bandeirantes, 3900 - 14040-901. Ribeirão Preto – SP, Brazil.

[†] Institute of Physics - IFSC - University of Sao Paulo.
Av. Trabalhador São Carlense,400 - 13560-970. São Carlos - SP, Brazil.

tatiana.marques@usp.br

Abstract. In this work gold nanoparticles (AuNP) were embedded in MAGIC-*f* gel and irradiated in a 250 kV x-ray clinical beam. The signal of non-irradiated gel samples containing AuNPs showed maximum difference of 0.5% related to gel without nanoparticles. Different AuNPs concentrations were studied: 0.10 mM, 0.05 mM and 0.02 mM, presenting dose enhancements of 106%, 90% and 77% respectively. Monte Carlo spectrometry was performed to quantify theoretical changes in photon energy spectrums due to AuNPs presence. Concordance between simulated dose enhancements and gel dosimetry measurements was better than 97% to all concentrations studied. This study evidences that polymer gel dosimetry as a suitable tool to perform dosimetric investigations of nanoparticle applications in Radiation Therapy.

1. Introduction

Nanoparticles have been extensively investigated in diagnostic radiology and radiation therapy [1-2]. Radiosensitization observed by several authors points out gold nanoparticles (AuNP) as the best candidates to be used as flagships of Radionanotherapy [3-4]. This technique is becoming an increasingly practical option as nanobio-interactions are mapped.

The dosimetric suitability of AuNP applications in radiation therapy is one relevant aspect that can justify its applicability in clinical environments [5]. From the dosimetric point of view, AuNP application in radiation therapy is motivated by the fact that photoelectric probability increases due to metal presence inside a biological target. Essentially, metallic nanoparticles kept inside target cells make it possible to handle effective atomic number and mass-attenuation coefficient in clinical targets improving dose delivery effectiveness [6].

Dosimetry evolved in Radionanotherapy is complex and precise investigations of changes in dose painting due to nanoparticles presence can be performed using gel dosimetry. Conditions of Radionanotherapy treatments can be experimentally simulated incorporating AuNP to tissue-equivalent dosimeters. In this work different concentrations of AuNP were embedded in MAGIC-*f* gel and dose enhancement was quantified by gel dosimetry and Monte Carlo simulation to irradiations in a clinical x-ray beam.

Journal of Physics: Conference Series **250** (2010) 012084 doi:10.1088/1742-6596/250/1/012084

2. Material and Methods

2.1. Gold nanoparticle synthesis
The synthesis of dendrimer encapsulated-nanoparticles consisted in the reduction of metallic precursors in presence of dendrimer polyamidoamine generation 4 (PAMAM G4). Briefly, in a 2.0mL of 1mMol L^{-1} gold tetrachloride acid aqueous solution ($HAuCl_4$), 2.0mL of the 1mMolL^{-1} PAMAM-G4 solution was added. After 15min under agitation, 2.0mL of formic acid (10% v/v) was added, which acted as reducing agent. The system was kept in the dark. After 2h, a red coloration appeared, indicating the gold nanoparticles formation. The PAMAM AuNPs were characterized using UV-Vis and dynamic scattering light measurements (DLS), revealing an average diameter of 2–3nm.

2.2. Nanoparticles incorporation in gel
MAGIC-*f* (*Methacrylic Ascorbic acid and Gelatin Initiated by Copper with formaldehyde*) [7] was prepared from 70% dehydrated gel at 40 °C. Four samples were isolated from the same batch, in which three of them contained the AuNPs. The sample not containing AuNPs served as control. Gel homogenization was achieved by routine mechanical mix without heating. Tree different AuNPs concentration were considered: 0.10mM (A), 0.05mM (B) and 0.02(C). Figure 1a presents the gel samples without nanoparticles with different polymerization levels. In figure 1b, gel containing different AuNP concentrations can be seen as different colors.

1.a 

 1.b

Figure 1 – Gel samples: (a) Polymerization levels of MAGIC-*f* samples irradiated with different doses; (b) Gold nanoparticles embedded in gel presenting visible color changing.

2.3. Irradiation procedures and NMR reading
Gel samples were irradiated in a Siemens Stabillipan ortovoltage clinical beam of 250kV at the Radiation Therapy facility of Hospital of Clinics of the Medical School from Ribeirão Preto - HCFMRP. MAGIC-*f* linearity of response and tissue equivalence for the beam studied were determined. A water box was positioned under the gel tubes to guarantee backscattering conditions. Control gel samples and samples containing AuNP were irradiated with 5Gy.

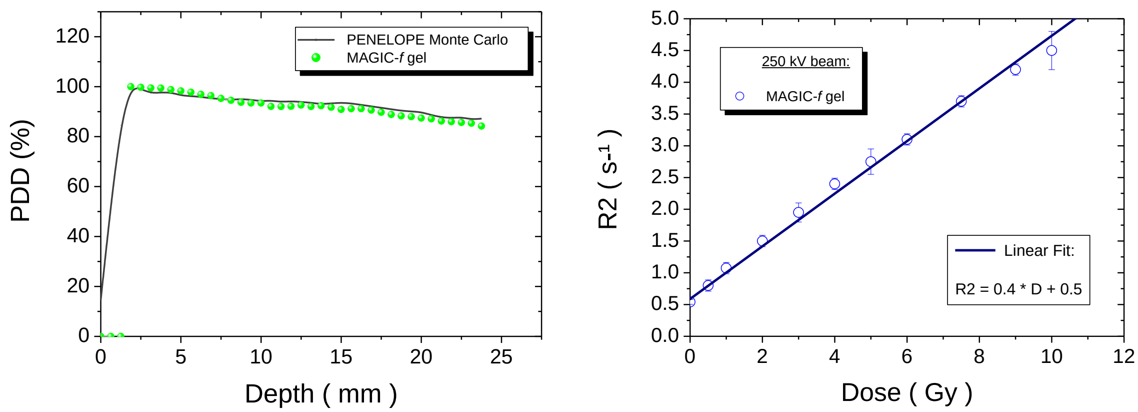
Dose measurement was made by relaxometry, which correlates dose and nuclear magnetic transversal relaxation rate (R2) [8]. Experiments were carried out in a Philips 3.0 Tesla Magnetic Resonance Imaging (MRI) scanner 24 hours after irradiation. A multi-spin echo sequence with 16 echoes, echo time of 15ms, repetition time of 4000ms, pixel size of 0.5x0.5mm^2 and two acquisitions averaged was used.

2.4. Monte Carlo simulations
Computational simulations of dose deposition were performed using PENELOPE Monte Carlo code [9]. Gold presence in gel was considered in the same experimental concentrations. Monte Carlo spectrometry was also performed using PENELOPE code to identify how the photon energy spectrum (PES) changes due to AuNP presence in gel. Scattered and absorbed components were identified and quantified in the PES to all nanoparticles concentrations studied.

Journal of Physics: Conference Series **250** (2010) 012084 doi:10.1088/1742-6596/250/1/012084

3. Results and Discussion

MAGIC-*f* response to the 250 kV x-ray beam was characterized by comparing experimental and Monte Carlo simulated percentage depth dose curves (PDD) (see figure 2a). Maximum difference in experimental and simulated PDDs was 2.96% found at 15mm depth. Linearity of response to MAGIC-*f* was verified considering a dose range from 0 Gy to 10 Gy. Figure 2b shows the R2 signal corresponding to the evaluated doses.

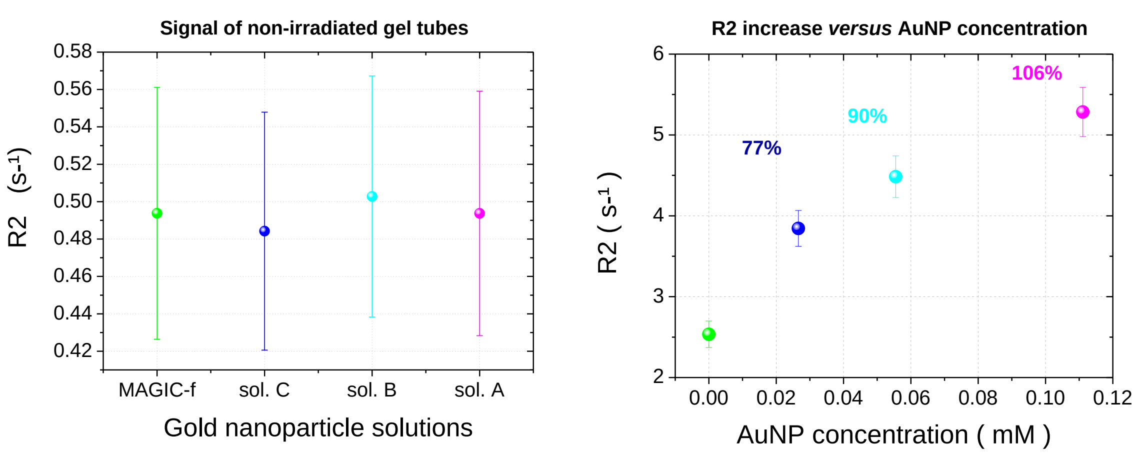


a. .b

Figure 2 – Dosimetric response of MAGIC-*f* to the 250 kV x-ray beam: (a) PDD curves comparison between PENELOPE Monte Carlo simulation and gel; (b) Dose linearity response of gel.

The signal of non-irradiated tubes containing and not containing AuNPs were evaluated. Chemical interactions between PAMAM AuNPs and gel were discarded considering the low R2 signal variation found (less than 0.5%). Figure 3a presents the respective R2 averaged from 3 non-irradiated tubes considered to each nanoparticle concentration.

The dose increase due to AuNPs presence in the tissue-equivalent gel was quantified comparing the R2 of all different nanoparticles concentrations irradiated with the same dose (5Gy). Concentration A presents an increase of 106% in R2 related to gel without AuNP; concentrations B and C present increases of 90% and 77% respectively (see figure 3b).

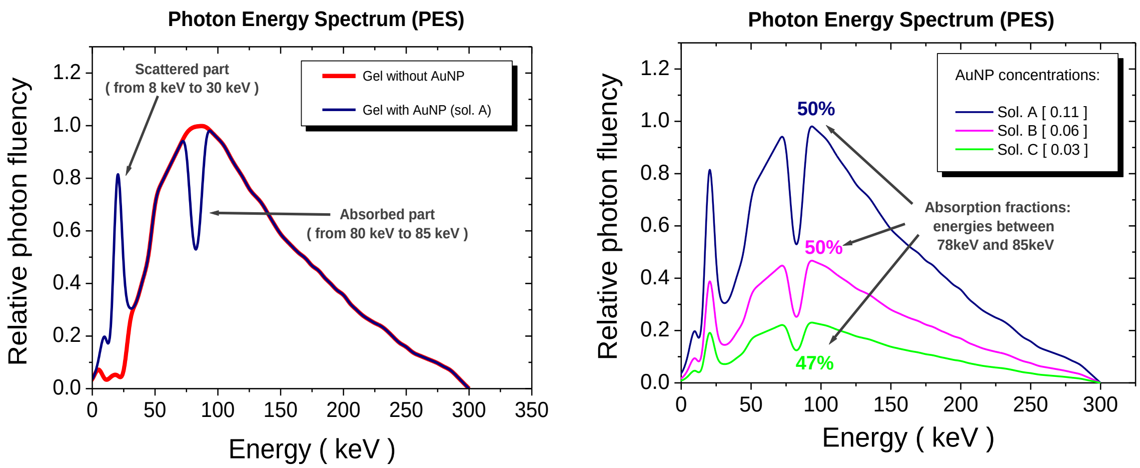


a. .b

Figure 3 – (a) Signal of non-irradiated gel samples with and without nanoparticles; (b) Dose enhancement measurements performed with MAGIC-*f* gel with different concentrations of AuNP.

Journal of Physics: Conference Series **250** (2010) 012084 doi:10.1088/1742-6596/250/1/012084

Monte Carlo spectrometry evidenced that the theoretical photon fluence absorption increases, resulting in 105%, 93% and 75% of dose enhancement when concentrations A, B and C of AuNP are present in gel respectively. Figure 4a shows a comparison between the PES inside gel without nanoparticles and gel containing concentration A of AuNP. It is possible to observe that the photon fluence increases between energies of 8 keV and 30 keV, indicating that incoherent scattering events occur in gold L-shells. This kind of interaction specially contributes to local dose increase because low energy photons are created with a short mean-free-path, resulting in low energy electrons created near the point where the primary photon was scattered. The absorbed part of the PES is also quantified in figure 4b. The absorption fractions in gold K-edge are referenced by the ratio between the photon fluencies in an energy range from 78 keV to 86 keV when AuNPs are not and are present in gel. That fraction is around 50% to all AuNPs concentrations studied. The absorption interactions also contribute to local dose enhancement due to photoelectron absorption.



a. .b

Figure 4 – Monte Carlo spectrometry inside MAGIC-*f* gel: (a) PES comparison between gel without gold nanoparticles and containing concentration A of AuNPs; (b) PES and absorption fraction inside gel containing concentrations A, B and C of AuNPs.

Dose enhancements verified by gel dosimetry and Monte Carlo simulation presented in this work instigate future investigations. Different biocompatible nanoparticles having different atomic numbers and other clinical beams can be investigated using polymer gel dosimetry aiming to optimize the application of nanoparticles in radiation therapy.

Acknowledgments

Authors are grateful to JL Aziani and to HCFMRP – USP for the essential technical contribution. This work was partially financial supported by CAPES / NANOBIOMED and CNPq. Technical and financial supports of CIDRA-USP are also appreciated.

References

[1] McMahon S.J., Mendenhall M.H., Jain S., *et al.*: “Radiotherapy in the presence of contrast agents: a general figure of merit and its application to gold nanoparticles”, Phys. Med. Biol. 53, 5635-5651 (2008).

[2] Hainfeld J.F., Slatkin D.N. and Smilowitz H.M.: "The use of gold nanoparticles to enhance radiotherapy in mice", Phys. Med. Biol. 49,N309–N315 (2004).
[3] Zhang X., Gao J., Buchholz T.A., *et al.:* "Quantifying tumor-selective radiation dose enhancements using gold nanoparticles: a monte carlo simulation study", Biomed. Microdev. 11, 925–933 (2009).
[4] Zhang X., Xing J.Z., Chen J., *et al*: *"*Enhanced radiation sensitivity in prostate cancer by gold-nanoparticles", Clin. Invest. Med. 31, E160-E167 (2008).
[5] Cho S.H., Jones B.L., Krishnan S.: "The dosimetric feasibility of gold nanoparticle-aided radiation therapy (GNRT) via brachytherapy using low-energy gamma-/x-ray sources", Phys. Med. Biol. 54, 4889-4905 (2009).
[6] Cho S.H. "Estimation of tumor dose enhancement due to gold nanoparticles during typical radiation treatments: a preliminary Monte Carlo study", Phys. Med. Biol. 50, N163-N173 (2005).
[7] Fernandes J., Pastorello B., Araujo D., *et al.:* "Formaldehyde increases MAGIC gel dosimeter melting point and sensitivity", Phys. Med. Biol. 53, N53-N58 (2008).
[8] De Deene Y.,Van de Walle R., Achten E., *et al.:* "Mathematical analysis and experimental investigation of noise in quantitative magnetic resonance imaging applied in polymer gel dosimetry", Sig. Proces. 70, 85-101 (1998).
[9] Salvat F., Fernández-Varea J.M., Sempau J.: *"*PENELOPE, a code system for Monte Carlo simulation of electron and photon transport", *Facultat de Física (ECM), Universitat de Barcelona, Spain,* 2009.