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Biodistribution of radioactive gold nanoparticles in mice

R.F.G.Gonçalves(1), L.O.Ladeira(2), K.Krambrock(2), A.H.Oliveira(1), A.V.Ferreira(3), A.P.Silveira(3), M.A.Soares(3), P.R.O.Silva(3), R.G.Santos(3) and M.V.B.Pinheiro(2)*

(1) Departamento de Engenharia Nuclear, Escola de Engenharia, Universidade Federal de Minas Gerais, Belo Horizonte, MG
(2) Departamento de Física, Universidade Federal de Minas Gerais, ICEx, Belo Horizonte, MG
(3) Centro de Desenvolvimento da Tecnologia Nuclear (CDTN), Comissão Nacional de Energia Nuclear, Belo Horizonte, MG
* Corresponding author (Pinheiro@fisica.ufmg.br).

Abstract – Gold nanoparticles have been synthesized, coated and irradiated by neutron flux. The radioactive coated-nanoparticles were intravenously injected in mice infected by Ehrlich tumor. The mice were sacrificed in several times after injection and their organs and tissues were analyzed in a gamma detector to determine the biodistribution of the nanoparticles. The results had shown that nanoparticles concentration in tumor is 100% higher than in healthful tissues.

Gold nanoparticles (AuNPs) represent a novel technology in the field of particle-based tumor targeting drug delivery, early-stage diagnosis and tumor radiotherapy [1]. In recent studies, AuNPs have been assayed in mice (2.7 g kg^{-1} animal) as X-Ray contrast agent for tumor diagnosis [2]. Unfortunately, this concentration becomes prohibitive for humans applications. In this study, we analyzed the biodistribution of neutron irradiated gold nanoparticles administered in mice (700 μg kg^{-1} animal). The studies involving neutron irradiation were realized at TRIGA Mark IPR-R1 reactor, operating at 100 kW to create a thermal and epithermal neutron flux of 6.6 x 10^{11} and 3.0 x 10^{10} n cm^{-2} s^{-1}, respectively. Over neutron flux, ^{197}Au (100% isotopic abundance) transmutes in ^{198}Au by neutron capture, emitting prompt gamma. The gold nanoparticles (AuNPs) were synthesized by Turkevich method [3]. The AuNPs were coated (AuNP-PVP) by a surfactant agent, poly(vinylpirrolidone) k30 (PVP k30), to hinder agglomeration in pH 7.4 and increase the blood clearance. These nanoparticles were irradiated for 5 minutes and submitted to neutron activation analysis (NAA). The neutron reaction ^{197}Au(n,γ)^{198}Au and gold concentration (103 μg mL^{-1}) were confirmed and the atomic force microscopy (AFM) showed diameters of 110 ± 20 nm for AuNP-PVP (Fig. 1). Toxicological studies involving non-irradiated nanoparticles (AuNPs-PVP) intravenously injected in healthful mice were realized and no toxic effects were detected 2, 14 and 30 days after injection. For biodistribution studies, AuNPs-PVP were neutron irradiated for 1 hour and mixed with saline 9.0% 9v:1v. After, 200-250 μL were intravenously injected in Swiss female mice implanted with Ehrlich tumor in the leg. The mice were sacrificed in different time periods and their organs, tissues, blood and urine were analyzed in a gamma detector with 39% efficiency for ^{198}Au gamma energy (411.8 keV). The amount of ^{198}Au injected in each mouse produced about 800,000 counts per minute (cpm). The tissues were counted for 60 seconds each one. The results had shown that AuNPs go preferentially to some organs like liver and spleen and the AuNPs-PVP's concentration in tumor is 100% higher than in healthful tissues in some time periods (Fig. 2), indicating that ^{198}AuNPs can be used as contrast agent for imaging in Single Photon Emission Tomography (SPECT), decreasing 10^2 – 10^3 times the amount of gold needed.

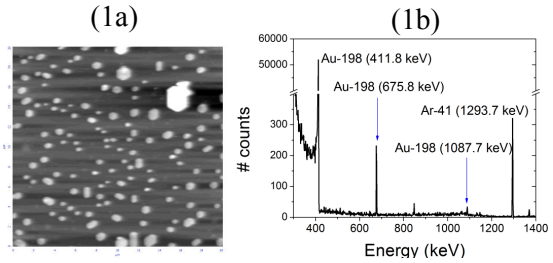

Figure 1: AuNP-PVP suspension, a) AFM image, b) and gamma spectrum.

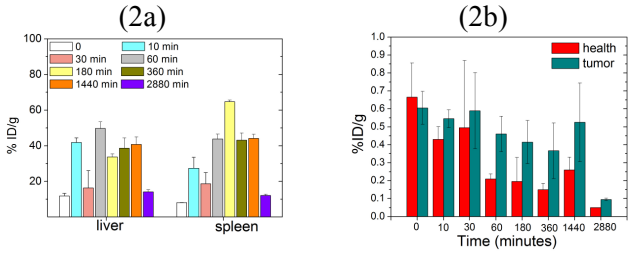

Figure 2: AuNPs biodistribution, a) in liver and spleen, b) and in health and tumor legs.

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[3] John Turkevich, Peter C. Stevenson, J. Hillier; The formation of colloidal gold (1953).