

**Purpose:** Microdosimetry is employed to estimate dose enhancement to endothelial cell nuclei, caused by radiation-induced photo/Auger electrons originating from gold nanoparticles (AuNP) targeting the tumor endothelium, during brachytherapy.

**Methods:** A tumor vascular endothelial cell (EC) is modeled as a slab of  $2\mu\text{m}$  (thickness)  $\times$   $10\mu\text{m}$  (length)  $\times$   $10\mu\text{m}$  (width). The EC nucleus is centrally located with  $5\mu\text{m}$  diameter and thickness of  $0.5 - 1\mu\text{m}$ , corresponding to nucleus size 5 - 10% of cellular volume, respectively. Analytic calculations based on the electron energy loss formula of Cole were carried out to estimate the dose enhancement to the nucleus caused by photo/Auger electrons from AuNP attached to the exterior surface of the EC. The nucleus dose enhancement factor (nDEF), representing the ratio of the dose to the nucleus with and without gold nanoparticles was calculated for different AuNP local concentrations. The investigated concentration range considers the non-uniform distribution of AuNPs, with significantly higher local concentration expected near the EC. Four brachytherapy sources were investigated, I-125, Pd-103, Yb-169, as well as 50kVp x-rays.

**Results:** For nucleus size 10 % of cellular volume, Pd-103, I-125, 50kVp, and Yb-169 yielded total nDEF values: 5.55 – 73.00, 4.81 – 58.29, 4.73 – 56.59, and 3.19 – 25.84, respectively over local concentration range of 7 – 140 mg/g. Meanwhile, for nucleus size 5 % of cellular volume, Pd-103, I-125, 50kVp, and Yb-169 yielded nDEF values of 6.38 – 89.49, 5.48 – 71.65, 5.39 – 69.87, and 3.51 – 32.31, respectively over similar concentration range.

**Conclusions:** The results predict that substantial dose enhancement to the sensitive nucleus of endothelial cells can be achieved by applying tumor vasculature-targeted AuNPs as adjuvants to brachytherapy, with low energy sources. Such magnitude dose enhancement may cause severe biological damage to tumor endothelial cells, without increased toxicity to healthy tissues not containing AuNPs.