AbstractID: 11613 Title: Comparison of the intratumoral distribution of targeted and non-targeted Cu-67-carrying composite nanodevices (CNDs)

Purpose: To investigate the tumor distribution of angiogenic microvascular targeted and non-targeted beta-emitting Cu-67-carrying composite nanodevices (CNDs) using an *in vivo* mouse tumor model.

Method and Materials: Composite nanodevices (CNDs) are third-generation "smart" nanoparticles synthesized from nanomaterials. We synthesized gold/dendrimer CND's (cRGD-AuCND) with certain peptides molecules, which target the proteins expressed in tumor microvasculature. The same constructs, but without targeting molecules (AuCND) were used as control. Labeling was achieved by complexing known activities of the beta emitter Cu-67 ions with the targeting and non-targeting CNDs in solution.
The solutions were introduced into a group of subcutaneous prostate-tumor-bearing mice via tail-vein injections. Sections of the tumors were resected and exposed on autoradiographic film. Autoradiographs were also produced of an agarose gel standard containing various concentrations of the same Cu-67 sample. These calibration films were digitized and analyzed using a threshold technique, and provided 32 regions of interest. Average pixel values of these regions were plotted versus the calculated number of beta events, and fit to a power law, to produce a sensitometric curve.

Results: The regions of interest of the calibration films varied between a high signal of 57 and a low signal of 177, based on 8-bit digital images. Images of tumor sections containing the targeted and non-targeted CND were analyzed using the sensitometric curve. The average relative activity of beta decays corresponding to the targeted cRGD-AuCND was 3.4 times higher than that of the non-targeted AuCND.

Conclusion: Based on analysis of autoradiographs, we have shown that targeted CND's are preferentially deposited in tumors. The relative activity of Cu-67 in tumor tissue was a factor of 3-4 greater for the targeted cRGD-AuCND than the non-targeted AuCND. In combination with other tumor image analysis techniques, these results will permit detailed quantitative intratumoral biodistribution and then microdosimetry of the nanodevices.