Simultaneous imaging and treatment of vulnerable plaques with tin-117m-DOTA-Annexin

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Tin-117m is a useful radionuclide both for radionuclide imaging (gamma emission 159 keV, 86%), and for radionuclide therapy (conversion electrons 141 keV, 114%). Sn-117m labeled Annexin V demonstrates promise for the noninvasive molecular imaging and treatment of active atheromatous disease [vulnerable plaque (VP), also known as thin-cap fibroatheroma (TCFA)] [1]. The rupture of VP's is a major cause of myocardial infarction and stroke. A majority of all significant cardiac events (~70%) leading to MI, including sudden death, are caused by the rupture of these thin-cap fibroatheroma lesions. VP is usually covered by a thin cap on the lumen side, and when ruptured, highly thrombogenic material is released that activates clotting cascade and induces thrombosis.

We have developed and used (i) Sn-117m electroplated coronary stents (Sn-117m stents), and (ii) Sn-117m-DOTA –Annexin [TA] for evaluating the possibility of simultaneous imaging and therapy of VP with this dual-purpose (theragnostic) radionuclide. At therapeutic doses, the conversion electrons from Sn-117m have been shown to reduce inflammation, and thus, are ideal for treating VP's, as their range in tissue (~300 μm) is approximately the same as the VP thickness in human coronary arteries. In hyperlipidemic rabbit aortas, TA was shown to bind to macrophage cells undergoing apoptosis, which are present in abundance in VP's. In relatively low doses, TA was able to image the plaque using traditional SPECT/CT cameras. Studies in a similar rabbit model, sacrificed 3d after Sn-117m-stent implantation [4 doses: 0 (cold tin), 30, 60, and 150μCi Sn-117m per 15-mm stent), upon histochemical analysis of proliferating macrophages and smooth muscle cells, demonstrated that inflammatory cells in the Sn-117m-stented segments were dramatically reduced in a dose-dependent manner. In recent studies in an Apo-E mouse VP model, TA has demonstrated a significant anti-inflammatory therapeutic effect. The plaque composition showed significantly less expression of macrophages in all treatment groups as compared to the control group. A clinical trial with TA, begun in 2010, is currently in progress [2]. The study involves human carotid endarterectomy patients who are dosed and imaged for VP, with histology as the comparison. The preliminary results thus far reveal SPECT-CT imaging of carotid in histologically proven unstable plaques.

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REFERENCES

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