

**Sn117m-DOXA-Annexin as a novel vulnerable plaque tracer. First time in humans trial.**

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**Background:** Cardiovascular disease is the main cause of death and disability in most developed countries as well as the major cause of disability. Acute cardiovascular events often involve the rupture of an atherosclerotic plaque. Optimal treatment of these patients should target the vulnerable plaques, which are at risk of rupturing, instead of stable atherosclerotic plaques. There are many imaging modalities attempting to identify vulnerable plaques, though none has succeeded in establishing a clinically useful high specificity test. Annexin-V is an apoptosis marker which occurs in Active Atheromatous Disease (AAD). Early in the course of apoptosis, the cell destined to die expresses the phospholipid phosphatidylserine (PS) on its outer leaflet. Annexin binds with nanomolar affinity to the PS expressed on the outer leaflet of the cell membrane, allowing specific identification and localization of these cells. Sn-117m labeled Annexin-V could be particularly useful for the non-invasive imaging and treatment of AAD in the carotid and coronary arteries. The half-life of Sn-117m is 14 days, and its decay involves two significant energy emissions: a low energy gamma photon and three major conversion electrons. The emitted gamma photon has an energy of 158 keV (86% abundance), so imaging in conventional gammacameras is possible.

**Methodology:** The first part of the trial had as an objective the assessment of biodistribution and radiological safety of a low dose of Sn117m-Annexin in patients selected to undergo a carotid endarterectomy. The second part (still undergoing) was performed with a higher dose of the tracer (determined by the first part's organ toxicity results) in order to enable a better image quality. All patients were followed with scintigraphic images up to 14 days after the injection. Blood and urine samples were collected to establish blood clearance and urinary excretion. Complete haematological, biochemical and liver parameters were measured in blood weekly until 4 weeks after injection. All patients underwent endarterectomy and the tissue sample was tested to obtain histological, histochemical and immunohistochemical confirmation of the presence of AAD and tracer activity within the lesion.

**Results:** 6 patients were injected with approximately 500 uCi of Sn117m-Annexin in the first part and 9 patients with 3 mCi of the tracer on the second part. Tracer activity in blood cleared after 24 hours. Urine tracer excretion at day 7 was less than 5% of total urinary activity. No significant clinical changes or blood test abnormalities were detected. Imaging of atherosclerotic plaques was not achieved in these patients, although tissue analysis confirmed the presence of the tracer on all inflammatory plaques. One patient had an abdominal aortic aneurism that showed Sn117m-Annexin uptake in the scintigraphy.

**Conclusion:** A novel inflammatory tracer, specifically targeting vulnerable atherosclerotic plaques, is presented. Biological safety and imaging capability is demonstrated. Clinical utility is still under study.

