Contribution ID: **43** Type: **poster contributions**

Heavy Metal (Gd - Er to U) loaded Nanoparticles for Indirect Radiation Therapy IRT of Cancer with Photons and Neutrons – SANS, (A)SAXS, Spectroscopy and Treatment Tests

Indirect radiation therapy IRT of cancer uses heavy metals as specific absorbers and local converters of external radiation into cell toxic secondary products, e.g. free radicals. The IRT principle can be applied with neutron and hard X-ray/ gamma photon radiation. Both can be focused by tomographic irradiation methods. The local radiotherapy effect can be enforced, if the heavy element can be deposited specifically in the tumor region by metal nanoparticles.

We have developed three kinds of biocompatible heavy metal nanoparticles: heavy metal liposomes, metal entrapping porous polymers (patent, PLGA), and lanthanide loaded magnetic nanoparticles, e.g.5% Gd, Er in Fe3O4. All metal carriers depicted a size of 100 - 200 nm for high load, bio-compatibility, and upper size limit < 0.5 µm, which avoids embolic problems.

The heavy metal load was adapted to the therapeutic sources according to their radiation spectrum and the human body transmission. For IRT with cold neutrons the optimized result was a double metal loading with Gd and excess Erbium, where the Erbium specifically catches the high energy photons (MeV) from the neutron capture of Gadolinium and converts them to soft X-rays and free radicals over Auger electrons, acting locally at the tumor site. For monochromatic synchrotron radiation (60-120 keV) and clinical LINAC sources Lanthanides of (A>65, Gd-Lu) and heavier elements (Pt, Au, Bi, U) were identified for suitable high body transmission at E > 60keV) by their high K-electron absorption energy and absorption coefficient ("white line" absorption).

The structure and metal load of the heavy metal nanoparticles for IRT, produced at GMP conditions, was investigated by a combination of SANS and DLS at ILL-D11, gamma spectros-copy at ILL-GAMS4-PN3 and by (A)SAXS at ESRF-ID01, DESY and BESSY-9T. Therapy tests with dummies, cancer cell cultures, pig tissue and tumor-rats where performed with neutrons at ILL-D22 with EMBL/CIBB Grenoble, with LINAC-source photons at the radiooncology clinics Gutenberg University Mainz, and monochromatic synchrotron photons at ESRF-ID17 with BioMedical facility BMF. The development resulted in a palliative treatment method for primary glioblastoma, which may be developed to a permanent healing method for other cancer types.

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