BIOLOGICAL BEHAVIOUR OF ^{90}Y-LABELED MICRO- AND NANOPARTICLES IN TUMOR-BEARING MICE

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Radioisotopes such as ^{90}Y that emit beta-particles are well known to be suitable for use in tumor therapy. In addition, the delivery of a variety of therapeutics using nanoparticles has become a large field of research in recent years. This study examined the biological behavior of three different micro- and nanoparticle formulations that carry the therapeutic ^{90}Y radioisotope. The first formulation was ^{90}Y-labeled citrate-coated superparamagnetic iron-oxide nanoparticles (^{90}Y-CA-SPIONs), the second was mesoporous silica-coated superparamagnetic iron-oxide nanoparticles (^{90}Y-Mag-MSN), and third formulation was ^{90}Y-labelled albumin microspheres (^{90}Y-AMS). All three formulations are shown to be stable over the relevant period of radioisotope decay. The sizes of particles were 22nm, 386nm, and 38μm for ^{90}Y-CA-SPIONs, ^{90}Y-Mag-MSN, and ^{90}Y-AMS, respectively. The biodistribution studies were done using tumor-bearing BALB/c mice. The results showed that, after the *i.v.* injection, the biodistribution was dependent on particle sizes. Thus, smaller particles (^{90}Y-CA-SPIONs and ^{90}Y-Mag-MSN) were taken up mainly by the liver and spleen (>90%ID), and larger particles (^{90}Y-AMS) were taken up entirely by the lungs. None of the formulations had a tumor uptake of more than 1%ID. After the direct intratumoral injection, all three formulations have shown to be stable, and radioactivity remained only in tumors during the four days of follow-up. This study confirms the delivery of nanoparticles to solid tumors after *i.v.* injection is a challenge due to the low uptake by tumor tissue. Nevertheless, all three examined materials have shown to be suitable for a direct intratumoral application, and ^{90}Y-AMS is suitable for radioembolization (SIRT) procedures.

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BIOLOŠKO PONAŠANJE ^{90}Y-OBELEŽENIH MIKRO- I NANOČESTICA KOD MIŠEVA SA TUMORSKIM KSENOGRAFTIMA

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Radioizotopi, kao što je ^{90}Y, koji emituju beta-čestice su pogodni za upotrebu u terapiji tumora. Pored toga, isporuka terapeutika pomoću nanočestica predstavlja poslednjih godina veliko polje istraživanja. U ovoj studiji je ispitivano biološko ponašanje tri različite formulacije mikro- i nanočestica obeleženih terapeutskim radioizotopom ^{90}Y. Prvu formulaciju su činile ^{90}Y-obeležene su perparamagnetne nanočestice gvožđe-oksida obložene citratom (^{90}Y-CA-SPIONs), druga je bila superparamagnetna nanočestica gvožđe-oksida obložena mezoporoznom silikom (^{90}Y-Mag-MSN), a treća formulacija je bila ^{90}Y-obeležena albuminska mikrosfera (^{90}Y-AMS). Pokazalo se da su sve tri formulacije stabilne tokom perioda poluraspada radioizotopa. Veličine čestica bile su 22 nm, 386 nm i 38 μm za ^{90}Y-CA-SPION, ^{90}Y-Mag-MSN i ^{90}Y-AMS, respektivno. Studije biodistribucije su urađene korišćenjem BALB/c miševa sa tumorskim ksenograftima. Rezultati su pokazali da, nakon *i.v.* injekcije, biodistribucija radioobeleženih čestica zavisi od njihove veličine. Prema tome, manje čestice (^{90}Y-CA-SPIONs i ^{90}Y-Mag-MSN) se uglavnom nakupljaju u jetri i slezini (>90%ID), a veće (^{90}Y-AMS) u plućima. Nakupljanje čestica u tumorima je bilo manje od 1%ID. Posle direktne lokalne intratumoralne injekcije, sve tri vrste radioobeleženih čestica su pokazale visoku stabilnost, tako da se radioaktivnost zadržala isključivo u tumorskom tkivu tokom četiri dana praćenja. Ova studija potvrđuje da je nakupljanje nanočestica u solidnim tumorima nakon *i.v.* injekcije izazov zbog malog preuzimanja od strane tumorskog tkiva. Ipak, sve tri ispitivane vrste čestica su se pokazale pogodnim za direktnu lokalnu intratumoralnu primenu, a ^{90}Y-AMS je pogodan i za terapiju radioembolizacijom (SIRT).

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