The combination of radionuclide-based imaging modalities such as single photon emission computed tomography (SPECT) and positron emission tomography (PET) with magnetic resonance imaging (MRI) is likely to become the next generation of clinical scanners. Hence, there is a growing interest in the development of SPECT- and PET-MRI agents [1]. These dual-modality agents may allow users to make the most of the high sensitivity of PET/SPECT and the high anatomical resolution and soft tissue contrast of MRI in a synergistic fashion. To this end, we have developed a new class of SPECT/PET-MR imaging agents based on the conjugation of radiolabeled bisphosphonates (BP) directly to the surface of superparamagnetic iron oxide (SPIO) nanoparticles (Figure 1) [2]. We demonstrate the high potential of the BP-iron oxide conjugation using radiolabeled BPs (\(^{64}\text{Cu}\) for PET or \(^{99m}\text{Tc}\) for SPECT), and Endorem/Feridex, a liver MRI contrast agent based on SPIO. The labeling of SPIOs with BPs can be performed in one step at room temperature if the SPIO is not coated with an organic polymer. Heating is needed if the nanoparticles are coated, as long as the coating is weakly bound as in the case of dextran in Endorem. The size of radiolabeled Endorem was characterised by TEM (5 nm, \(\text{Fe}_3\text{O}_4\) core) and DLS (106 ± 60 nm, \(\text{Fe}_3\text{O}_4\) core + dextran). EDX, Dittmer-Lester and radiolabeling studies demonstrate that the BP is bound to the nanoparticles and that it binds to the \(\text{Fe}_3\text{O}_4\) cores of Endorem, and not its dextran coating. The bimodal imaging capabilities and excellent stability of these nanoparticles were confirmed in vivo using MRI and nanoSPECT-CT or nanoPET-CT imaging, showing that the radionuclides and Endorem co-localise in the reticuloendothelial system (liver and spleen) and the lymph nodes, as expected for particles of the composition and size of Endorem. To the best of our knowledge, these are the first examples of radiolabeling SPIOs with BP conjugates and the first examples of radiolabeling SPIO nanoparticles directly onto the surface of the iron oxide core, and not its coating. This work lays down the basis for a new generation of SPECT/PET-MR imaging agents in which the BP group could be used to attach functionality to provide targeting, stealth/stability and radionuclides to \(\text{Fe}_3\text{O}_4\) nanoparticles and other inorganic materials of biomedical interest using very simple methodology readily amenable to GMP.
References


Figures

**Figure 1**