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Development and Pre-clinical Evaluation of New ^{64}Cu-NOTA-Folate Conjugates for PET Imaging of Folate Receptor-Positive Tumors

Authors : Norah Al Hokbany, Ibrahim Al Jammaz, Basem Al Otaibi, Yousif Al Malki, Subhani M. Okarvi

Abstract : Objective: The folate receptor is over-expressed in a wide variety of human tumors. Conjugates of folate have been shown to be selectively taken up by tumor cells via the folate receptor. In an attempt to develop new folate radiotracers with favorable biochemical properties for detecting folate receptor-positive cancers. Methods: we synthesized ^{64}Cu-NOTA- and ^{64}Cu-NOTAM-folate conjugates using a straightforward and simple one-step reaction. Radiochemical yields were greater than 95% (decay-corrected) with a total synthesis time of less than 20 min. Results: Radiochemical purities were always greater than 98% without high-performance liquid chromatography (HPLC) purification. These synthetic approaches hold considerable promise as a rapid and simple method for ^{64}Cu-folate conjugate preparation with high radiochemical yield in a short synthesis time. In vitro tests on the KB cell line showed that significant amounts of the radio conjugates were associated with cell fractions. Bio-distribution studies in nude mice bearing human KB xenografts demonstrated a significant tumor uptake and favorable bio-distribution profile for ^{64}Cu-NOTA- and ^{64}Cu-NOTAM-folate conjugate. The uptake in the tumors was blocked by the excess injection of folic acid, suggesting a receptor-mediated process. Conclusion: These results demonstrate that the ^{64}Cu-NOTAM-folate conjugate may be useful as a molecular probe for the detection and staging of folate receptor-positive cancers, such as ovarian cancer and their metastasis, as well as monitoring tumor response to treatment.

Keywords : folate, receptor, tumor imaging, ^{64}Cu-NOTA-folate, PET
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