

## Synthesis of a $^{99m}\text{Tc}$ -labeled substance P derivative for detection of glioblastoma tumors

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**Background and Aims:** Malignant gliomas are the most common primary brain tumors in adults with a high mortality risk and still associated with a poor prognosis despite advances in medical sciences. Neurokinin1 receptors (NK1R) are over expressed in all malignant glioma stages including astrocytomas (grade I/II/III) and glioblastoma (grade IV). The distribution density of NK1R correlates with the degree of malignancy as well. Substance P (SP) is a member of tachykinin family neuropeptides with specific affinity for NK1R. This study investigated the labeling of a SP analog with  $^{99m}\text{Tc}$  for imaging of NK1R positive tissues.

**Methods:** A modified derivative of SP was designed and synthesized using a standard F-moc strategy. The crude peptide was purified by semi-preparative RP-HPLC method and then characterized by analytical HPLC and LC/Mass. The purified peptide was labeled with  $^{99m}\text{Tc}$  on its specified conjugation site. Labeling yield and radiochemical analysis were performed by ITLC and HPLC methods equipped with a gamma detector. The stability of radiopeptide was checked in the presence of human serum at 37 °C in 24 h periods. Biodistribution of radiopeptide was studied on normal mice and the NK1R binding internalization and externalization rates were studied in human glioblastoma cell lines.

**Results:** A labeling yield of >95% was obtained and peptide conjugate showed good stability in human serum in vitro. An acceptable specific binding to cell lines was observed ( $15 \pm 60\%$  at 4 h). In vivo distribution studies in normal mice showed a low uptake in bone, liver, blood and muscles. A high uptake was occurred in kidneys, intestine, colon and salivary glands.

**Conclusions:** This study could promote the peptide receptor radiation therapy (PRRT) for Glioblastomas by  $^{186/188}\text{Re}$  or  $^{131}\text{I}$  labeled SP analogs in the future.

**Keywords:**  $^{99m}\text{Tc}$  labeling; Substance P; Glioblastoma; Cell line