The goal of this research is to cyclize octreotide analogues with $^{99m}$Tc and $^{186/188}$Re radiometals to be used as diagnostic and therapeutic agents for neuroendocrine tumors, respectively. Several series of octreotide analogues that differ in their sequences, and/or coordination systems ($S_2N_2$ and $S_3N$) were developed. Their in vitro receptor binding affinity toward somatostatin receptors was measured via IC$_{50}$ studies.

In vitro stability studies were carried out under physiological conditions on $^{99m}$Tc-cyclized analogues in phosphate buffered saline, mouse serum, and under high cysteine concentration. The only analogue that expressed high receptor binding affinity was not stable at the tracer level; however, the other analogues were stable at the tracer level but at the expense of their receptor affinity.

The effect of metal-cyclization on Tyr$^3$-octreotate’s receptor binding site was determined via three-dimensional molecular structure calculation, using two-dimensional NMR experiments as experimental constraints. From the obtained structures, it was concluded that the metal-cyclized Tyr$^3$-octreotate’s receptor binding site configuration was, to some extent, similar to that of the usually disulfide-cyclized counterpart.