Tc-99m labeled tissue-type plasminogen activator: Preparation, stability and preliminary imaging of thrombus-bearing rats

Kazuo Itoh,* Eriko Tsukamoto,* Toshiya Nishibe,** Shoki Sakurama,***
Masahiro Ieko,*** Tatsuzo Tanabe** and Masayori Furudate*

*Department of Nuclaer Medicine, **Second Department of Surgery, and
***Second Department of Internal Medicine, Hokkaido University School of Medicine

Tissue-type plasminogen activator (t-PA) is a thrombolytic agent that directly binds to fibrin formed in clots. In terms of radiolabeling and nuclear imaging, t-PA has several advantages in Tc-99m labeling: it is stable in acidic solution at pH 3, which is suitable for labeling Tc-99m by a method of stannous reduction and blood disappearance after administration is rapid, which is desirable for imaging targets using short-lived radionuclides.

Recombinant t-PA was labeled with Tc-99m by a method of stannous reduction without significant degradation of biochemical activity, over 95% of which was retained after the labeling procedure. Labeling efficiency in paper chromatography was over 98%. The moiety of hydrolyzed Tc-99m that was not eluted through the Sephadex column was estimated to be less than 10%. Tc-99m labeled t-PA, however, appeared to become unstable when diluted with normal saline. Nevertheless, in *in vitro* fibrin binding, Tc-99m labeled t-PA showed high affinity with fibrin: 80% of 100 ng/ml of Tc-99m t-PA bound to 10^{-5} mol of the fibrinogen. Preliminary animal studies also showed a concentration of Tc-99m labeled t-PA at fresh thrombi formed in the inferior vena cava.

Tc-99m labeled t-PA appears to have potential for thrombus imaging and the preparation of an instant kit.

Key words: recombinant tissue-type plasminogen activator (t-PA), Tc-99m labeling, scintigraphy, thrombus imaging