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In vivo distribution of Tc-99m labeled recombinant tissue-type plasminogen activator in control and thrombus-bearing rats

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In vivo distribution of Tc-99m labeled recombinant tissue-type plasminogen activator (Tc-99m-rt-PA) was studied in control rats and thrombus-bearing rats. To compare fibrin binding *in vivo* with that *in vitro*, Tc-99m-rt-PA binding to fibrin gel *in vitro* was also imaged.

Rapid blood clearance and accumulation into the liver and kidneys were observed in both control and thrombus-bearing rats. Accumulation in the stomach, which indicates instability of labeled rt-PA *in vivo*, was very low until two hours after injection. Tc-99m-rt-PA accumulation in the clots was higher than that in skeletal and heart muscles, although it was lower than in blood, liver, and kidneys. Administration of aprotinin, an antifibrinolytic agent, significantly prolonged clot accumulation of Tc-99m-rt-PA at 30 minutes after injection. These results suggest that fibrinolysis is responsible for the low rt-PA concentration in the clots. A scintigram of a thrombus-bearing rat demonstrated increased radioactivity at the clot forming site. On the other hand, Tc-99m-labeled human albumin, which was used as a control, was not accumulated in the clot. Tc-99m-rt-PA binding to fibrin gel *in vitro* was clearly imaged.

By comparison, *in vivo* fibrin binding of Tc-99m-rt-PA was much lower than *in vitro*. The reasons for low thrombus uptake *in vivo* may be: 1. biochemical inactivation of extrinsically administered rt-PA by t-PA inhibitor. 2. fibrinolysis by rt-PA activated plasminogen. Overcoming these limitations will enable Tc-99m-rt-PA to reach the stage of clinical trials.

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