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Novel Method of Greatly Enhanced Delivery of Liposomes to Lymph Nodes[1]

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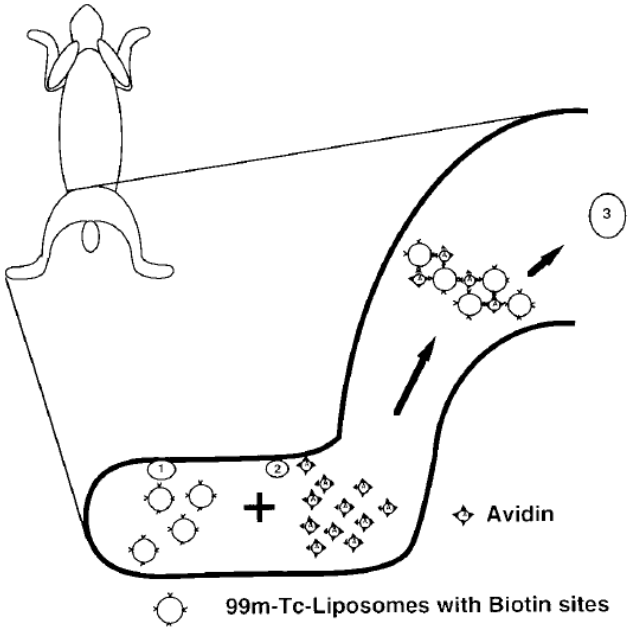
Intravenously administered liposomes are versatile carriers for drugs, contrast agents, biologics, and DNA. Liposomes and other colloidal particles are currently under investigation as lymph node delivery vehicles. After s.c. injection, conventional liposomes move into the lymphatic vessels, but are poorly retained in each draining lymph node (<2% injected dose). In this report, we describe a novel method for greatly enhancing the retention of liposomes in the lymph nodes. This system is comprised of a s.c. injection of biotin-coated liposomes in an area where lymph node targeting is desired, followed by an adjacent s.c. injection of avidin. As the avidin moves through the lymphatic vessels, it causes aggregation of biotin-coated liposomes that are also in the process of migrating through lymphatic vessels. These aggregated liposomes become trapped in the next encountered lymph node. In the present study, experimental rabbits were s.c. administered biotin-coated liposomes in both hind feet, followed by an adjacent injection of avidin, whereas control rabbits were administered biotin-coated liposomes in both hind feet without the avidin. At 24 h, rabbits receiving avidin retained 13.7% of the injected liposomes in popliteal nodes and 2.3% in iliac nodes, whereas control rabbits retained only 1.7% of the liposomes in popliteal nodes and 0.3% in iliac nodes. Blood and liver uptake of the biotin-coated liposomes was greatly decreased in the experimental rabbits receiving avidin. This novel liposome delivery system may prove useful for the delivery of chemotherapeutic drugs, vaccine antigens, and biologic agents to lymph nodes.



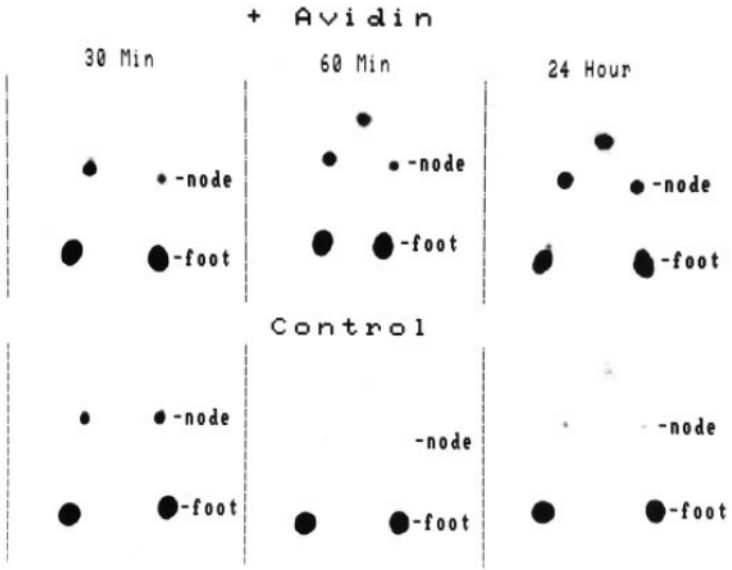


Fig. 3. Characteristic scintigraphic images of the legs and lower abdomen of rabbits acquired at 30 min, 60 min, and 24 h after s.c. injection of ^{99m}Tc-biotin-coated liposomes. Images of an experimental rabbit (+avidin) are depicted (top panel) compared with a control rabbit (bottom panel). The increased uptake by the popliteal nodes in the experimental animal is clearly visualized in the images acquired at 60 min and 24 h.