

Title	Lymphatic uptake of liposomes after intraperitoneal administration primarily occurs via the diaphragmatic lymphatics and is surface property dependent
Keywords (up to 5)	Lymphatic drug delivery, intraperitoneal administration, liposome
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Abstract	<p>The lymphatics play an important role in many diseases including cancer and critical illness. In the past, these diseases have been treated with small molecule drugs that have limited lymphatic distribution leading to reduced therapeutic efficacy¹. Lymphatic targeting is improved following interstitial (SC, ID) administration in nano-sized carriers. However, this results in limited access to the deep lymphatics draining the abdominal and thoracic organs^{1,2}. Intraperitoneal (IP) administration may provide greater access due to proximity. Thus, the study aimed to: (1) determine the impact of liposome surface properties (charge and derivatisation) on lymphatic uptake following IP administration; and (2) identify the major sites of lymphatic access from the peritoneal cavity. Radiolabelled, 80-160 nm liposomes with negative, neutral, or positive surface charge, or that were PEGylated, were prepared. Liposome size and charge was confirmed by DLS and cryo-TEM. Rats were IP administered 1 ml of the liposome formulations. Lymph and blood were collected periodically for 6 h. Lymph was collected from the thoracic lymph duct at either the abdomen or the jugular-subclavian junction (JSJ). After the study, lymph nodes (LNs) were collected. Thoracic lymph recovery at the abdomen was low for all liposomes (<4% of dose). In contrast, thoracic lymph recovery at the JSJ was very high (>10% of dose) for all except the positive liposomes. Up to 10 fold greater recovery was measured in the mediastinal LNs compared to mesenteric LNs. Together this data suggests that lymph access after IP administration mainly occurs above the abdomen at the diaphragm. In addition, the data confirms the potential to deliver drugs to the deep lymphatics via IP administration in liposomes. Illnesses involving the deep lymphatics may thus be better treated by IP administration of drugs in nano-sized carriers.</p>
References	<ol style="list-style-type: none"> 1. Trevaskis et al., Nat. Rev. Drug. Discov. 2015, 14, 781-803 2. Yadav et al., J. Control. Release., 2018, 272, 17-28