The study examined the impact of size on lymphatic particle distribution through intrapleural (ipl.) administration. Aminopolystyrene of three sizes, 0.29 µm, 2.18 µm, and 11.2 µm were radiolabeled with 111In and their biodistributions were evaluated in rats after ipl administration. Animals received either particles of three different sizes (4 mg, 200 µCi/animal) or unconjugated 111In Indium as control. The percentage of injected dose (%ID) per organ or sample was determined for left (L) and right (R) mediastinal lymph nodes (LN), blood, lung, and pleural wash. The biodistribution of 2.18 µm 111In-aminopolystyrene was further investigated at 6 h, 24 h, 48 h, and 72 h following ipl administration to examine the possible particle retention time. The 2.18 µm particles had significantly higher uptake in both LLN and RLN compared to other sizes. The systemic uptake was minimal. At 72 h, there was still 3.2 ± 3.2% and 2.1 ± 1.8% of injected dose retained in the LLN and RLN, respectively. Scintigraphic imaging revealed significant accumulation of the radioactivity in mediastinal nodes. Particle size has significant impact on lymphatic particle distribution through ipl administration. Approximately 2 µm seems to be a suitable size.