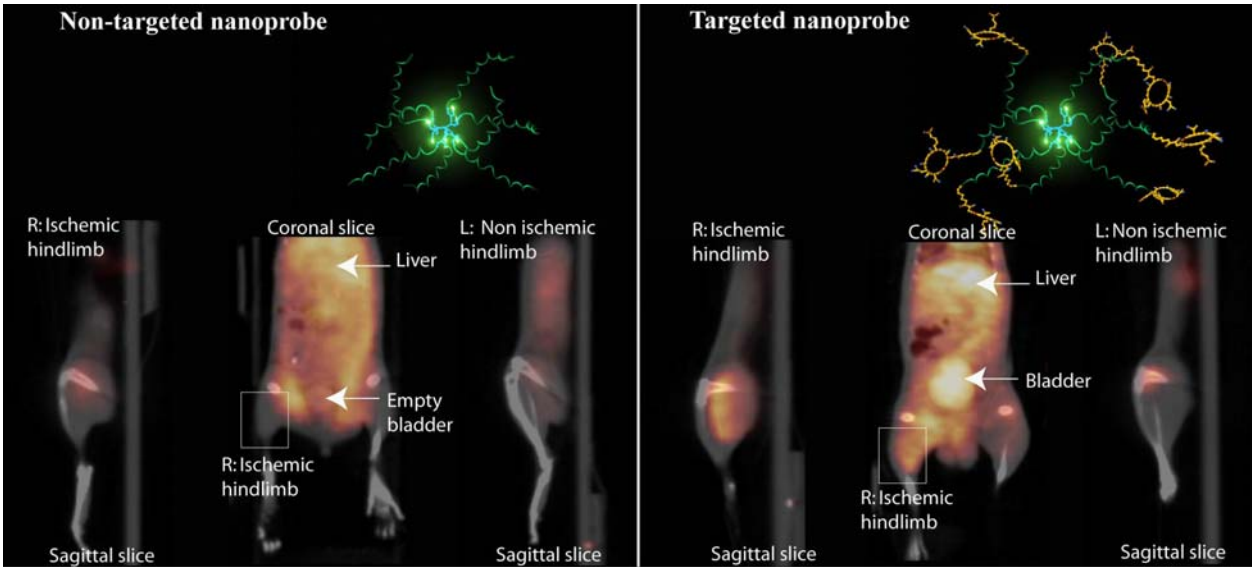
Biodegradable Nanoparticles to Image New Blood Vessels

Angiogenesis, the formation of new blood vessels, plays an important role in both cardiovascular diseases and in cancer. The ability to monitor angiogenesis non-invasively would be helpful in evaluating the management of disease therapies. A multi-institutional collaboration funded by the NHLBI Programs of Excellence in Nanotechnology has developed biodegradable dendrimers, branched nanoparticles that can be labeled with radioisotopes. The radioisotopes allow detection in the body using positron emission tomography, an advanced imaging technique that permits accurate 3D localization and quantification of the nanoparticles. The dendrimers also carry groups that protect the particles from being rapidly removed from the blood by the body's immune defense systems, and targeting groups that bind to $\alpha_v\beta_3$ integrins, proteins found specifically on new blood vessels, giving selective imaging of angiogenesis.



Addition of targeting agent to the dendrimer (right panel) increases uptake of the radiolabeled dendrimer to ischemic hindlimb of mouse where formation of new blood vessels is increased

The labeled dendrimer probes accumulate specifically in ischemic hindlimb tissue of mice, where blood vessels are being formed to restore blood flow. Omitting the targeting ligand from the nanoparticles greatly reduced the accumulation of the probe in the ischemic limb, showing that the signal was due to the labeled probe binding to the integrin proteins on the new blood vessels. These dendrimer probes will allow neoangiogenesis to be followed non-invasively in patients with atherosclerosis, peripheral artery disease, and cancer, and facilitate monitoring of therapies to increase or decrease angiogenesis.

Almutairi A., Rossin R., Shokeen M, Hagooly A, Ananth A, Capoccia B, Guillaudea S, Abendschein D, Anderson CJ, Welch MJ, and Frechet JMJ: Biodegradable dendritic positron-emitting nanoprobes for the noninvasive imaging of angiogenesis. *Proceedings of the National Academy of Sciences USA* 106(3)685-690, Jan 20 2009.

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