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PRODUCT INFORMATION AND INSTRUCTIONS

VivoVist™

VivoVist™: super contrast, long blood half-life nanoparticle
X-ray contrast agent for *in vivo** use
Best Performance • Best Price

Product Name:	**VivoVist™**
Catalog Number:	**1301-5X0.25ML (5 vials, each 0.25 mL, containing75mg at 300 mg/mL)** **1301-25X0.25ML (25 vials, each 0.25 mL, containing75mg at 300 mg/mL)** **1301-2ML (1 vial of 2 mL, containing 600 mg at 300 mg/mL)**
Appearance:	**White opalescent solution**
Quantity:	**1 vial contains 75 mg alkaline earth metal in biocompatible nanoparticles** **Packaged as 300 mg/mL solution in phosphate buffered saline, pH 7.4**
Revision:	**1.3 (February 2025)**

*not approved for human use.

Introduction

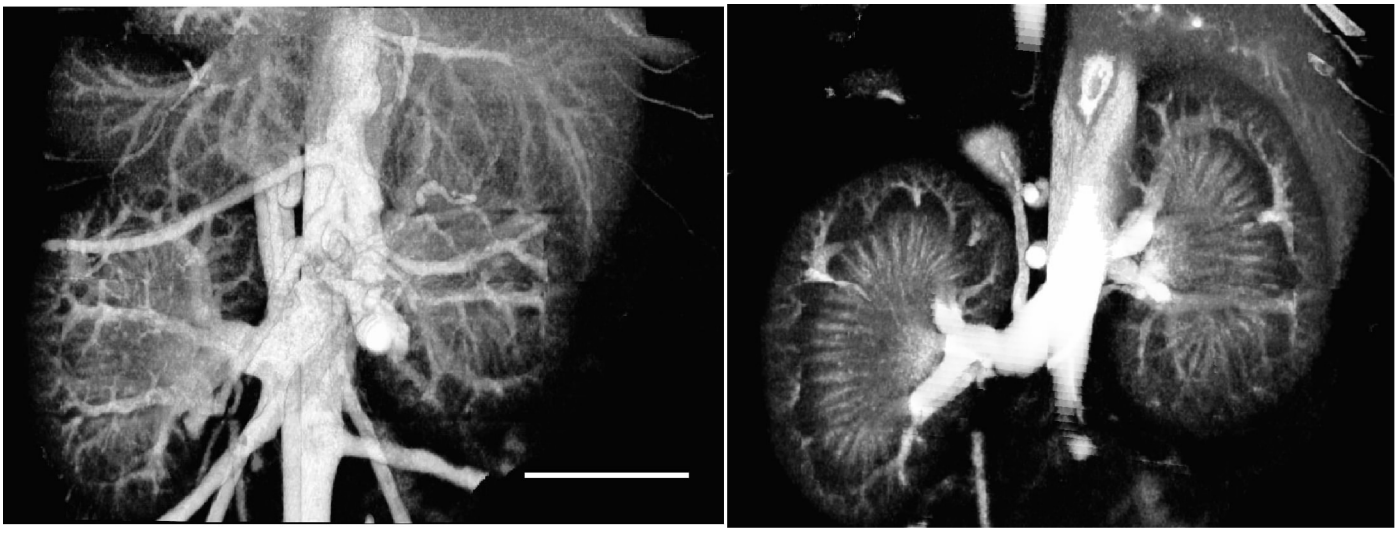
VivoVist™ is a novel nanotechnology contrast agent based on alkaline earth metal nanoparticles. VivoVist™ enables greatly enhanced X-ray imaging of blood vessels, tumors, and other tissues and organs.

Unique features and advantages of VivoVist™ include:

- Very high CT contrast, approximately 3-4 times that of alternatives. Initial blood concentration of 50 mg/mL (5%) gives >3500 HU.
- Long blood residence time: 14 hour blood half-life.
- Most affordable pricing
- Does not discolor skin.
- Low toxicity (4 g/kg is well-tolerated).
- Low osmolality, even at high concentrations.
- Easy to inject into small mouse tail vein blood vessels (typical injection volumes 0.08-0.25 mL).
- Can be imaged using MicroCT, clinical CT, planar X-ray, or mammography units.
- Enhances radiotherapy X-ray dose to tumors and other targets.

- Affordable rat imaging

The major difference will be in the results:



Live mouse microCT imaging with VivoVist™. Image taken shortly after tail vein injection of 2g/kg VivoVist with a Scanco VivaCT 80. Bar=5mm.

VivoVist™ is particularly useful for *in vivo* live animal microCT imaging, for studies of tumors, stroke, atherosclerosis and other vascular conditions, organ function, and other biological structural and functional analyses.

Contents

Each vial of VivoVist™ contains 0.25 mL of 300 mg/mL alkaline earth metal nanoparticles. **NOTE**: this is the concentration of alkaline earth metal, which does not include other atoms in the nanoparticle. It is supplied in phosphate buffered saline (PBS: 20 mM sodium phosphate with 150 mM sodium chloride, pH 7.4).

Physical Properties

The nanoparticle solution is opalescent white in color and may be diluted in water or PBS. For purification or exchange into other solvents, it may be pelleted at 5-10 kg and resuspended; sonication is recommended.

Storage

This product is shipped at ambient temperature. Upon receipt, the VivoVist™ nanoparticle solution should be stored at 4°C. For extended periods of one month or longer, it should be stored at -20°C.

INSTRUCTIONS FOR USE

NOTE: because of the density of VivoVist™, the nanoparticles may settle over time. Mix well before using by flicking vial with finger (about 10 times), vortexing or shaking thoroughly. Sonication is not typically needed but may be used. We suggest removing the label and observing that upon inversion all pellet has been resuspended in the mobile phase.

For use at >1g/kg, a slow injection time (e.g., 10 sec) is recommended, and at **3g/kg (1 standard vial in a 25g mouse) it is required**.

VivoVist™ is supplied ready to inject. A typical volume for intravenous injection into a mouse (for example into the tail vein), is 0.08 - 0.25 mL of the 300 mg/mL solution. For calibrated imaging, the amount should be scaled by animal weight. For example, for 1g/kg (body weight) in a 25 g mouse, 25 mg should be used. At 300 mg/mL, this is 0.083 mL. For 3g/kg in a 25 g mouse, 75 mg should be used. At 300 mg/mL, this is 0.25 mL (one standard vial).

Longitudinal Studies: for studies lasting several days more than one injection is possible, but the limit has not been established. There is long term residence in liver and spleen. Caution: Even with only one initial injection, if the injection is not smooth and the needle is outside the vein (a "missed" injection), the concentrated VivoVist™ can be deposited locally in the tail (evidenced by a white stationary "slug". This very concentrated material may cause local blockage and tail damage over time. Therefore, for longitudinal studies, the injections should be faultless.

Caution: most microCT units rotate the beam slowly around the animal. If the imaged region moves during this period, resolution will be compromised. The region MUST be immobilized. Some units offer gated imaging timed with breathing or heartbeat (mouse is 600 beats/min).

VivoVist™ may be diluted with PBS as needed. Typically, 1 g/kg gives very good imaging contrast. 3g/kg gives super contrast. Since the maximum tolerated dose (MTD) is >4 g/kg, larger or multiple injections are feasible.

Rat imaging: Good rat vascular imaging can be obtained at 0.54 g/kg. This equates to injecting 1.8 vials of VivoVist™ (134 mg) in a 250 g rat.

Co-injection with other agents: Combination may make the injection volume objectionably too large. This may be countered by pelleting the VivoVist, then bringing up in other co-injectates.

More specifically:

(A) Spin 2 seconds ("short" on Eppendorf tabletop centrifuge) to get all drops off lid into liquid volume. Transfer to a 1.5 mL Eppendorf tube and spin at 5 kg for 5 min in a tabletop centrifuge (all white material should then be in pellet). Discard supernatant.

(B) Mix with other agents to the desired volume and resuspend the particles by flicking with finger, inversion, vortexing strongly and place in a room temperature bath sonicator (e.g., 42 KHz 240 W) for 2 min or sonicate briefly with a tip sonicator.

Animals: Normal chow contains bone meal bits that show up as bright dots in the stomach, intestines, and abdomenal area. This greatly interferes with the imaging. Feed animals bone-free chow for 2-3 days before use if imaging this region. One source for this is Teklad Custom research, diet TD.05109, Purified diet without mineral mix, ½ inch diameter pellets, from Envigo (https://tekladapp.inotivco.com/ 800-483-5523).

Image Display & Analysis

When to scan: highest vascular contrast is immediately after IV injection, although some vessels can be contrasted and seen even 2-3 days later.

The contrast may be difficult to see from the raw data slices provided by the microCT because they are thin and noisy. Use a reconstruction program to better visualize blood vessels and other details.

At the highest resolution there are fewer counts per voxel so the images may look noisy. If desired, you can use the program to combine voxels, which reduces noise and improves visibility, but at the cost of some resolution loss.

Another way to improve image quality is to image for a longer time (more photons/voxel).

Most microCT units rotate the source around the animal, typically one revolution in 20 min to 1 hour. If the animal moves in that time this will degrade resolution upon reconstruction (which assumes no motion). Therefore, for best results, immobilize the region of interest as best as possible. The mouse heart beats at 600 beats/min, so detailed heart imaging requires gated data collection; the same goes for breathing artefacts.

X-ray Instruments

Mammography: these instruments are suitable for small animal imaging. Use of lower kVp (e.g., 22 kVp) is recommended to take advantage of the L edge alkaline earth metal absorptions. Exposures are typically 1 sec or less for a mouse, so live imaging is possible. Resolution can be < 0.1 mm.

Clinical CT: 80-100 kVp (lower kVp setting) gives the greatest contrast. Imaging time is typically a few seconds, with resolution ~0.3 mm.

MicroCT: these provide higher resolution (to even 2 microns), but the tube power is typically ~100 times less than a clinical unit. Fine area detectors mean that many tiny pixels must each receive enough counts. This requires a much longer imaging time (with many microCT scanners, 20 minutes - 2 hours) than with a clinical CT (a few seconds). Many units also slow the tube rotation down such that only 1 revolution is done in the selected imaging time (e.g., 1 hour). If the animal moves during collection of this data set, the back projection 3D reconstruction will be errant and resolution degraded. This places significant constraints for live animal imaging, and motion must be minimized, such as by immobilizing the leg or other organ or limb of interest, if highest resolution is desired. Some units offer gated imaging, and some offer a fast acquisition time (~1 min) with reduced resolution.

Cabinet X-ray units: various cabinet (refrigerator-like) X-ray units provide imaging of animals, including those from Precision X-ray (https://precisionxray.com/) and Xstrahl (https://xstrahl.com/).

Technical Assistance Available.

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