The VX2 carcinoma is a widely used model of transplantable neoplasia in the rabbit. It has been used extensively for neoplastic imaging studies, either via implantation directly in an organ to create a solid tumor, or via intravenous administration of a single-cell suspension to create pulmonary metastases. These methods create neoplasia in a known location.

To create a more realistic scenario, given that radiologists in the clinic must use contrast agents to detect neoplastic lesions in unknown locations, our goal was to create a model of widespread, unpredictable metastasis for evaluation of novel tumor avid contrast agents. We hypothesized that to test the efficacy of a novel tumor avid contrast agent, a single-cell suspension injected intra-arterially would generate widespread, small, unpredictable metastases, creating a more accurate "real world" model of the imaging challenges that radiologists face.

Materials and Methods

1. Animals. 2 SPF New Zealand White rabbits, weighing 2.75 - 3.25 kg.
2. VX2 Carcinoma Model. a. VX2 Cell Suspension. A suspension of 8-15 x 10^6 cells/ml was prepared from tumor tissue collected from donor tumor passage rabbits.
   b. Anesthesia. EMLA cream (2.5% lidocaine/2.5% prilocaine) was applied to the dorsal pinna prior to intra-arterial catheter placement.
   c. VX2 Inoculation. 0.5 ml of the cell suspension was administered intra-arterially through a 23-gauge catheter placed in the auricular artery. Another 0.5 ml of the cell suspension was administered IM in the biceps femoris.
   d. Monitoring. Rabbits were palpated daily to assess tumor progression, and monitored for dyspnea. Once the tumor in the biceps femoris reached 1.5 cm in diameter, it was assumed that metastasis from intra-arterial administration would also be present, and the rabbits were imaged.
3. Imaging. a. Anesthesia. Rabbits were pre-medicated with 0.15 mg acepromazine IV, and then induced and maintained with isoflurane via facemask (1 - 2%). b. Magnetic Resonance Imaging (MRI). A novel contrast agent 3Gd HPPH was injected into the auricular vein (30 umol Gd/kg, 10 umol Gd-HPPH/kg), and the animals were imaged at 1.5 T (GE Sigma HDX TX-1.5) in the "vascular" phase and also at 24 hr. in one rabbit, as well as in the hepatic phase, at 24 hr and 48 hr in a second rabbit. For the head and neck, coronal fat-sat T2 T208 cm and coronal three-pd post-contrast F208 images were generated; the kidneys, liver, and spleen were imaged with coronal fat-sat T2 T208 cm and coronal three-pd images. c. Postmortem Tumor Vascularisation/Computed Tomography (PET/CT). 0.93 mg (34.1 MBeq) of Fluorine-18 Fluorodeoxyglucose (FDG) was injected intravenously into each rabbit and at 30 min each subsequent PET/CT (GE Discovery ST, TX 25 cm).

FDG-PET/CT

Materials and Methods, cont.

4. Endpoints and monitoring. a. Rabbits were monitored daily for signs of dyspnea, cyanosis, lethargy, and inappetence. b. Inappetence was treated with supplemental feedings of highly palatable foods, liquid diet, and increased monitoring. c. Dyspnea and/or cyanosis was an endpoint for humane euthanasia.
5. Necropsy. a. After the 24 hour MRI rabbit #1 was euthanized by IV injection of Pentobarbital Sodium, 390 mg/kit. b. After the 48 hour MRI rabbit #2 had respiratory arrest before recovery from anesthesia.

Conclusion: intra-arterial injection of VX2 carcinoma cell suspension in rabbits provides a practical approach for generating widespread, unpredictable metastasis to effectively evaluate novel tumor-avid contrast agents in a large animal model.

References