Diagn Interv Radiol 2026; DOI: 10.4274/dir.2026.263989

INTERVENTIONAL RADIOLOGY

PICTORIAL ESSAY

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Development and angiographic utilization of the Oncopig liver cancer model: a comprehensive pictorial review

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ABSTRACT

Image-guided locoregional therapies are central to the management of liver cancer. Large-animal models are valuable preclinical tools for advancing interventional oncology because they allow testing with standard clinical imaging platforms and devices. The Oncopig™ is a genetically engineered porcine model that enables site-specific tumor formation through inducible expression of *KRAS*^{G12D} and *TP53*^{R167H} following exposure to Cre recombinase. This pictorial essay illustrates the technical methodology for liver tumor induction in Oncopigs and demonstrates the angiographic use of tumor-bearing animals for evaluation of transarterial therapies. Liver tumors were induced using an *ex vivo* transgene activation approach in which liver biopsy specimens were incubated with an adenoviral vector expressing Cre recombinase and injected percutaneously into the liver under ultrasound guidance. Tumor development occurred in 34/37 (92%) induction sites across 17 Oncopigs and was confirmed by contrast-enhanced computed tomography. Hepatic arteriography using standard clinical devices enabled selective catheterization of tumor-feeding arteries. This pictorial essay provides a technical guide for investigators studying liver-directed therapies in a translational large-animal model.

KEYWORDS

Hepatic arteriography, interventional oncology, large animal model, liver tumor induction, preclinical liver cancer model

Image-guided locoregional therapies (LRTs), including transarterial therapies, are a cornerstone of hepatocellular carcinoma (HCC) management.[1] Innovations in catheter technologies, embolic materials, pharmacological agents, and combinations with systemic therapies represent promising strategies to further improve patient outcomes.[2,3] Preclinical evaluation of these emerging approaches requires large-animal models that replicate human hepatic anatomy and are compatible with clinical interventional devices.[4] Pigs represent a valuable translational model due to their similarity to humans in terms of anatomy, physiology, and drug metabolism.[5,6] The Oncopig™ is a genetically engineered porcine model that enables site-specific tumor development through inducible expression of porcine *KRAS*^{G12D} and *TP53*^{R167H} following exposure to Cre recombinase.[7] Liver tumor induction in Oncopigs has been described in several prior studies evaluating liver-directed LRTs.[8-11] This pictorial essay illustrates the workflow for liver tumor induction in Oncopigs and demonstrates angiographic utilization of tumor-bearing animals for transarterial therapy. This technical guide provides a practical reference for investigators seeking to evaluate LRTs in a clinically relevant large-animal model.

Study animals

The results reported in this essay are based on tumor inductions in 17 male Oncopigs (age 3.5–4 months). Oncopigs were obtained from the University of Illinois Urbana-Champaign. All procedures were approved by the Institutional Animal Care and Use Committee (IACUC) (protocol code: ACC #20-110). Trained veterinary staff supported daily animal maintenance; pre-, peri-, and post-procedural care; procedural anesthesia; and euthanasia.

Handling editor: Sonay Aydın

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Received 28 March 2026; revision requested 14 May 2026; last revision requested 06 June 2026; accepted 06 June 2026.

Epub: 14.09.2026

DOI: 10.4274/dir.2026.263989

You may cite this article as: Elkhadragy L, Jordan LR, Blanco D, Guzman G, Gaba RC. Development and angiographic utilization of the Oncopig liver cancer model: a comprehensive pictorial review. *Diagn Interv Radiol*. 14 September 2026 DOI: 10.4274/dir.2026.263989 [Epub Ahead of Print].

Animal preparation

Tumor induction procedures were performed under general anesthesia with perioperative analgesia. The Oncopigs received intramuscular (IM) injections of 2.2–3.3 mg/kg of xylazine and 4.4–5.5 mg/kg of telazol for anesthetic induction. Other anesthetic regimens may also be used, in accordance with institutional veterinary and IACUC recommendations. For analgesia, 0.4 mg/kg of meloxicam was administered subcutaneously immediately before the procedure and orally once daily for 3 days thereafter. The animals were placed in left lateral recumbency, and the abdominal skin was shaved and sterilized (Figure 1).

Reagent preparation

The reagents required for Oncopig liver tumor induction include adenoviral vectors expressing Cre recombinase (AdCre) and a sterile 2-M calcium chloride solution in phosphate-buffered saline (PBS). Each liver biopsy specimen is incubated with 10^9 plaque-forming units of AdCre. Adenoviral vectors can be produced in house[12] or obtained commercially. The tumor inductions described herein utilized AdCre under the control of a cytomegalovirus promoter (Ad5CMVCre; University of Iowa Viral Vector Core, Iowa City, IA, USA). Because repeated freeze/thaw cycles reduce viral vector titers, aliquoting the AdCre into small volumes upon arrival and storage at –80°C is recommended. In accordance with biosafety precautions, AdCre handling and aliquoting must be performed in a certified Class II biosafety cabinet.[13] A sterile 2-M calcium chloride solution in PBS can be prepared in advance and stored at 4°C.

Main points

- Oncopigs™ are genetically engineered porcine models that enable site-specific tumor formation through inducible expression of *KRAS*^{G12D} and *TP53*^{R167H} transgenes.
- Liver tumors are induced by incubating liver biopsy specimens with an adenoviral vector expressing Cre recombinase (AdCre) and injecting the biopsy–AdCre mixture into the Oncopig liver.
- Tumor development can be confirmed with contrast-enhanced computed tomography or ultrasound.
- Tumor-bearing Oncopigs can be used for hepatic arteriography and testing liver-directed locoregional therapies.
- This model provides a clinically relevant translational platform for interventional oncology research.

Shortly before the procedure, the required volume of AdCre was thawed on ice. Then, PBS containing calcium chloride was added to each tube containing AdCre to a total volume of 1 mL, and the solution was mixed gently by pipetting or inverting the tube. The solution was incubated for 15 minutes at room temperature before being combined with the liver biopsy specimen.

Liver tumor induction

Under ultrasound guidance, liver biopsy specimens were obtained from anesthetized Oncopigs using an 18-gauge core needle biopsy device (Figure 2). Multiple biopsy specimens can be obtained in the same procedure setting. Each specimen was placed in a tube containing AdCre solution and incubated for 30 minutes (Figure 3). During this time, gelatin sponge was cut into small pieces (2–3 mm^2) and placed in a 3-mL syringe. Gelatin sponge serves as a scaffold to facilitate retention of the biopsy–AdCre suspension at the injection site and to reduce leakage into surrounding tissues or the peritoneal cavity following injection.[8] Following incubation, the biopsy–AdCre mixture was aspirated into a 3-mL syringe and mixed with the gelatin sponge by repeatedly passing it through a three-way stopcock to macerate the tissue and create a homogenous mixture of approximately 1-mL total volume (Figure 4). The resulting slurry was then injected percutaneously into the liver of the same Oncopig using a 16-gauge needle under ultrasound guidance (Figure 5). Up to four sites can be inoculated in each Oncopig liver, with two in each liver lobe. Injecting multiple sites provides flexibility for targeting accessible tumors using LRTs, allows assessment of potential abscopal effects in untreated tumors, and ensures that the animal can still be used for therapeutic testing if tumor induction fails at one site. Injection sites should be well separated, safely accessible, and deep enough to prevent leakage of the injected material into the peritoneum. In the experiments described, 14/17 (82%) Oncopigs received two induction injections each, and 3/17 (18%) received three induction injections each.

Biosafety precautions

As with all experiments involving viral vectors, appropriate biosafety precautions must be taken when handling AdCre,[13] and institutional biosafety committee approval must be obtained prior to initiating experiments. Adenoviruses are classified as Risk Group 2 agents, which are associated with human disease that is rarely serious and for

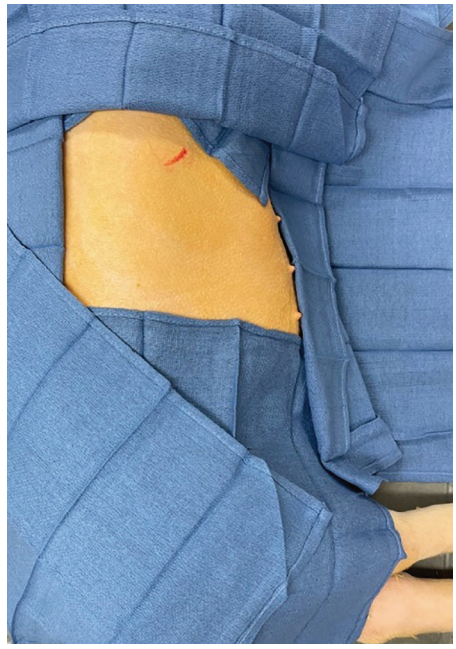

Figure 1. Preparation of Oncopigs for liver tumor induction. Animal positioned in left lateral recumbency to facilitate percutaneous liver access. Abdomen shaved, sterilized, and draped in standard surgical fashion.

which preventive or therapeutic interventions are often available. Transmission by direct contact, ingestion, aerosol exposure, or percutaneous injury may cause mild respiratory illness or conjunctivitis in healthy adults. Work involving adenoviruses generally requires Biosafety Level 2 (BSL-2) containment and procedures during preparation, manipulation, and injection. These precautions include restricted laboratory access, appropriate signage and laboratory setup, personnel training, decontamination of waste prior to disposal, and personal protective equipment to prevent skin or mucous membrane exposure.[13] Personal protective equipment for *in vivo* tumor induction procedures includes an N-95 respirator, a face shield, gloves, a disposable coverall or suit, and shoe covers. A 0.5% sodium hypochlorite solution (10% bleach) should be used to decontaminate surfaces and materials potentially contaminated with the adenovirus, including pipette tips and tubes. Animals that receive adenovirus injections should be housed under animal BSL-2 containment for 72 hours, followed by reclassification to animal BSL-1 housing after a complete cage change.

Tumor imaging

Two weeks after tumor induction, the Oncopigs underwent contrast-enhanced abdominal computed tomography (CT) to confirm tumor development (Figure 6a–c). This imaging interval was selected based on

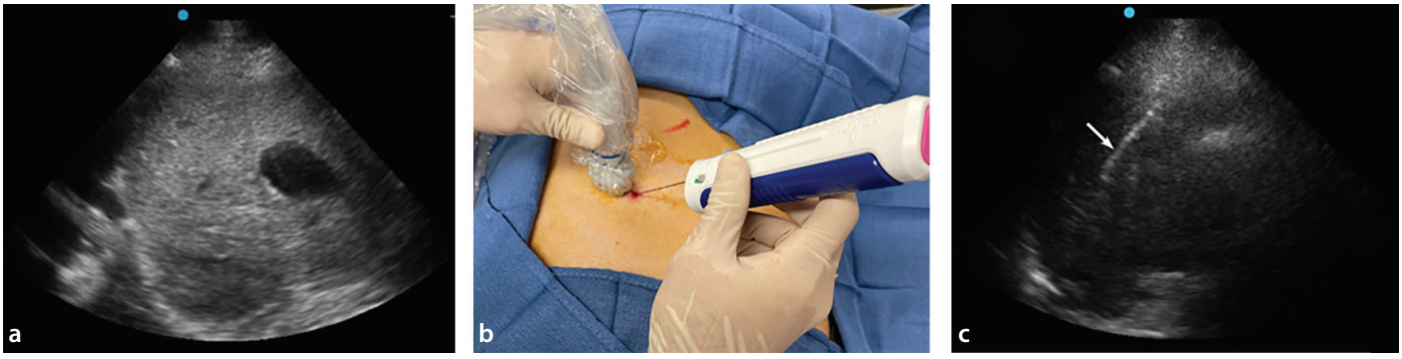

Figure 2. Obtaining liver biopsy under ultrasound guidance. **(a)** Ultrasound image prior to biopsy showing normal porcine liver tissue. **(b)** Under ultrasound guidance, 18-gauge core liver biopsy obtained from anesthetized Oncopig using an automated biopsy device (BioPince Ultra Full Core Biopsy Device; Argon Medical Devices, Plano, TX, USA). **(c)** Ultrasound image showing core needle biopsy in liver (arrow).

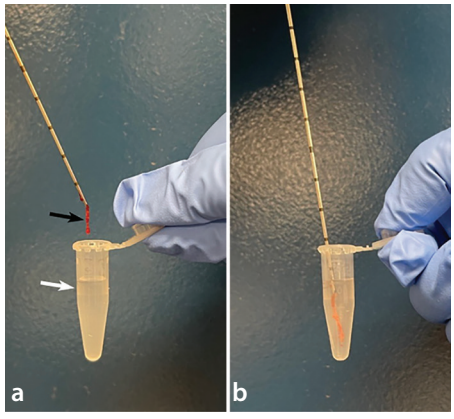

Figure 3. Incubation of Oncopig liver biopsy with adenoviral vector expressing Cre recombinase (AdCre). **(a)** Liver biopsy specimen (black arrow) placed in tube containing prepared AdCre solution (white arrow). **(b)** Biopsy–AdCre mixture incubated for 30 minutes at room temperature.

prior studies[8] and our experience demonstrating reliable tumor development within approximately 2 weeks following induction. The animals were sedated with IM injections of xylazine (2.2–3.3 mg/kg) and telazol (4.4–5.5 mg/kg) prior to imaging. Out of 37 tumor induction sites, a total of 34 tumors were detected by CT, with a mean tumor diameter of 1.8 cm (range, 1.2–2.4 cm). If CT imaging is not available, ultrasound may alternatively be used to confirm tumor development (Figure 6d).

Tumor angiographic utilization

The animals underwent hepatic arteriography in a fluoroscopy suite 3–5 days following imaging (Figure 7a–d). Following anesthetic induction with IM xylazine and telazol, the animals were endotracheally intubated and maintained under 1%–3% inhaled isoflurane anesthesia throughout the procedure. Arterial access was obtained via the common femoral artery with placement of a 5-French sheath. A 5-French catheter was used to access the celiac artery, and a 2.4-French microcatheter was then advanced into the seg-

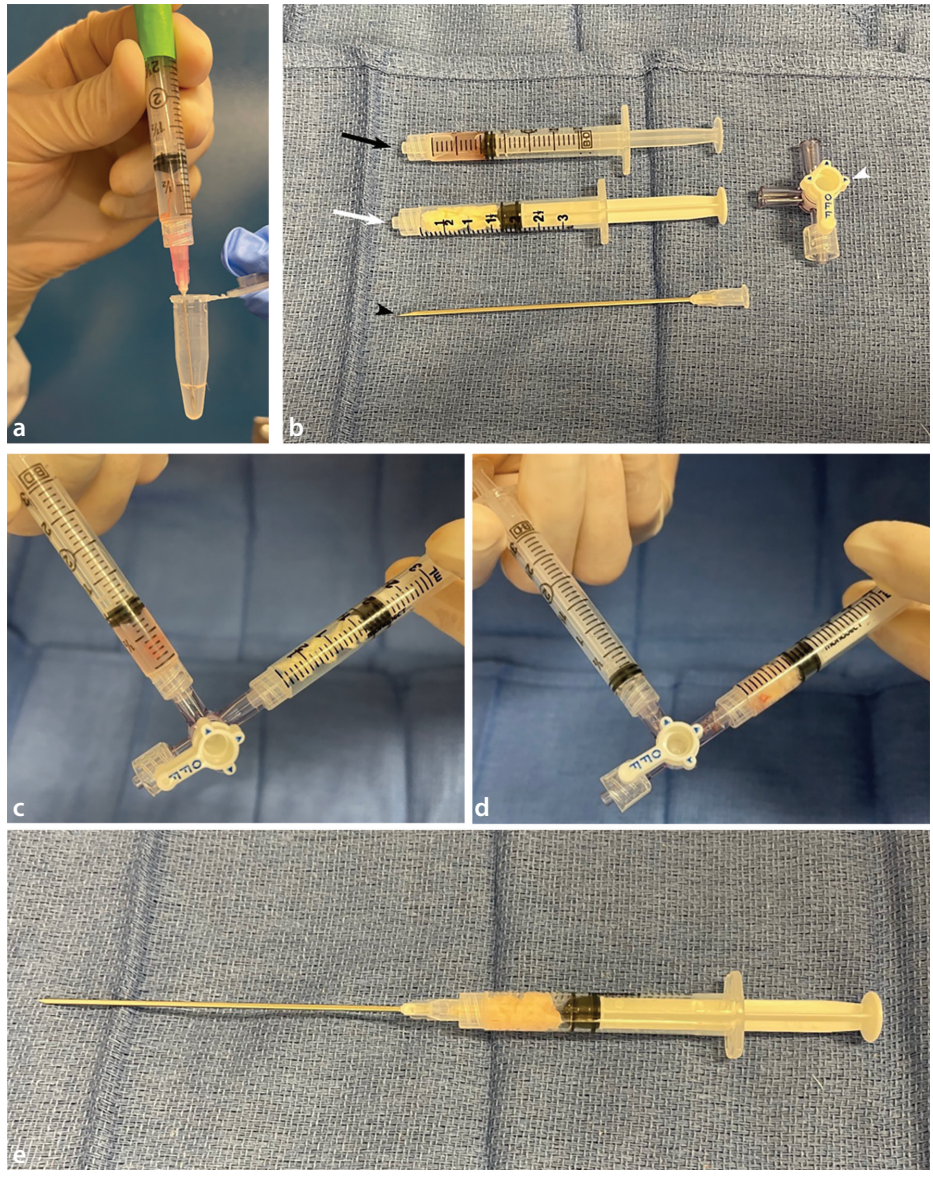

Figure 4. Mixing liver biopsy–adenoviral vector expressing Cre recombinase (AdCre) with gelatin sponge. **(a)** After 30 minutes of incubation, biopsy–AdCre mixture aspirated into 3-mL syringe. **(b)** Gelatin sponge (Surgifoam; Ethicon, Somerville, NJ, USA) cut into small fragments and placed in 3-mL syringe (approximately one-quarter of one sheet used per injection site). Photograph shows materials needed for injection, including a syringe containing biopsy–AdCre suspension (black arrow), a syringe containing gelatin sponge fragments (white arrow), a three-way stopcock (Cook Medical, Bloomington, IN, USA) (white arrowhead), and a 16-gauge 4-inch needle (Air-Tite Products Co., Inc., Virginia Beach, VA, USA) (black arrowhead). (c, **d)** Biopsy–AdCre suspension combined with gelatin sponge fragments by passing 4–5 times through three-way stopcock to macerate tissue and create slurry. **(e)** Syringe containing biopsy–AdCre and gelatin sponge suspension attached to 16-gauge needle.

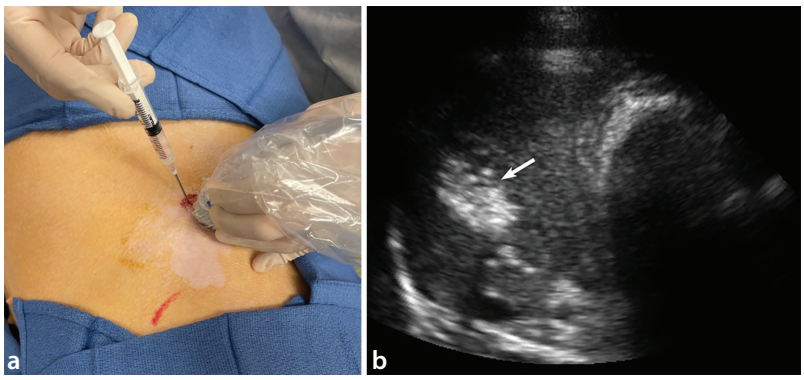

Figure 5. Ultrasound-guided percutaneous injection of the biopsy–adenoviral vector expressing Cre recombinase (AdCre) and gelatin sponge suspension. **(a)** Suspension injected percutaneously into liver of the same Oncopig under ultrasound guidance. **(b)** Ultrasound image demonstrates injected biopsy–AdCre and gelatin sponge suspension as focal hyperechoic area (arrow) within hepatic parenchyma.

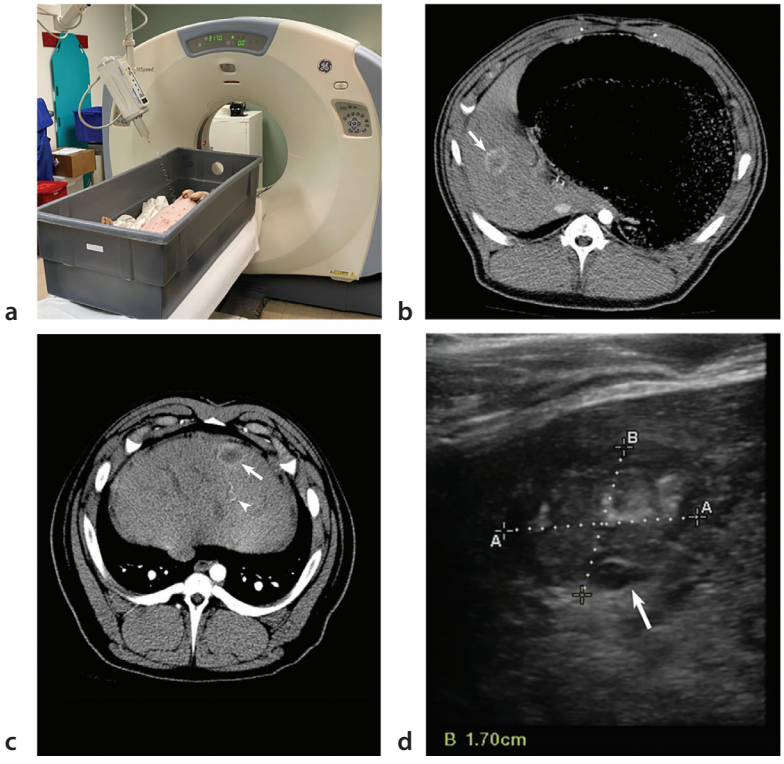

Figure 6. Confirmation of tumor formation by contrast-enhanced computed tomography (CT) or ultrasound. **(a)** Photograph of Oncopig undergoing CT imaging. Multiphase contrast-enhanced CT scans performed using a standard human clinical liver imaging protocol consisting of a non-contrast phase, followed by arterial phase at 30–35 s, portal venous phase at 60–70 s, and delayed phase at 180 s after intravenous administration of 120–150 mL of iodinated contrast injected at a rate of 4–5 mL/s. **(b)** Contrast-enhanced arterial phase CT demonstrating enhancing tumor (arrow) in right liver lobe posterior segment. **(c)** Contrast-enhanced arterial phase CT demonstrating enhancing tumor (arrow) in left liver lobe lateral segment, with perfusing left hepatic artery (arrowhead). **(d)** Ultrasound image shows discrete, mixed echogenicity liver mass (arrow).

mental arterial supply of the hepatic tumor. Catheter position can be confirmed using cone-beam CT (Figure 7e). Subsequently, LRTs such as chemoembolization (Figure 7f) and radioembolization can be performed. Herein, all Oncopigs (n = 17) underwent transarterial chemoembolization (TACE) with doxorubicin. After completion of the procedure and removal of all devices, hemostasis at the arterial access site was achieved with 10 minutes of manual compression.

Tumor response to LRTs can be assessed using cross-sectional imaging, similar to clinical practice. Contrast-enhanced CT performed 7 days after TACE demonstrated the absence of contrast enhancement within the treated lesion in all animals, consistent with complete response (Figure 8).

Tumor harvest and characterization

The timing of euthanasia should be determined according to the experimental objectives. In this study, the Oncopigs were euthanized 4 days after liver angiography and TACE using a commercial euthanasia solution containing sodium pentobarbital and sodium phenytoin, administered intravenously at a dose of 1 mL per 10 lb of body weight. Following euthanasia, midline and transverse incisions were made to expose the abdominal cavity, and the liver was removed. Tumors were harvested for downstream analyses (Figure 9a). Tissue sections for histologic evaluation were fixed in 10% neutral buffered formalin, and samples intended for genomic and transcriptional analyses were flash-frozen and stored at –80°C. Tumor development occurred in 34/37 (92%) inoculation sites. Harvested tumors were evaluated histologically and demonstrated poorly differentiated carcinoma accompanied by immune cell infiltrates (Figure 9c, d).

Discussion

Large-animal models are important for preclinical evaluation of novel LRTs. Although mouse models of HCC are widely available,[14] their small size precludes the ability to test LRTs. The Oncopig is a transgenic porcine model that enables temporal and site-specific tumor induction. This pictorial essay describes the development and angiographic utilization of Oncopig liver tumors using an *ex vivo* transgene activation approach (Figure 10).

Tumor induction success rates have been high across studies using this approach. In this cohort, tumors developed in 34/37 (92%) induction sites in male Oncopigs. Although only male Oncopigs were utilized in this study to reflect the epidemiologic male predominance of HCC, similar success rates were reported by Nurili et al.,[8] who observed tumor formation in 44/48 (92%) sites across 18 female Oncopigs. These findings suggest that tumor induction is robust across sexes.

In this study, AdCre was used for tumor induction. The AdCre dose utilized in this study was selected based on the previously published approach described by Nurili et al.[8] Adeno-associated virus (AAV) vectors may represent an alternative approach, as they are less immunogenic than adenoviruses and require only BSL-1 animal containment. However, AAV use in this model has not yet been evaluated.

An alternative method for developing liver tumors in Oncopigs involves *in vitro* transgene activation in isolated hepatocytes followed by autologous implantation of transformed cells.[15,16] Although this ap-

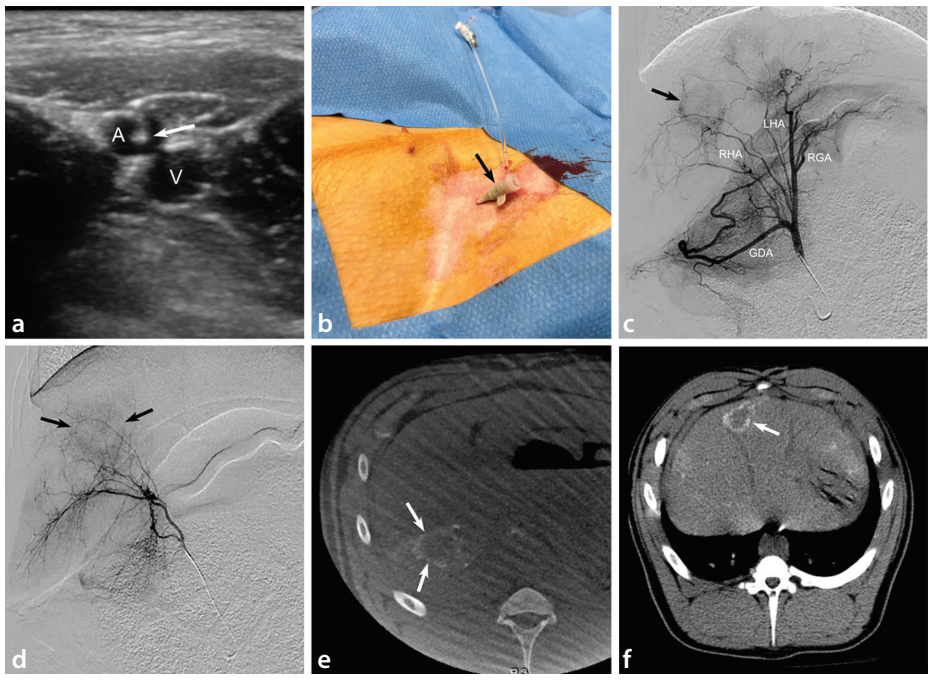

Figure 7. Angiographic utilization of tumor-bearing Oncopigs. **(a)** Ultrasound image demonstrating common femoral artery **(A)** and vein **(V)**, with 21-gauge needle (Micropuncture Access Set; Cook, Bloomington, IN, USA) access (arrow) into common femoral artery. **(b)** Placement of 5-French vascular sheath (Pinnacle; Terumo, Somerset, NJ, USA) (arrow) into common femoral artery. **(c)** Celiac arteriography performed using 5-French catheter (Sos Omni Selective; AngioDynamics, Queensbury, NY, USA). Hepatic arteriography subsequently performed after placement of coaxial 2.4-French microcatheter, showing hypervascular liver tumor (arrow) and hepatic vascular anatomy (gastroduodenal artery: GDA, right hepatic artery: RHA, left hepatic artery: LHA, right gastric artery: RGA). **(d)** Selective right posterior hepatic arteriogram demonstrating hypervascular tumor (arrows). **(e)** Cone-beam computed tomography (CT) scan performed from right posterior hepatic artery demonstrating arterial perfusion of hypervascular tumor (arrows). **(f)** Non-contrast CT following conventional transarterial chemoembolization demonstrating ethiodized oil accumulation within liver tumor (arrow).

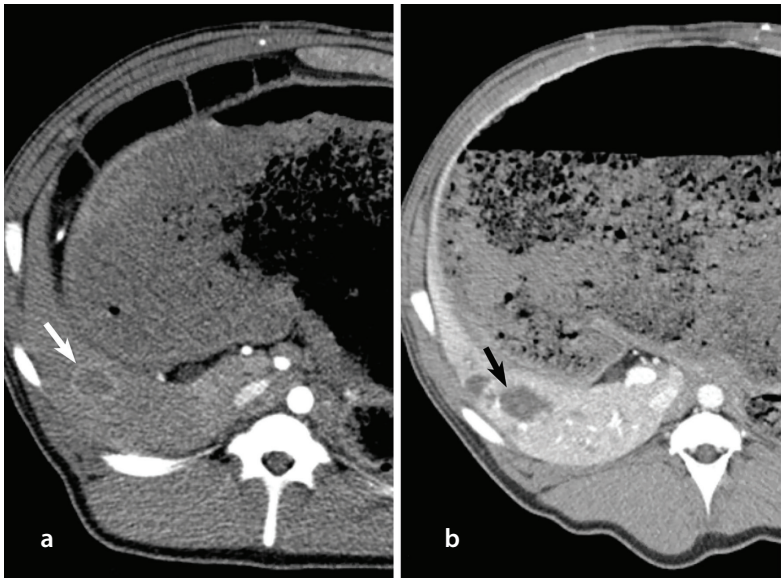

Figure 8. Evaluation of therapy response by imaging. **(a)** Pre-treatment contrast-enhanced computed tomography (CT) demonstrating enhancing liver tumor (arrow). **(b)** Post-treatment contrast-enhanced CT after transarterial chemoembolization illustrating tumor non-enhancement (arrow), consistent with radiologic complete response.

proach enables hepatocyte-specific transgene expression and facilitates *in vitro* gene editing of Oncopig HCC cells,[17] it is more labor intensive, resource demanding, and time consuming than the *ex vivo* approach described here.

Although the described approach enables rapid and reproducible tumor induction, the model has several limitations. These include tumor regression, which has been reported in Oncopig liver tumors as well as other tumor types developed in the Oncopig model.[8,18] Tumor regression is thought to be related, at least in part, to anti-tumor immune responses characterized by cytotoxic T-cell and inflammatory immune cell infiltration.[19] Consequently, this model may be best suited for short-term interventional studies performed shortly after tumor induction, prior to the onset of tumor regression. In the present study, angiographic procedures were performed approximately 2 weeks following tumor induction to maximize the likelihood of treating viable tumors. Additional longitudinal studies with serial imaging are needed to more fully characterize tumor growth kinetics and regression patterns in this model and to further inform optimal timing for therapeutic interventions.

Additional limitations include the absence of liver cirrhosis, a common comorbidity in patients with HCC,[1] and the fact that induced tumors in this model demonstrate poorly differentiated histologic features and may not fully recapitulate human HCC histopathology.[8,18] Given that porcine hepatic arterial anatomy differs slightly from human hepatic arterial anatomy,[20] procedural planning and catheterization approaches may need to be adapted. Nevertheless, the porcine hepatic vasculature is sufficiently comparable for translational angiographic and catheter-based interventional studies, and published studies support the applicability of human angiographic devices in the Oncopig.[8-11] Despite these limitations, the Oncopig model represents a valuable translational platform for evaluating liver-directed LRTs in a clinically relevant large-animal setting.[18]

Acknowledgements

We thank the veterinarians and staff at the University of Illinois Chicago (UIC) animal facility for their support with pig procedures and husbandry, the UIC Research Histology Core, and the UIC Research Tissue Imaging Core for technical support. Oncopig™ was developed at the University of Illinois and is commercially licensed to Sus Clinicals, Inc. Figure 10 was created with BioRender.com.

Footnotes

Conflict of interest disclosure

R.C.G. reports research contracts from Sus Clinicals, Inc.; consulting fees from Lytos Therapeutics; participation on Sus Clinicals,

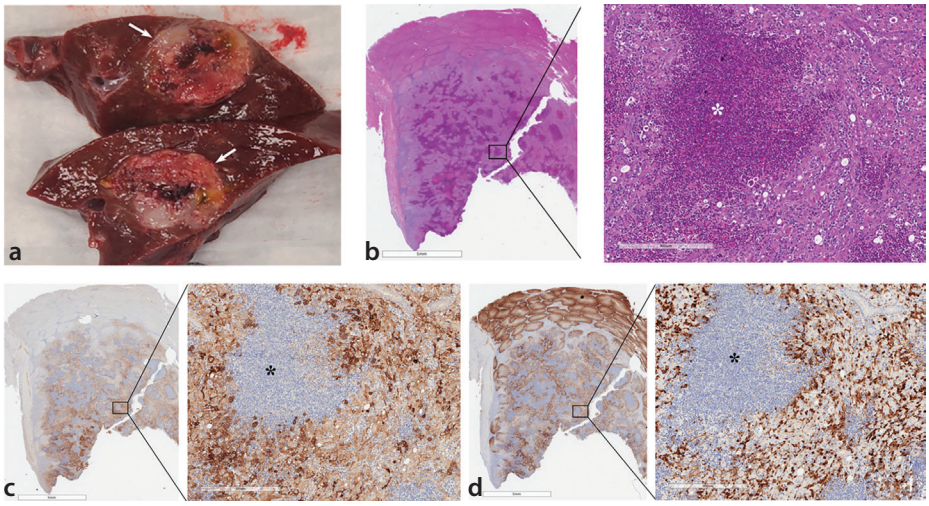

Figure 9. Tumor harvest and histologic characterization. **(a)** Representative picture of tumor (arrows) harvested from liver following resection. **(b–d)** Hematoxylin and eosin-stained section **(b)** of Oncopig liver tumor. Immunohistochemical staining for *KRAS*^{G12D} **(c)** demonstrating positively stained tumor cells (brown color), confirming expression of the induced transgene. Immunohistochemical staining for Arginase-1 (hepatocyte/hepatocellular carcinoma marker) **(d)** depicting positive staining (brown color) in *KRAS*^{G12D}-positive tumor cells as well as adjacent normal liver tissues. Overall, histological analysis demonstrates poorly differentiated carcinoma accompanied by immune cell infiltrates, including lymphocytes, eosinophils, and neutrophils. Tumor comprising pleomorphic neoplastic cells with coarse chromatin and high nuclear-to-cytoplasmic ratio that stained positive for Arginase-1 and *KRAS*^{G12D}. Tumor also contained clusters of Arginase-1-positive and *KRAS*^{G12D}-positive cells histopathologically consistent with high-grade dysplasia. Within the tumor were islands (*) containing dystrophic microcalcification and apoptotic cells. Scale bars: 5 mm (low-magnification images) and 300 µm (high-magnification images).

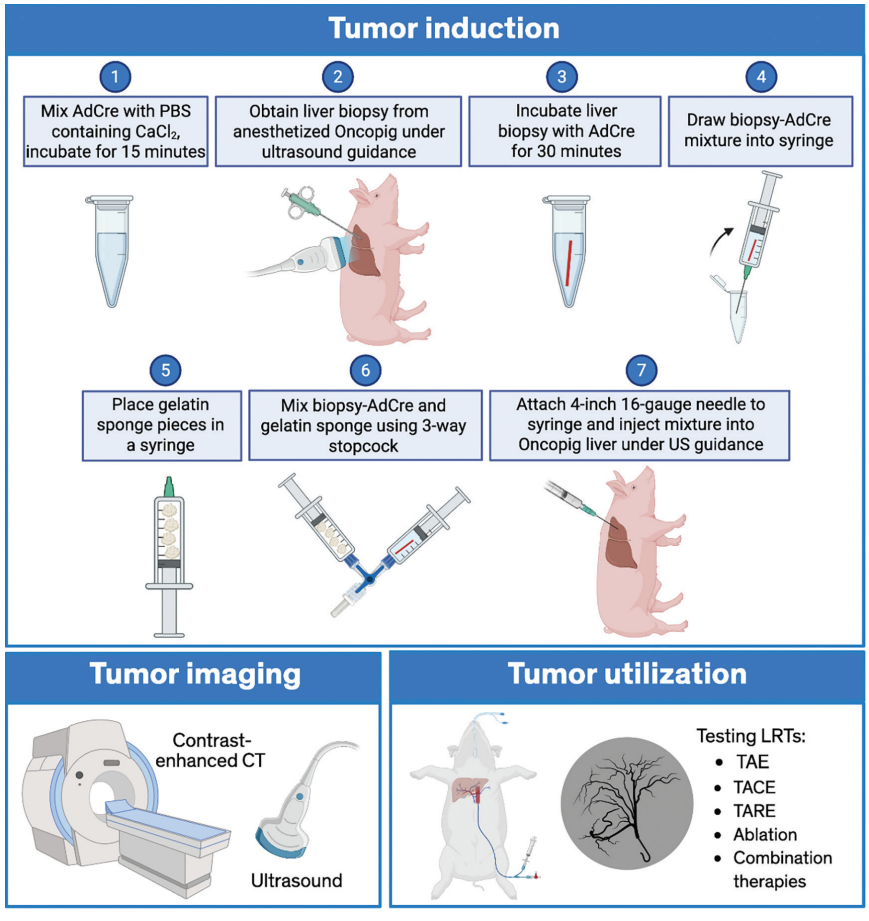

Figure 10. Schematic overview of Oncopig liver tumor induction and angiographic utilization. AdCre: adenovirus expressing Cre recombinase, PBS: phosphate-buffered saline, CaCl2: calcium chloride, TAE: transarterial embolization, TACE: transarterial chemoembolization, TARE: transarterial radioembolization.

Inc. Scientific Advisory Board, Fluidx Medical Technology Advisory board, and Kaveri University Advisory board; and stock or stock options in Sus Clinicals, Inc. The remaining authors declare no conflicts of interest.

Funding

This work was supported by the National Cancer Institute [1R01CA283548] and contracts from Guerbet USA LLC and Sus Clinicals, Inc.

References

1. Llovet JM, Kelley RK, Villanueva A, et al. Hepatocellular carcinoma. *Nat Rev Dis Primers*. 2021;7(1):6. [Crossref] Erratum in: *Nat Rev Dis Primers*. 2024;10(1):10. [Crossref]
2. Greten TF, Mauda-Havakuk M, Heinrich B, Korangy F, Wood BJ. Combined locoregional-immunotherapy for liver cancer. *J Hepatol*. 2019;70(5):999-1007. [Crossref]
3. Llovet JM, De Baere T, Kulik L, et al. Locoregional therapies in the era of molecular and immune treatments for hepatocellular carcinoma. *Nat Rev Gastroenterol Hepatol*. 2021;18(5):293-313. [Crossref]
4. Aravalli RN, Golzarian J, Cressman EN. Animal models of cancer in interventional radiology. *Eur Radiol*. 2009;19(5):1049-1053. [Crossref]
5. Hou N, Du X, Wu S. Advances in pig models of human diseases. *Animal Model Exp Med*. 2022;5(2):141-152. [Crossref]
6. Lunney JK, Van Goor A, Walker KE, Hailstock T, Franklin J, Dai C. Importance of the pig as a human biomedical model. *Sci Transl Med*. 2021;13(621):eabd5758. [Crossref]
7. Schook LB, Collares TV, Hu W, et al. A genetic porcine model of cancer. *PLoS One*. 2015;10(7):e0128864. [Crossref]
8. Nurili F, Monette S, Michel AO, et al. Transarterial embolization of liver cancer in a transgenic pig model. *J Vasc Interv Radiol*. 2021;32(4):510-517.e3. [Crossref]
9. Cournoyer L, Liu Y, Jaroch DB, et al. Pressure enabled drug delivery (PEDD) of nelitolimod increased therapeutic delivery, reduced immunosuppression, and improved efficacy in porcine and murine liver tumor models. *Front Oncol*. 2025;15:1655794. [Crossref]
10. Jaroch DB, Liu Y, Kim AY, Katz SC, Cox BF, Hullinger TG. Pressure-enabled drug delivery significantly increases intra-arterial delivery of embolic microspheres to liver tumors in a porcine model. *J Vasc Interv Radiol*. 2025;36(3):499-504.e1. [Crossref]
11. Schachtschneider K, Arepally A, Blanco D, et al. Preclinical evaluation of Yttrium-90 radioembolization in the Oncopig liver cancer model. *J Vasc Interv Radiol*. 2024;35(3 Suppl):S226. [Crossref]

12. Dumitrescu M, Trusca VG, Fenyo IM, Gafencu AV. An efficient method for adenovirus production. *J Vis Exp*. 2021;(172). [Crossref]
13. Collins DE, Reuter JD, Rush HG, Villano JS. Viral vector biosafety in laboratory animal research. *Comp Med*. 2017;67(3):215-221. [Crossref]
14. Santos NP, Colaço AA, Oliveira PA. Animal models as a tool in hepatocellular carcinoma research: a review. *Tumour Biol*. 2017;39(3):1010428317695923. [Crossref]
15. Gaba RC, Elkhadragy L, Boas FE, et al. Development and comprehensive characterization of porcine hepatocellular carcinoma for translational liver cancer investigation. *Oncotarget*. 2020;11(28):2686-2701. [Crossref]
16. Schachtschneider KM, Schwind RM, Darfour-Oduro KA, et al. A validated, transitional and translational porcine model of hepatocellular carcinoma. *Oncotarget*. 2017;8(38):63620-63634. [Crossref]
17. Elkhadragy L, Regan MR, M Totura W, et al. Generation of genetically tailored porcine liver cancer cells by CRISPR/Cas9 editing. *Biotechniques*. 2021;70(1):37-48. [Crossref]
18. Elkhadragy L, Gaba RC, Niemeyer MM, Schook LB, Schachtschneider KM. Translational relevance and future integration of the oncopig cancer model in preclinical applications. *Annu Rev Anim Biosci*. 2025;13(1):465-481. [Crossref]
19. Overgaard NH, Principe DR, Schachtschneider KM, et al. Genetically induced tumors in the oncopig model invoke an antitumor immune response dominated by cytotoxic CD8β+ T cells and differentiated γδ T cells alongside a regulatory response mediated by FOXP3+ T cells and immunoregulatory molecules. *Front Immunol*. 2018;9:1301. [Crossref]
20. Nykonenko A, Vávra P, Zonča P. Anatomic peculiarities of pig and human liver. *Exp Clin Transplant*. 2017;15(1):21-26. [Crossref]