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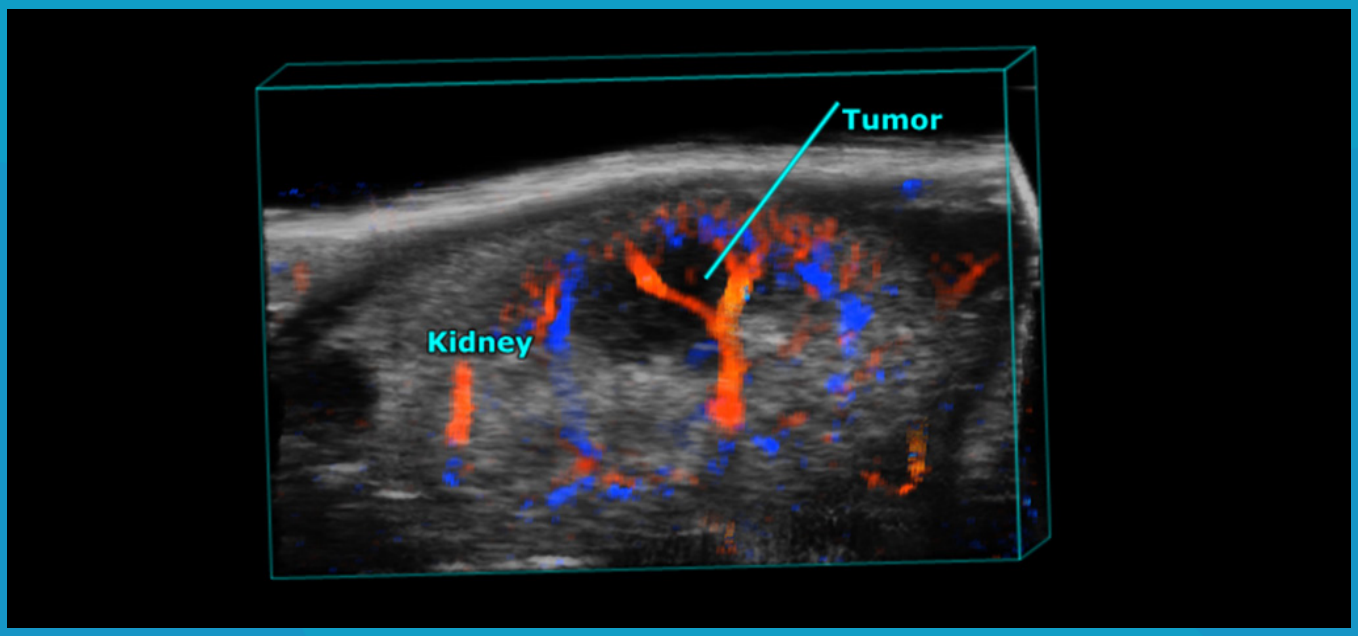

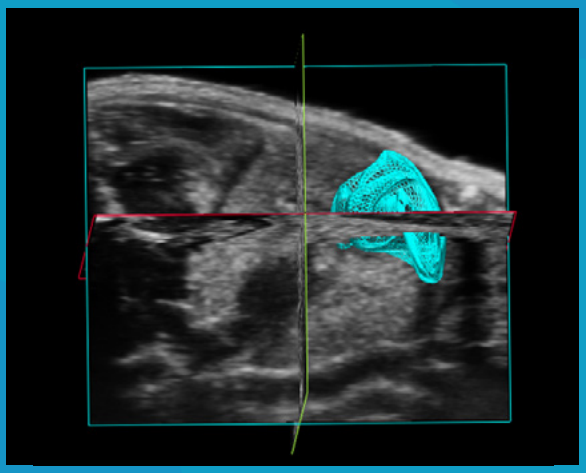

Ultrasound and Photoacoustics for Cancer Research

Key Publications

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PANCREATIC CANCER

Abou-Elkacem, L. *et al*. Thy1-Targeted Microbubbles for Ultrasound Molecular Imaging of Pancreatic Ductal Adenocarcinoma. *Clin. Cancer Res.* clincanres.2057.2017 (2018). doi:10.1158/1078-0432.CCR-17-2057

Huynh, A. S. *et al*. Development of an orthotopic human pancreatic cancer xenograft model using ultrasound guided injection of cells. *PLoS One* **6**, e20330 (2011).

Sastra, S. A. & Olive, K. P. Quantification of Murine Pancreatic Tumors by High-Resolution Ultrasound. in *Methods in Molecular Biology* **980**, 249–266 (2013).

Pysz, M. A. *et al*. Vascular Endothelial Growth Factor Receptor Type 2–targeted Contrast-enhanced US of Pancreatic Cancer Neovasculature in a Genetically Engineered Mouse Model: Potential for Earlier Detection. *Radiology* **274**, 790–799 (2015).

Snyder, C. S. *et al*. Complementarity of ultrasound and fluorescence imaging in an orthotopic mouse model of pancreatic cancer. *BMC Cancer* **9**, 106 (2009).

FEATURED PUBLICATION SUMMARY

Huynh, A. S. *et al*. Development of an orthotopic human pancreatic cancer xenograft model using ultrasound guided injection of cells. *PLoS One* **6**, e20330 (2011).

Research Question: *Can an orthotopic pancreatic cancer xenograft model be developed minimally invasively using ultrasound-guided injection?*

- Human pancreatic cancer xenografts studied
- Comparison done for tumor uptake and growth between image-guided needle injection (IGNI) of cells versus surgical implantation
- Tumor growth monitored weekly using high-frequency ultrasound
- 100% take rate for tumor models produced from two cell lines using IGNI
- There was no difference in tumor growth between the models
- In vivo and ex vivo fluorescence showed higher correlation in the IGNI models versus the surgical model due to absence of scar tissue

Image-guided injection of cancer cells represents a non-invasive, precise and reproducible method of orthotopic pancreatic cancer model development.

PROSTATE CANCER

Fagerland, S. M. T. *et al*. Ultrasound-Mediated Delivery of Chemotherapy into the Transgenic Adenocarcinoma of the Mouse Prostate Model. *Ultrasound Med. Biol.* **46**, 3032–3045 (2020).

Aalinkeel, R. *et al*. Nanotherapy silencing the interleukin-8 gene produces regression of prostate cancer by inhibition of angiogenesis. *Immunology* **148**, 387–406 (2016).

Singh, S. *et al.* Quantitative volumetric imaging of normal, neoplastic and hyperplastic mouse prostate using ultrasound. *BMC Urol*. **15**, 1–11 (2015).

Xuan, J. W. *et al.* Functional neoangiogenesis imaging of genetically engineered mouse prostate cancer using three-dimensional power Doppler ultrasound. *Cancer Res*. **67**, 2830–9 (2007).

KIDNEY CANCER

Ingels, A. *et al*. Ultrasound Molecular Imaging of Renal Cell Carcinoma: VEGFR targeted therapy monitored with VEGFR1 and FSHR targeted microbubbles. *Sci. Rep*. **10**, 7308 (2020).

Noord, R. A. V. A. N. et al. Tissue-directed Implantation Using Ultrasound Visualization for Development of Biologically Relevant Metastatic Tumor Xenografts. *In Vivo (Brooklyn)*. **791**, 779–791 (2017).

Linxweiler, J. *et al*. Experimental imaging in orthotopic renal cell carcinoma xenograft models: comparative evaluation of high-resolution 3D ultrasonography, in-vivo micro-CT and 9.4T MRI. *Sci. Rep*. **7**, 1–10 (2017).

LIVER CANCER

Zhang, Y. *et al*. Contrast-Enhanced Multispectral Photoacoustic Imaging for Irregular Hepatectomy Navigation: A Pilot Study. *ACS Biomater. Sci. Eng.* **6**, 5874–5885 (2020).

Yu, Q. *et al*. Label-free Visualization of Early Cancer Hepatic Micrometastasis and Intraoperative Image-guided Surgery by Photoacoustic Imaging. *J. Nucl. Med*. jnumed.119.233155 (2019).

Graham, K. C. *et al*. Three-dimensional high-frequency ultrasound imaging for longitudinal evaluation of liver metastases in preclinical models. *Cancer Res*. **65**, 5231–7 (2005).

FEATURED PUBLICATION SUMMARY

Lavaud, J. *et al*. Noninvasive monitoring of liver metastasis development via combined multispectral photoacoustic imaging and fluorescence diffuse optical tomography. *Int. J. Biol. Sci*. **16**, 1616–1628 (2020).

Research Question: *Can Angiostamp800 act as a targeted photoacoustic (PA) contrast agent in the detection of liver metastasis?*

- Using PA and fluorescence (fDOT) imaging, Angiostamp800 and ICG were used to monitor liver metastasis in a mouse model
- PA imaging showed increased liver HbT signal, relating to tumor angiogenesis, and decreased oxygen saturation (sO2), reflecting hypoxia development
- Multispectral imaging of ICG showed a decrease in signal during metastasis development, correlating with decrease in liver function
- ICG imaging alone was unable to differentiate between disease stages
- PA imaging of tumor targeting Angiostamp800 allowed differentiation between healthy, early and advanced stages of liver metastasis

PA imaging provided higher significance in the discrimination between metastatic stages versus fDOT.

BRAIN CANCER

Li, W. *et al*. MicroRNA-378 enhances radiation response in ectopic and orthotopic implantation models of glioblastoma. *J. Neurooncol*. **136**, 63–71 (2018).

Lavaud, J., Henry, M., Coll, J. L. & Josserand, V. Exploration of melanoma metastases in mice brains using endogenous contrast photoacoustic imaging. *Int. J. Pharm*. **532**, 704–709 (2017).

Askoxylakis, V. *et al*. Preclinical Efficacy of Ado-trastuzumab Emtansine in the Brain Microenvironment. *JNCI J. Natl. Cancer Inst*. **108**, 1–10 (2016).

Kloepper, J. *et al*. Ang-2/VEGF bispecific antibody reprograms macrophages and resident microglia to anti-tumor phenotype and prolongs glioblastoma survival. *Proc. Natl. Acad. Sci*. **113**, 4476–4481 (2016).

LUNG CANCER

Lee, H. *et al*. Development and evaluation of a CEACAM6-targeting theranostic nanomedicine for photoacoustic-based diagnosis and chemotherapy of metastatic cancer. *Theranostics* **8**, 4247–4261 (2018).

Ghaddar, N. *et al*. Detection of Lung Tumor Progression in Mice by Ultrasound Imaging. *J. Vis. Exp*. **2020**, 1–8 (2020).

FEATURED PUBLICATION SUMMARY

Raes, F. *et al*. High Resolution Ultrasound and Photoacoustic Imaging of Orthotopic Lung Cancer in Mice: New Perspectives for Onco-Pharmacology. *PLoS One* **11**, e0153532 (2016).

Research Question: *To validate ultrasound (US) and photoacoustics (PA) as robust, non-invasive, nonradiative tools to assess therapeutic efficacy in mouse models of cancer.*

- Orthotopic lung cancer model used to monitor and characterize tumor growth with various imaging modalities (US, PA, CT and bioluminescence)
- CT used clinically to monitor tumor growth; radiation is a concern
- US can accurately measure tumor size in vivo; correlates well with CT
- Vascularity was measured with contrast enhanced ultrasound and Power Doppler
- PA used to detect differences in oxygenation and hypoxia within the tumor
- Targeted contrast revealed VEGFR2 distribution correlated with tumor hypoxia

Validates US and PA as high-throughput, longitudinal method for studying efficacy of anticancer therapies.