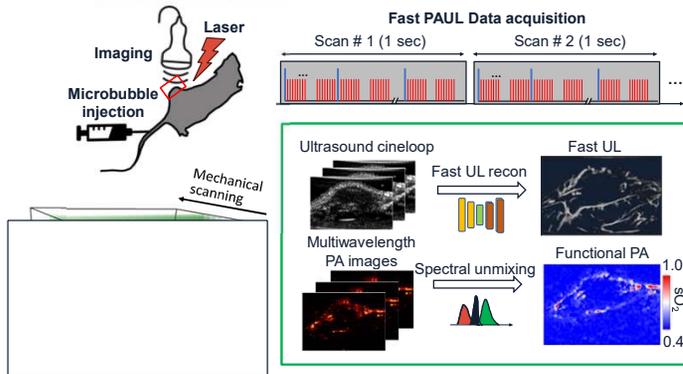


INTRODUCTION

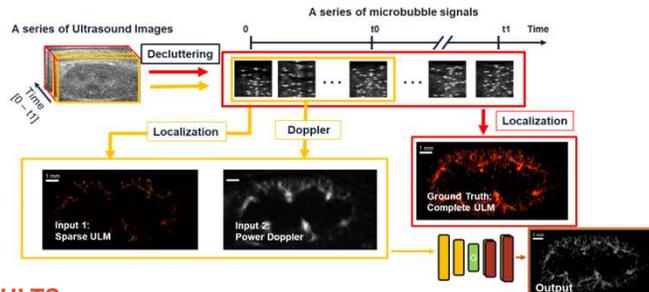
Combining photoacoustic (PA) imaging with microbubble-based ultrasound localization (UL) imaging enables **high-resolution**, in vivo visualization of anatomical, structural, physiological, and molecular features of tumor microenvironment in **deep tissue**. However, the inherently slow acquisition speed of UL imaging (typically >1 minute per frame) renders 3D imaging of the tumor microenvironment impractical—**requiring over 4 hours of continuous contrast agent injection** with mechanical scanning. To address this, we developed a deep learning–accelerated PAUL imaging approach to speed-up 3D tumor microenvironment visualization.

METHODS

Deep learning enhanced Fast PAUL imaging system



Training workflow of deep learning model

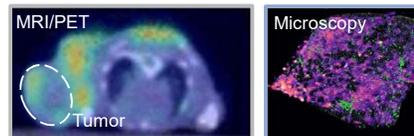
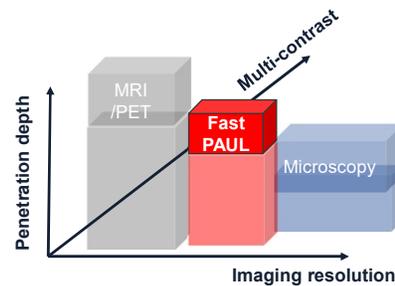


RESULTS

Deep learning massively accelerates PAUL imaging

Power Doppler offers an overview of tumor vasculature but lacks details of small vessels. Sparse UL generated by microbubble-localization has finer vasculature but incomplete vessel reconstruction. A deep learning model combining power Doppler and sparse UL creates DL-UL image for a complete and fine-grained view of tumor vasculature.

Understanding the tumor microenvironment remains challenging due to limitations in current imaging tools — some (optical microscopy) can only capture shallow details, while others (MRI/PET) penetrate deeper but blur the details. In this study, we aim to develop advanced ultrasound imaging to uncover the hidden details buried deep within tumors.



RESULTS

Fast PAUL imaging visualizes whole tumor molecular fingerprint

Fast PAUL imaging reveals a **stronger accumulation** of tumor-targeting probes compared to non-targeting probes. These results are further validated by fluorescence imaging of excised tumors labeled with the targeting probes.

Fast PAUL imaging tracks angiogenesis and hypoxia dynamics during tumor growth

Fast PAUL imaging reveals a **progressive decline** in tumor vasculature density and oxygen saturation during tumor growth

CONCLUSIONS

In this study, we developed a deep learning–accelerated, multi-parametric fast PAUL imaging technique to probe the tumor microenvironment with high resolution and deep tissue penetration. Leveraging deep learning enhancement, the system enables 3D mapping of tumor vasculature, oxygenation, and molecular features. Fast PAUL imaging reveals critical characteristics of the tumor microenvironment, offering valuable insights for early detection of tumor progression and the development of personalized treatment strategies.

ACKNOWLEDGEMENTS

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