Multi-modal Assessment of Longitudinal Growth of Liver Metastases in a Mouse Model of Colon Carcinoma

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INTRODUCTION

The liver is a common site for distal metastases in colon and rectal cancers, and if detected early has an improved prognosis. A number of studies in the clinical domain have analyzed the relative merits of different imaging modalities for improved and earlier detection of liver metastases. To the best of our knowledge, such a rigorous study has not been undertaken in preclinical research. Here, we present a longitudinal, multi-modality study that assesses two imaging techniques for liver metastases in a mouse model of colon carcinoma: high-field T2-weighted MRI and contrast-enhanced microCT.

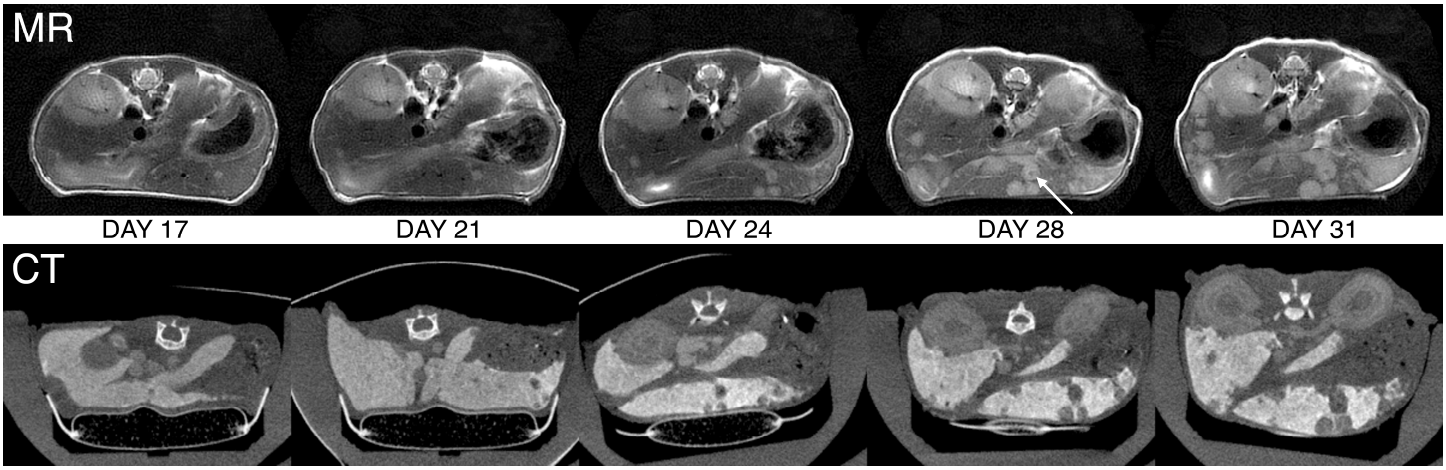
METHODS

All animal studies were approved by the Duke Institutional Animal Care and Use Committee. The liver tumor model implant was performed at Piedmont Research Center. Female athymic nude mice were implanted with 5 x 10^6 HT29 colon carcinoma cells in a volume of 50µl with a 25-gauge needle in the spleen. After a 2-minute pause post-injection, a splenectomy was performed and the surgical site was closed. The procedure was conducted under isoflurane anesthesia. Animals were allowed to recover for 9 days, after which they were imaged twice a week for a total of 7 time-points with both high-field MRI and microCT. Mice were anesthetized using isoflurane delivered by nose cone. They were breathing on their own and all physiological signals were continuously monitored. Following the completion of the last imaging experiment, the mice were either euthanized with anesthesia-overdose or were perfusion-fixed for histology.

MR Protocol: Imaging was performed on a 7T GE Signa Scanner with high-performance gradient coils. 2-shot PROPELLER [1] was used to obtain ungated, heavily T2-weighted images with TE = 67.37ms, TR = 3s. Multi-slice axial datasets covering the entire abdominal region (125µm in-plane, 1mm slice) were acquired in ~30 minutes. (figure, top row)

CT Protocol: Imaging was performed on a microCT system consisting of an x-ray tube with a 0.8mm focal spot and a cooled CCD camera [2]. A liposomal (blood pool) contrast agent, Lp-I (0.4ml/25g) [3] was administered 18 hours prior to imaging. Each scan consisted of 300 projections with a 0.65° step angle, acquired at 80 kVp, 160 mA, and 10ms exposure. Respiratory-triggered datasets with 88µm isotropic resolution were acquired in ~5 minutes. (figure, bottom row)

RESULTS



DISCUSSION AND CONCLUSION

Both high-field MRI and microCT were sufficiently simple and fast to permit rapid acquisitions required for high-throughput studies, and were also sufficiently non-invasive to allow multiple scans. We imaged up to 8 mice/day with both MR and CT, for a total of 7 imaging time-points. Each modality has its strengths (and weaknesses). MicroCT has higher spatial resolution and isotropic datasets enabling resections in any plane. With a respiratory-triggered acquisition of ~5minutes, microCT is more conducive for high-throughput studies than MRI (~30 minutes). T2-weighted MRI has higher contrast-to-noise ratio than contrast-enhanced microCT (between viable liver and metastatic tumors). Additionally, heterogeneity within the tumors (arrow in figure) can also be seen in the MR images. We speculate that this represents different stages of tumor growth. We believe that this technique could be used in the future to quantify additional tumor properties in this model, compared to tumor detection alone. Finally, MRI is less invasive than microCT, which requires both contrast injections as well as radiation dose, and is thus more suitable for longitudinal studies.

REFERENCES

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ACKNOWLEGGEMENTS

Imaging was performed at Center for In Vivo Microscopy, Duke University, supported by NIH/NCRR/NCI (P41 RR005959, U24 CA092656).