Echo-planar imaging improves staging of murine model of lung cancer

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Introduction

Lung cancer remains the leading cause of cancer death in the United States [1]. Despite the excellent soft tissue contract afforded with MRI, clinical application of this modality to lung cancer is limited because of relatively long scan times and sensitivity to motion. These problems are exacerbated in the laboratory where researchers investigating small animal models of human lung cancer desire an ability to non-invasively monitor the progression of the disease despite very fast respiratory and cardiac motion. In both the clinic and the laboratory, CT is the preferred method for accomplishing this. In small animals, however, reduced tissue contrast can make the accurate identification of tumor boundaries difficult, especially when the tumors abut the pleura or invade the thoracic wall. A number of approaches have been suggested to allow MRI to be used as a tool to monitor the state of lung tissue, most often relying on hyperpolarized gasses, edema, or allergic response to provide sufficient contrast. These methods generally employ gated T_1-weighted spin-echo imaging techniques to reduce motion artifacts, or fast gradient-echo sequences that reduce scan times as well [2]. For the study of solid lung tumors, we have found that the intrinsic soft tissue contrast of T_2-weighted echo-planar imaging (EPI) provides an excellent means for the non-invasive characterization of small animal models of lung cancer.

Methods

Nude mice were injected with NCI-H460 cells (human large cell lung carcinoma). MR and CT images were acquired 3 and 5 weeks after injection, after which animals were euthanized and frozen for cross-sectional block-face photographic imaging.

MR images were acquired on a 4.7T Biospec (Bruker Biospin, Billerica, MA) using micro-imaging gradients (maximum amplitude 950 mT/m; minimum rise time 70μs) and a 35-mm linear birdcage-style resonator. The acquisition protocol included a respiratory-gated T_2-weighted multi-shot EPI sequence (TE_{eff}=35ms; TR=2 respiratory cycles, about 5s; matrix size 128x128; 8 shots) and pre- and post-contrast, T_1-weighted, respiratory- and cardiac-gated, fast, spoiled gradient echo (FSPGR) sequence (TE=1.3ms; TR=1 cardiac cycle, about 200ms; matrix size 128x128). Contrast was delivered (Magnevist, 0.4 mL/kg) via tail-vein catheter. With animal placement, localizing scans, and each of these sequences, the overall protocol required about 20 minutes per animal.

CT images were acquired on a RS-9 micro-CT scanner (GE Medical Systems, London, Ontario). A respiratory-gated acquisition protocol (80 kVp, 450 mA) yielded images with isotropic 91μm resolution with a scan time of approximately 25 minutes per animal.

Results & Discussion

T_2-weighted spin-echo EPI exploits the susceptibility-induced low signal content of normal lung tissue to provide excellent contrast between solid tumor and healthy lung. EPI images also provided excellent contrast between tumor tissue and other adjacent soft tissues, including atelectasis. FSPGR images provided improved anatomic coverage, but tumor could not be distinguished from collapsed lung except by the rapid enhancement of lung tissue following administration of contrast. In cases where tumor abutted the thoracic wall, it was impossible to identify tumor boundaries from CT images, as illustrated in Figure 1.

Fast imaging methods such as EPI can be employed to allow the excellent soft tissue contrast of MRI to be used for non-invasive monitoring of lung tumors in small animal models of cancer. This has provided immediate benefit to researchers by helping to identify animals in which inoculation led to tumor prior to initiation of expensive experimental therapies. Improved positive identification may lead to experimental treatments that can begin at earlier stages of the disease, providing an opportunity to non-invasively and longitudinally observe the biology of the disease and its response to therapy.
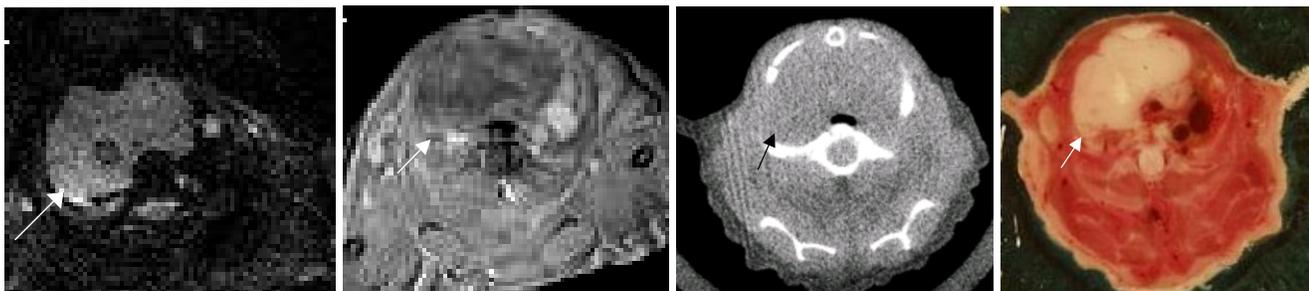
Figure 1: Representative axial images of the cranial aspect of the thorax, demonstrating the utility of MR in visualizing an intrathoracic tumor. Left to right: T2-weighted multishot EPI image clearly illustrating tumor boundary; T1-weighted FSPGR image with reduced enhancement of the tumor compared to atelectasis; CT image in which the tumor boundary is not identifiable; photograph of the corresponding frozen section.

References

[1] Cancer facts & figures 2004. Atlanta, GA: American Cancer Society, Inc; 2004.
[2] Schuster DP, et al. *Am J Respir Cell Mol Biol* **30**(2): 129-38, 2004.