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Quantitative Preclinical Magnetic Resonance Imaging of Lung Tumor Burden

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The recent article, “Imaging Primary Lung Cancers in Mice to Study Radiation Biology,” by Kirsch, *et al.* (1), makes a compelling case for the use of non-invasive imaging for longitudinal studies of tumor growth. In the research reported therein, micro-computed tomography (micro-CT) was employed for detection of lung tumors “below 1 mm³” in volume and a strong linear correlation between the tumor volume as determined by micro-CT and that determined by histology was demonstrated, though the volume calculated by micro-CT consistently overestimated the size of the tumors compared with histology.

The authors offer the opinion that micro-CT is superior to MRI for imaging lung tumors because of “the better contrast between the air and the soft tissue, whose interface can cause artifacts in MRI”. While we enthusiastically second the arguments regarding the power of *in vivo* imaging for longitudinal studies of tumor growth, we wish to offer a forceful counter point to this claim. In fact, MRI offers excellent capabilities for *absolute* quantification of lung-tumor burden, a capability that is often unappreciated by preclinical imaging scientists focused on high-energy-radiation methods.

Previously published reports from our laboratory have demonstrated the utility of respiratory-gated MRI experiments for quantitative measurement of lung-tumor growth in several different murine tumor models (2-6). In particular, this laboratory has employed MRI to detect lung tumors as small as 0.5 mm in diameter (0.065 mm³ volume) (5), has successfully correlated MRI-derived tumor volumes with histologic measures (3-6), and has monitored longitudinal tumor growth over a period of many months in cohorts of mice (4). Because MRI uses very low energy (non-ionizing) radio-frequency radiation, animals are not exposed to potentially therapeutic doses of radiation.

The idea that micro-CT is superior to MRI for imaging lung tumors because of air and soft tissue interface-induced MRI artifacts, reflects a common misconception. While normal lung tissue is not observable by standard MRI methods because of the tissue’s low water content and the presence of significant mesoscopic magnetic-susceptibility-induced magnetic field

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inhomogeneities (the air/tissue interface issue), this proves to be a marked advantage when targeting the detection and quantification of lung tumors. The lack of background MR signal from lung parenchyma ensures remarkably high MR image contrast. While magnetic-susceptibility-induced inhomogeneities will, at some point, limit achievable resolution with standard MRI pulse sequences, in our experience, these susceptibility effects do not cause observable image artifacts at 4.7 tesla.

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