In Vivo 1H/19F UTE Imaging of Lung Disease

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Introduction

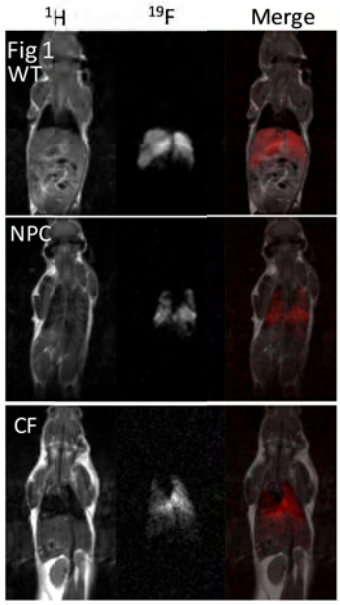
Diagnosis and treatment of many illnesses could be improved by MRI of lung inflammation and functional compromise. However, such imaging using traditional MRI methods is difficult. Recently, ^{19}F MRI of perfluorocarbon emulsions have shown sensitivity to the presence of macrophages and monocytes in areas of inflammation [1,2]. In this work, we present ^{1}H and ^{19}F spin-echo and Ultrashort TE (UTE) MRI to obtain 2D and 3D volumetric images of mouse models of cystic fibrosis (CF) and Niemann-Pick type C (NPC) disease. The UTE techniques used allow for motion insensitive 3D imaging of lung tissue and inflammation-associated perflorocarbon accumulation.

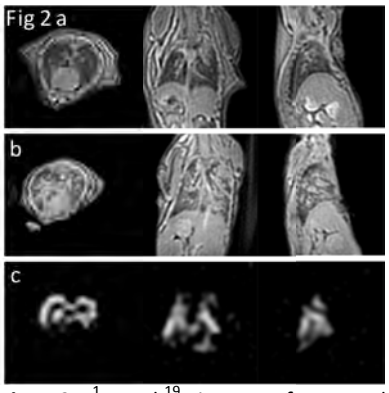
Methods

Nanoemulsions of approximately 200 nm diameter droplets were prepared with 40% vol/vol Perfluoro-15-crown-5-ether in PBS. 40 µL of nanoemulsion was diluted with 160 µL of saline and injected into adult CF, NPC, and control mice via the tail vein. MR imaging was carried out 18 hours post-injection on a Bruker BioSpec 7T MRI system using a dual tuned ^{1}H/^{19}F volume coil (m2m Corp). Animals were anesthetized using 1.5% isoflurane in O_2 and maintained at 37 °C via heated air. ^{1}H (2 mm slice thickness) and ^{19}F (whole body projection) spin-echo (SE) images (TE = 10 ms, TR = 500 ms) were acquired. 3D ^{1}H UTE (TE = 40 µs, TR = 10 ms, flip angle = 5°, 400 micron isotropic resolution) and 3D ^{19}F UTE (TE = 40 µs, TR = 10 ms, flip angle = 5°, 800 micron isotropic resolution) images were also acquired in the same imaging session.

Results

Images in Fig. 1 show clear accumulation of ^{19}F signal in the liver and spleen of the control mouse, which is the natural clearance pathway of the emulsion [1]. In contrast, ^{19}F signal accumulation is mainly observed in the lungs of NPC and CF mouse. UTE images, as shown in Figs. 2 and 3, provide volumetric information and 3D lung structure. ^{1}H UTE images in Fig. 2 clearly show increased signal in the lungs of the NPC mouse compared to the lungs of the control mouse. The increased signal in the lungs corresponds directly to the presence of ^{19}F signal due to the accumulation of macrophages. To investigate the imaging results, bronchial alveolar lavage was performed on the mice, which showed accumulation of alveolar foamy macrophages; approximately 5x elevation in the lungs of the NPC mice compared to the control. While the ^{1}H UTE images of CF mice (Fig. 3) do not show extensive abnormal signal in the lungs, the ^{19}F UTE images show dramatic accumulation of the nanoemulsions in the lungs with very little signal from the liver and spleen.





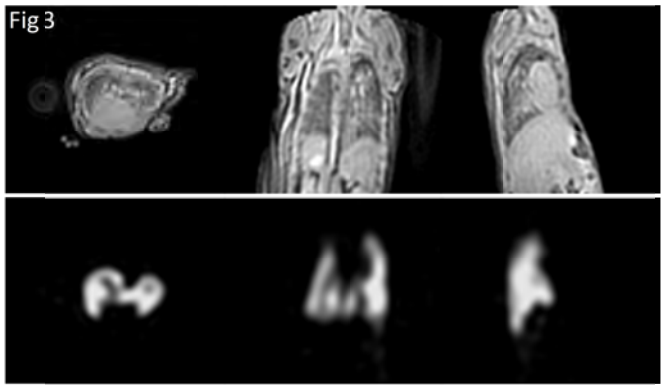


Fig 1: 2D ^{1}H and ^{19}F images of a control, NPC, and CF mouse at 18hrs post nanoemulsion injection. Images of the control show ^{19}F signal accumulation primarily in the liver. Images of the NPC and CF mice show ^{19}F signal accumulation primarily in the lungs.

Fig 2: 3D ^{1}H UTE image of a control mouse (a) and NPC mouse (b) and corresponding 19F UTE images of the NPC mouse. The ^{19}F UTE images were acquired with 4 averages in 8 min.

Fig 3: 3D 1H and 19F UTE images of a CF mouse. ^{19}F UTE images were acquired with 8 averages in 17 min.

Conclusion

Lung pathology was able to be visualized in CF and NPC mice via ^{1}H and ^{19}F MRI. 3D ^{1}H UTE allowed for motion-insensitive imaging of lungs. 3D ^{19}F UTE imaging of perfluorocarbon nanoemulsions enabled in vivo visualization of macrophage accumulation.

References

[1] Giraudeau et al. NMR Biomedicine. 2010. [2] Ebner et al. Circulation. 2010.