3D Ultra Short TE MRI for Whole Subject Imaging of Perfluorocarbon-Labeled Cell Biodistribution

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INTRODUCTION

Cellular MRI is an emerging field that has the potential to make significant contributions to biomedical sciences. The ability to image cell distributions in deep tissues can provide a better understanding of biological processes as well as make a significant impact on the clinical diagnosis and treatment of numerous diseases. Perfluorocarbon-based nanoemulsions are a class of cellular MRI agents that have gained attention in recent years because ^{19}F MRI is highly selective for the labeled cells with no background signal. For detecting fluorine-labeled cells, significant signal averaging is generally employed to overcome the low ^{19}F spin density. This can result in long scan times, when respiratory and/or cardiac gating is necessary for image acquisition and generally precludes 3D imaging on live subjects. The radial acquisition scheme of a 3D ultra short TE sequence (UTE3D) is less sensitive to motion artifacts than conventional phase encoding acquisition of k-space. In this study we explore the feasibility of using a ^{19}F-UTE3D sequence to image whole subject biodistribution of perfluorocarbon labeled immune cells. We applied this technique to a hetertopic heart and lung transplantation model of acute allograft rejection in rats.

METHODS

An abdominal heterotopic working heart and lung transplantation model was used with Dark Agouti to Brown Norway transplantation rat pairs (1). The transplanted hearts exhibit similar cardiac outputs and ventricular pressure close to those in native hearts. Mild (Grade 1A or B) rejection develops by post-operation day (POD) 2.5-3.5; grade 2 rejection develops on POD 4.5-5.5; whereas the moderate to the severe (Grade 3A) rejection develops after POD 6-7. Immune cells, macrophages, are labeled *in vivo* by direct intravenous injection of perfluorocarbon nanoemulsion, VS-1000 (Celsense, Pittsburgh PA). Animals were imaged at 7 Tesla on a Bruker Biospec AV3 system. A ^{19}F-UTE3D (TR/TE = 10/0.02 ms, 0.8 x 0.8 x 1.6 mm resolution, matrix = 80^3-100^3, NA = 8-16) experiment was used to image nearly the entire subject. Conventional ^{1}H scans can then be used for anatomical context.

RESULTS AND DISCUSSION

We recently showed that following a direct *i.v.* injection of a perfluorcarbon nanoemulsion, circulating monocytes and macrophages are labeled, and ^{19}F MRI can detect labeled-macrophage accumulation in the rejecting grafts. (2). Consistent with our previous studies, immediately following the injection of VS-1000, a UTE3D image shows that the ^{19}F signal is found in the vasculature (Fig.1A). The signal is observed in the native and transplanted (Tx) heart cavities and the major vessels. At 24 hrs, the UTE3D reveals the 3D biodistribution of VS-1000 labeled cells (Fig 1B). ^{19}F-UTE3D signal identifies ^{19}F-labeled macrophage accumulation in the transplanted heart and lung, and signal can also be found in the spleen and liver, consistent with RES clearance of the nanoemulsion. We show that whole subject 3D ^{19}F images can be collected in less than 60 min and can provide anatomical reference without the use of conventional ^{1}H scans. The ^{19}F-UTE3D can be generally applied to cellular imaging studies and the simplicity of animal preparation, and independence of pilot scans is favorable for increased throughput and screening.

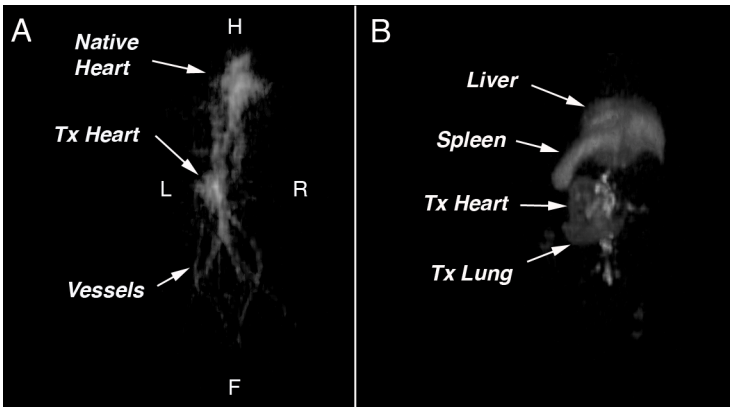

Figure 1. Volume rendering of ^{19}F-UTE3D images following a 1 mL injection of VS-1000 on POD 5 (A) and 24 hrs post-injection on POD 6 (B). The acquisition times for A and B were 20 and 60 min, respectively.

AKNOWLEDGEMENTS

Supported by grants from the National Institutes of Health (RO1 HL081349 and P41 EB001977).

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