Improved diagnosis of tumor tissues with QUESPOWR MRI

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Introduction: The Quantification of Exchange as a function of Saturation Power On the Water Resonance (QUESPOWR) method is introduced as a simple way to detect tissues with fast exchanging labile protons with small chemical shifts. This method uses the OPARACHEE MRI pulse sequence[1] to measure water signal as a function of RF power, and uses QUESPOWER linear fitting methods (that are similar to linear variations of QUESP fitting methods)[2] to estimate the average chemical exchange rate for each pixel. Simulations and phantom studies were used to evaluate QUESPOWR MRI. Demonstrations with an in vivo mouse model of mammary carcinoma showed that QUESPOWR MRI can detect tumor tissues with great sensitivity and specificity.

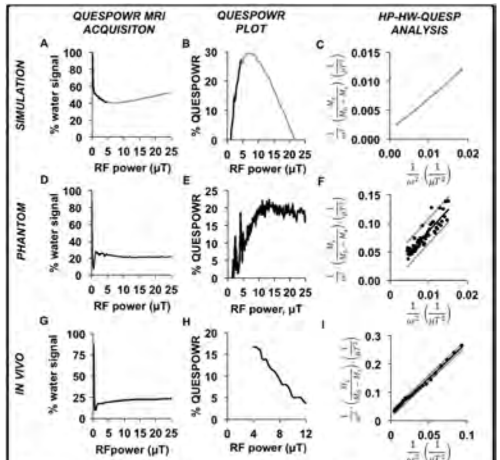
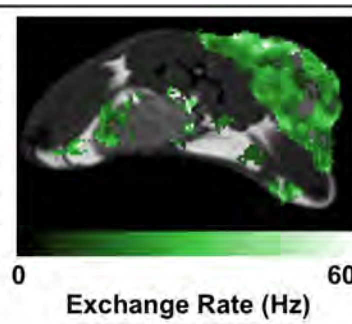


Figure 1. Simulations showed A) % water signal from QUESPOWR MRI with endogenous biomolecules with a small chemical shift and slow chemical exchange rate, B) which was converted to a QUESPOWR plot, C) and analysed with the HP-HW-QUESP method. D-F) Experimental phantom studies of iopamidol confirmed simulated results. G-I) An *in vivo* study showed that two regions of the tumor showed similar results.

Methods and Results: Simulations were performed to determine the percentage change water signal generated by OPARACHEE MRI over a range of RF powers using the WALTZ16* pulse train; this series of images is known as a QUESPOWER MRI (Fig. 1A). The simulations were performed for samples with large and small chemical shifts relative to water, and fast and slow chemical exchange rates. The water signal was renormalized and inverted to create a QUESPOWR plot that was similar to a QUESP plot (Fig. 1B).[3] The portion of this plot at high power was analyzed with HP-HW-QUESP (Fig. 1C),[2] which measured the chemical exchange rates used for initially simulating the % water signals.

Experimental phantoms of iopamidol (Isovue®) were prepared at 0-79 mM and pH 6.21 – 7.26. QUESPOWR MRI was acquired with RF powers of 0-25 μT for the WALTZ16* pulse train. The % water signal (Fig. 1D) was renormalized and inverted (Fig. 1E) to create a QUESPOWR plot, and the linear HP-HW-QUESP method was fit to these results to measure chemical exchange rates (Fig. 1F). This experimental result confirmed simulated results. Three mice with a subcutaneous MCF7 tumor were imaged with QUESPOWR MRI. The % water signals of two tissue regions (Fig. 1G) were renormalized and inverted to create a QUESPOWR plot (Fig. 1H), and HP_HW-QUESP was used to measure chemical exchange rates (Fig. 1I). The analysis was repeated on a pixelwise basis to create a parametric map of chemical exchange rates (Fig. 2). A linear variational Bayesian inference with an uninformative prior was used to avoid overfitting the results. The parametric map fit almost all pixels in the tumor and a few pixels in the bladder, but did not adequately fit pixels in non-fat, normal tissues.

Figure 2. A parametric map of chemical exchange rates using QUESPOWR MRI. QUESPOWR only identifies pixels of the tumor and bladder that have low extracellular pH. This technique is "blind" to non-fat tissues with neutral extracellular pH.



Discussion: Simulations and experimental phantom studies showed that QUESPOWR MRI can detect endogenous species with small chemical shifts and slow chemical exchange rates, which challenges the assumption that OPARACHEE MRI can only apply to exogenous paraCEST MRI contrast agents. Importantly, the simulations and phantom studies showed that the HP-HW-QUESP analysis can only analyze QUESPOWR MRI that involve species with small chemical shifts and slow chemical exchange rates, *such as endogenous biomolecules at low pH*. Remarkably, the *in vivo* study showed that HP-HW-QUESP analysis of QUESPOWR MRI can *only identify pixels of the tumor and bladder that have low extracellular pH*. Because QUESPOWR MRI is "blind" to tissues with neutral extracellular pH, this method has outstanding sensitivity and specificity for tumor diagnosis.

References: 1. Vinogradov, et al., J Mag Res 2005, 176:54-63. 2. Randtke, et al., Magn Reson Med 2014, 71:1603-1612. 3. McMahon, et al., Magn Reson Med 2006, 55:836–847.