# Mapping brown adipose tissue through intermolecular double-quantum magnetic resonance imaging at 7 Tesla

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## Introduction

Nowadays, obesity caused by excessive accumulation of white adipose tissue (WAT) killed more people than malnutrition in the world. Recently, another adipose tissue, called brown adipose tissue (BAT) with potential to resist obesity by 'burning' WAT, was found in adults [1]. However, only a few adults have BAT. Many studies are engaging in getting BAT back to adults, so it is meaningful to map the BAT in the body. Current regular method for imaging BAT is PET/CT, which is costly and only sensitive to active BAT. For MRI, chemical shift imaging and localized spectroscopy can pick out BAT when it exists alone, but fail when it mixes with other cells, which is often the case in vivo, especially during the treatment of using BAT to combat obesity. Branca and co-workers demonstrated that two-dimensional (2D) intermolecular zero-quantum coherence (iZQC) spectroscopy could probe BAT at cellular scale [2], but failed to tell exactly where BAT was. Herein we proposed an approach marrying a novel two-point Dixon algorithm and intermolecular double-quantum coherence (iDQC) to map pure BAT image of rats.

## Theory and method

IDQC arises primarily from the coherences between spins within a macroscopic separation called dipolar correlation distance $d_c$ ($d_c \approx 100$ μm in our study). The diameter of adipose cells is about 30 ~ 200 μm, so iDQC can be used to probe spins at the cellular level. WAT cells are rich of fat spins but less water spins while water spins almost equals fat spins in BAT cells, and most of other tissue cells are rich of water spins. Theoretically, iDQC signals from BAT are different from WAT and other tissues at cellular scale. At this scale, only one predominant fat-fat coherence between fat and fat spins exists in WAT with a frequency of $\omega_{fat-fat} = \omega_{fat} + \omega_{fat} = 2\omega_{fat}$ ; water-water ( $\omega_{water-water} = \omega_{water} + \omega_{water} = 2\omega_{water}$ ), fat-fat, and water-fat ( $\omega_{water-fat} = \omega_{water} + \omega_{fat}$ ) coherences exist in BAT; and almost only one predominant water-water coherence exists in other tissues. With the characteristic frequency of water-fat iDQC signals of BAT at cellular scale, Dixon technique can be applied to solely reconstruct BAT image based on water-fat iDQC signals, even when it mixes with other tissues.

Raw iDQC signals were obtained using a modified CRAZED sequence (Fig. 1). Simulation and rat experiments were performed to test this method. A model containing two spin systems with chemical shifts of 1.3 ppm and 4.8 ppm to mimic fat and water in the upper and lower parts respectively was used for simulations. Animal MRI experiments were taken on a Varian 7 T/160 mm MRI scanner. All animal procedures were approved by the Institutional Animal Care and Use Committee of Xiamen University.

## Results and discussion

Figure 2 shows the simulation results using traditional Dixon and iDQC-Dixon methods. For the traditional Dixon method, the fat and water can be well separated (Fig. 2a and b). Differently, iDQC-Dixon method can separate the signals according to their positions relative to the interface of two components, shown in Fig. 2c and d. This is because water-water and fat-fat coherence signals are from water and fat parts separately, and water-fat coherence signal is only form the protons at the interface of two parts within $d_c$. With proper echo time, water-fat signal will be in anti-phase status compared with water-water and fat-fat signals. The simulation results prove that the iDQC-Dixon method can effectively separate the iDQC signals within a distance of 100 μm. It has the ability to give a new contrast image based on the different chemical compositions and microstructures. Figure 3 shows the experimental results on the scapular region of a three-week old rat. Distribution of BAT in rat and the selected slice of scapular region for experiments marked by a rectangular frame are shown in Fig. 3(a). BAT regions are successfully mapped by the iDQC-Dixon method at cellular scale which is beyond the ability of traditional Dixon method. The BAT regions are all validated by PRESS and hematoxylin and eosin stain (H&E) (Fig. 3d and e).

## Conclusion

A method combining iDQC with Dixon was proposed to separate different iDQC signals at micron scale. It can distinguish BAT from other tissues even when it mixes with other tissues, thus can be applied to monitor the dynamic process of BAT in resisting obesity.

## Acknowledgment

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## References

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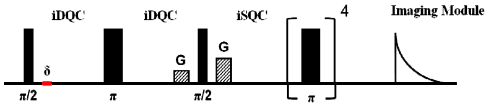


**Fig. 1** Modified CRAZED pulse sequence. δ is a delay for Dixon method.

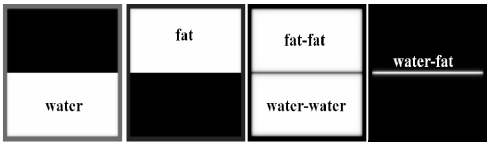


**Fig. 2** Simulated results of a fat-water two-layer model from traditional Dixon method (a, b), and iDQC-Dixon method (c, d). (a) Separated water image; (b) separated fat image; (c) separated water-water and fat-fat image; and (d) separated water-fat image.

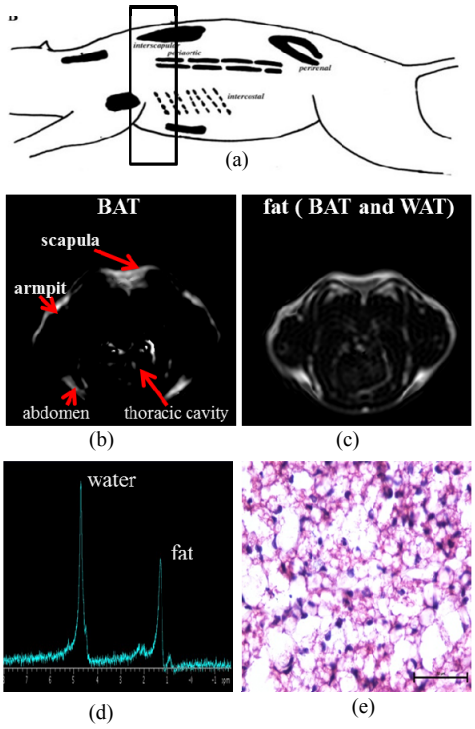


**Fig. 3** (a) Distribution of BAT in rat and the selected slice for scan; (b) separated water-fat coherence image of BAT only of a three-week old rat obtained from iDQC-Dixon method. The BAT regions are labeled by red arrows; (c) fat only image corresponding to (b) obtained from traditional Dixon method; (d) $^1$H spectrum of BAT obtained from PRESS; (e) H&E stain of BAT (×40).