ISMRM Workshop on Cerebral Perfusion
March 2004, Venice, Italy

Potential and Limitations of Oxygen-17 MR Perfusion Measurements

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The purpose of this communication is to discuss an MR application that seems very far fetched, but – in the opinion of the author – a quite valid proposition. The "pros and cons" are briefly described below.

Oxygen-17 is by far the best *in vivo* and *in vitro* tracer of water molecules (*1-4*). It is a stable, non-toxic isotope with a natural abundance of 0.037 %. At 3.7 % enrichment, it can be detected 10,000 times faster, with a very large signal-to-background ratio. Its observation can be compared with seeing the light of a little candle in a totally dark room (see Figure 1).

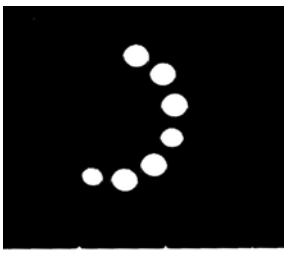


Figure 1a. Proton image of seven capillaries filled with (from top to bottom) natural abundance (NA) water, 10% $H_2{}^{17}O$, NA, 20% $H_2{}^{17}O$, NA, NA, and 40 % $H_2{}^{17}O$.

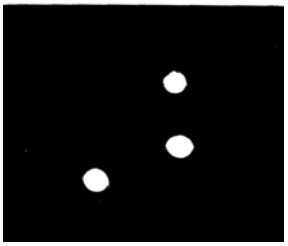
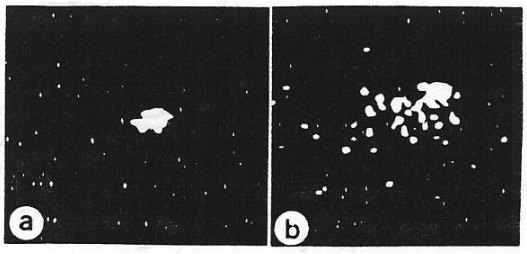


Figure 1b. O-17 image of the same set of capillaries shown above. It is seen that only O-17 enriched water is detected (the NA water contains too little O-17 to be seen).

The fundamental difference between oxygen and proton (or deuteron) is that the latter could not be specifically associated with a given molecule of water because it "hops" extremely rapidly from molecule to molecule in very complicated exchange/tunneling patterns. Thus, oxygen is the true marker of the water molecule.

There are two observation avenues for O-17 water perfusion. The first is *via* a bolus injection. Figure 2 illustrates the perfusion of $H_2{}^{17}O$ through the wall of a coronary artery in an isolated human heart (*5*).

Figure 2. (a) Transverse O-17 MR image of a coronary artery in an isolated human heart immediately after ligation and injection of a bolus of 20% O-17 enriched water.
(b) Image taken after 15 minutes clearly shows extent of perfusion.



The second is "from within the cell" into the interstitial volume, then into tissues and the blood stream. This is the "nascent mitochondrial water" resulting from cell bioenergetics in organisms breathing O-17

enriched air (*4*, *6-9*). Figure 3 illustrates the temporal progression of labeled metabolic water in the mouse brain.

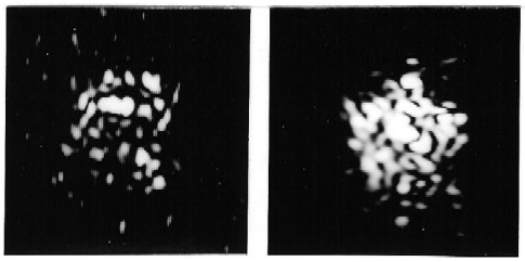


Figure 3. Left: Oxygen-17 MR image of a mouse head (16 mm slice) taken 23 minutes after being placed in a respirator filled with air enriched with 45% $^{17}O_2$. Right: after 46 minutes.

Arguments in favor of O-17 MRI perfusion methods: highly specific label; demonstrated detectability with adequate sensitivity (short relaxation times, fast pulse repetition); feasibility of mathematical modeling. Complementary brain function information, particularly in conjunction with interleave spectroscopic ^{1}H - ^{17}O - ^{31}P imaging (*10-13*).

Arguments against (in order of importance): very high cost of the isotope; low spatial resolution; (arguably) label redistribution via circulation.

Conclusion: worth giving it a serious try.

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