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RESEARCH

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Photoacoustics sheds light on brain function

Photoacoustic imaging could prove an optimal method for tracking brain function throughout disease progression. The non-invasive technique, which uses pulsed laser light to generate acoustic waves, can create high-resolution images of absorbing structures such as blood vessels. And as the absorption properties of haemoglobin depend on its oxygenation, photoacoustics can monitor brain activity by revealing local changes in blood oxygenation, volume and flow.

Researchers at Washington University in St. Louis, MO, (WUSTL) have used photoacoustic microscopy (PAM) to obtain high-resolution *in vivo* images of the mouse brain in response to differing oxygen levels. The technique, they propose, could prove invaluable in the controlled study of neurological disease progression and treatment in preclinical mouse models (*J. Biomed. Opt.* **14** 020502).

"Photoacoustic imaging can image through the intact scalp and skull of small animals *in vivo* at high spatial resolution," said Lihong Wang, director of director of WUSTL's Optical Imaging Laboratory. "Other high-resolution optical imaging techniques, such as confocal microscopy and two-photon microscopy, require removal of the scalp and thinning of the skull. Photoacoustic imaging is also relatively low in cost and works in real time."

Oxygen response

The researchers tracked the real-time blood-oxygenation dynamics of individual cortex vessels in response to changes in inhaled oxygen level. They first recorded an *in vivo* PAM image of the mouse-brain vasculature at 570 nm, a wavelength at which optical absorption is independent of oxygenation status. This image was used to identify the vasculature associated with the somatosensory cortex and determine five blood vessels of interest.

The five vessels were imaged using PAM at 561 nm, a deoxyhaemoglobin-dominant wavelength, and at 570 nm. The acquisition time for each multi-wavelength scan was 10 s. During image acquisition, the researchers induced hyperoxic and hypoxic states by alternating the oxygen levels delivered to the animal between 100% and 5%, respectively. The animal received three bouts of 5% oxygen with a return to baseline (100% oxygen) between each stint.

"The two forms of haemoglobin, oxy- and deoxyhaemoglobin, have different absorption spectra," Wang explained. "The use of dual laser wavelengths allows us to estimate the relative concentrations of both forms and thereby monitor the haemoglobin oxygenation."

The initial step from hyperoxia to hypoxia was initiated at 6.1 minutes. After a 27 s lag time, the 561 nm photoacoustic signal from each vessel increased by roughly 20%. The maximum increase varied between vessels (from about 17% to 24%), but no significant correlation between maximum response and vessel diameter was observed. The forward response time (from 10% to 90% of maximum response) was 63 s, with no significant variation between the five vessels studied.

At 12.2 minutes, the researchers ended the hypoxic challenge with a step exposure to 100% oxygen. This decreased the levels of deoxyhaemoglobin in the cortex vessels and, in turn, decreased the 561 nm photoacoustic signal. The reverse response time (from 90% to 10% of the maximum) was 16 s. The three repeated hypoxic challenges produced similar results each time.

An equivalent experiment using 5% oxygen as the baseline showed comparable results, with a forward response time of 14 s, a reverse response time of 61 s and a lag time of 28 s when transitioning from hyperoxia to hypoxia.

Unexpectedly, the switch from 5% to 100% oxygen increased the 570 nm photoacoustic signal, in contradiction to the expected decrease in blood flow during hyperoxia. One possible reason for this could be that the decrease in optical absorption caused by higher vasoconstriction in smaller surrounding vessels leads to more light being incident on the imaged vessel. This change in local fluence can overwhelm effects due to the change in haemoglobin concentration in that vessel.

"We have received a National Institutes of Health grant to develop 3D quantitative photoacoustic imaging, which will help understand the root cause of this unexpected observation," Wang told *medicalphysicsweb*.

Wang and colleagues concluded that these results demonstrate the potential of PAM to non-invasively track the oxygenation dynamics of multiple cortex vessels via the haemodynamic response. They note that a high degree of correlation was observed between the dynamic oxygenation profiles and the oxygen step-change profiles.

Ultimately, this work could provide a simple means by which to monitor the longitudinal effects of human-like neurological disease on brain function, using transgenic mouse models. "Two companies are commercializing our technology," Wang noted. "We want to make the technology available to the broad research community, which is expected to impact biomedical research."

About the author

Tami Freeman is Editor of *medicalphysicsweb*.