PHOTOACOUSTIC IMAGING

Real-time tomography of the human brain

Arrays of ultrasonic transducers arranged hemispherically around the head enable the mapping of haemodynamic changes in the brain via photoacoustic computed tomography at resolutions down to 350 micrometres and 2 seconds.

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Neural activity can be monitored non-invasively via local changes in blood flow, blood perfusion and blood oxygenation that are then mapped to brain function. Functional magnetic resonance imaging (fMRI) — the standard technique for imaging brain haemodynamics — can provide such information at high spatial resolution and across the entire brain. However, the temporal resolution of fMRI is low, the device has to be housed in dedicated facilities, and it cannot be used with patients bearing ferromagnetic implants because it requires a strong magnetic field. An fMRI scan collects up to 130,000 voxels, but such large amounts of data can require extensive data correction[1]. And the narrow size of the gantry and loud sounds during device operation make fMRI unsuitable for infants and for people suffering from claustrophobia. Alternatively, positron emission tomography can be used for neuroimaging, but it requires the administration of radioactive tracers and has poor spatial resolution.

Functional photoacoustic computed tomography (fPACT) is instead label-free,

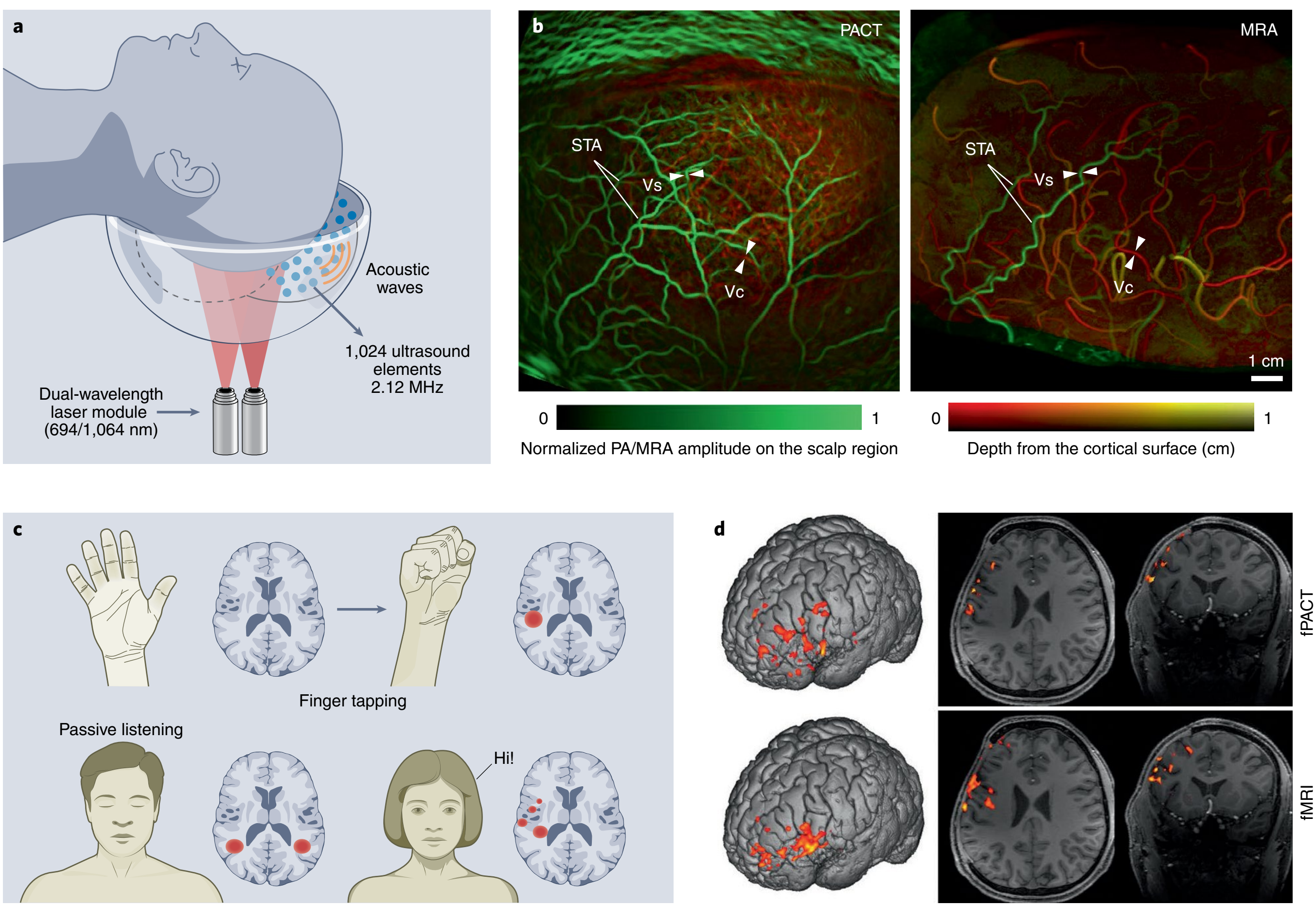

Fig. 1 | Functional photoacoustic computed tomography (fPACT) of the adult brain. a, fPACT with dual-wavelength illumination and 1,024 ultrasound transducer elements with a central frequency of 2.12 MHz. **b**, fPACT angiography and magnetic resonance angiography (MRA) of the same brain section. STA, superficial temporal artery; Vs, scalp vessel; Vc, cortical vessel. **c**, Different cognitive tasks (speaking, finger tapping, lip puckering, tongue tapping and passive listening) activate different areas of the brain. **d**, Haemodynamic responses (overlaid on a three-dimensional representation of the brain (left) and on actual MRI brain scans (right)) measured by fPACT and fMRI for the same brain while speaking one word. Panels **b** and **d** reproduced with permission from ref. [2], Springer Nature Ltd.

and it allows for real-time imaging at high resolution. In photoacoustic imaging, light irradiated by pulsed lasers into tissue generates heat, which causes the local thermoelastic expansion of the tissue. This causes transient changes in pressure that can be detected by conventional ultrasonic transducers. fPACT can map neural activity in the brain by imaging oxygen saturation in blood (owing to the fact that activated neurons consume more oxygen, and that oxyhaemoglobin and deoxyhaemoglobin have different absorption coefficients) and by discriminating venous blood from arterial blood. However, subtle changes in perfusion and oxygenation have long fallen beyond the limits of detection of the technology. Writing in *Nature Biomedical Engineering*, Lihong Wang and colleagues now report an implementation of fPACT that allows for the real-time functional imaging of the adult human brain at resolutions of 350 µm and 2 s (ref. [2]).

To capture subtle changes in brain haemodynamics, real-time fPACT needs to differentiate small signals from background noise. Wang and co-authors used lasers with two wavelengths (1,064 nm and 694 nm) to separate the relative contributions from oxyhaemoglobin and deoxyhaemoglobin, and to optimize the system for depth of penetration (for wavelengths longer than about 1,000 nm, light scattering and light absorption in tissue are reduced). Also, the authors developed a hemispherical detector housing 1,024 ultrasonic transducer elements with a central frequency of 2.12 MHz (Fig. 1a) to reduce artefacts and to collect data with a panoramic field of view (about 10 cm, through an acoustic window provided via craniectomy). Moreover, the photoacoustic signals were amplified via one-to-one mapping (that is, each transducer element was linked to a single pre-amplifier), thus limiting background noise and signal crosstalk.

fPACT has been used to image mouse brains, yet computed tomography of the human brain is much more challenging owing to its larger size (approximately 2,400-fold in volume) and thicker skin (2.5 mm versus 0.2 mm). Wang and co-authors quantitatively validated the fPACT system in patients who had hemicraniectomy (that is, portions of their cranium removed) by comparing the vasculature in the cortex and scalp with magnetic resonance angiography (Fig. 1b). The performances of fPACT and fMRI (at 7 T) were also compared for the mapping of brain function (Fig. 1c). The participants were asked to perform five different tasks: speaking, finger tapping, lip puckering, tongue tapping and passive listening. For the speech task, fPACT detected neural activity in Broca's area (a brain region involved in speech function; Fig. 1d); and for the finger-tapping task, it detected activity in the primary motor cortex. Unlike fMRI, which depends on paramagnetic deoxyhaemoglobin for contrast, fPACT can quantify the contrasts from oxyhaemoglobin and deoxyhaemoglobin, and therefore determine oxygen saturation and cerebral blood volume. However, the authors' implementation of fPACT limited the imaging depth to up to 11 mm below the cortical surface, and required that the participants shave their heads (to improve the signal-to-noise ratio). Also, the signal-to-noise ratios achievable may decrease substantially when imaging intact heads (rather than heads after hemicraniectomy). Alternative light-illumination schemes, transducer arrays, wider fields of view and contrast agents could improve the penetration depth of fPACT[3,4]. Studies with a larger number of participants and thorough comparisons with fMRI will better establish the performance of fPACT technology and the clinical settings for which it is most useful. So far, only one protocol for photoacoustic imaging has been approved by the United States Food and Drug Administration (for imaging the breast)[5].

Overall, the technology for fPACT needs improvements in imaging processing to account for the acoustic heterogeneity of the skull and to balance reconstruction quality and computational cost. However, Wang and co-authors' fPACT technology should be suitable for integration with machine-learning algorithms for faster image processing as well as with smaller optical sources and advanced ultrasonic transducers for increased sensitivity and resolution[6–8]. Hardware for photoacoustic imaging is much more amenable to miniaturization than hardware for fMRI, and it is thus enticing to imagine a future where wearable 'photoacoustic helmets' could continuously monitor brain activity in real time for hours or days. ❐

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Competing interests

The authors declare no competing interests.