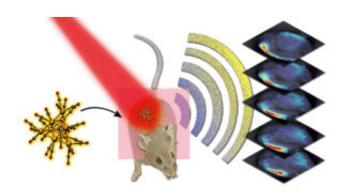


Compound boosts contrast of photoacoustic images

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When injected into a mouse, osmium carbonyl clusters (left) enhance the contrast of photoacoustic images, which are obtained by using near-infrared laser light (red) to excite acoustic waves (purple and yellow). Credit: The Royal Society of Chemistry

An agent for enhancing the contrast of photoacoustic imaging—an emerging imaging modality that involves 'listening' to the sound generated by laser light—has been developed by A*STAR researchers.

Photoacoustic imaging is an intriguing way to capture a picture of biological tissue in the body. Researchers shine ultrashort pulses of near-infrared laser light on to the region to be imaged. Tissue absorbs the light, causing it to heat up and expand and the expansion generates sound waves that are picked up by an ultrasound detector and used to generate an image.



Since it does not use ionizing radiation, photoacoustic imaging is safer than X-ray imaging and combines the advantages of optical imaging (good contrast) with those of ultrasound imaging (high spatial resolution and tissue penetration). Currently it is mainly used in research laboratories, but it has several potential clinical applications.

Compounds known as contrast agents are used to boost the contrast of photoacoustic images. While metal carbonyl clusters—molecules with metal atoms at their centers and limbs of carbon monoxide—have high photoacoustic contrasts, the contrast peaks at wavelengths that are too low to be useful for photoacoustic imaging.

Now, Malini Olivo at the A*STAR Singapore Bioimaging Consortium and co-workers have discovered a way to shift the optical absorption of metal carbonyl clusters to longer wavelengths. They found that using metal cores that have high nuclearity pushes the optical contrast into the near-infrared range (680 to 1,000 nanometers), which is so important for photoacoustic imaging.

When they injected osmium carbonyl clusters into the bloodstream of mice, they observed up to a four-fold enhancement in the photoacoustic signal from certain tissues, compared to that obtained with metal carbonyl clusters that have a low nuclearity.

"We demonstrated the potential of high-nuclearity carbonyl clusters of ruthenium and osmium as photoacoustic contrast agents in whole-body preclinical imaging," says Olivo. "The clusters exhibit low toxicity, high stability and superior photoacoustic stability compared to the clinically approved near-infrared dye indocyanine green."

More broadly, the study emphasizes a neglected class of compounds. "This work highlights the potential biological applications of organometallic complexes, which have not been well explored," says



Olivo.

"Metal-based therapeutic and imaging agents are becoming increasingly important. The in vivo evaluation of this class of clusters provides insights into the toxicity of such compounds, which should help to reduce the stigma associated with heavy-metal toxicity."

The team intends to improve the biocompatibility of the clusters and also functionalize the clusters with certain ligands to enable targeted imaging.

More information: Zhiyong Lam et al. High nuclearity carbonyl clusters as near-IR contrast agents for photoacoustic in vivo imaging, *J. Mater. Chem. B* (2016). DOI: 10.1039/C6TB00075D

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