Vascular imaging is indispensable to visualise cancer. Since solid cancers require neovascularisation (the process by which new vascular structures assemble) for their growth and progression, this imaging technique is useful for the diagnosis of cancer. Understanding of the blood supply to the tumour results in precise diagnosis and favourable treatment outcomes. Dr Masakazu Toi and Dr Yoshiaki Matsumoto at the Department of Breast Surgery, Kyoto University Graduate School of Medicine, harness the high-resolution ability of photoacoustic imaging, detecting light-induced ultrasound mostly from haemoglobin, to visualise tumour-associated vessels in the human breast in vivo.

The human heart pumps approximately five litres of blood around the body each day through our circulatory system, the network of blood vessels that deliver oxygenated blood to all organs and tissues, and remove blood containing waste products. However, many diseases are caused by changes in the circulatory system, or by unwanted changes to blood vessel growth and formation. For example, vascular dementia is a common type of dementia caused by reduced blood flow to the brain. Heart attacks, some cancers and diseases that induce defects in collagen, a protein that makes many of the body's tissues, can also be caused by abnormal blood supply. Angiogenesis, or the formation of new blood vessels from pre-existing vessels, is particularly relevant in cancer as solid tumours require a good blood supply to survive and grow.

Diagnostic imaging techniques are employed to characterise and monitor circulatory diseases. In particular, angiography is a technique that uses X-rays to check blood vessels. Angiographies involve injecting a special dye into the blood, as blood vessels do not show up well on normal X-rays. Other techniques such as CT and MRI scans are also used. One disadvantage of these types of imaging techniques is that they involve a contrast agent, such as the dye used in angiographies, and this is not well tolerated by some patient groups. Also, it can be dangerous for children to be exposed to high levels of the radiation often used in these imaging methods.

Due to the above challenges, there is a need for imaging techniques for blood vessels which do not require invasive approaches. One such technique is photoacoustic imaging (PAI). This is a novel imaging approach that does not require contrast agents or expose patients to radiation.

**PAI works by using a phenomenon called the photoacoustic effect. In essence, this is the formation of sound waves following the absorption of light by a particular material. The material absorbs the light which in turn raises the temperature of the material and causes it to expand. This expansion generates sound. The sound signals emitted can then be detected by a computer and analysed to determine the 3D position of the subject – in this case, the blood vessels. PAI has the dual advantages of high tissue specificity and contrast due to the optical measurements, and high spatial resolution due to the ultrasonic wave measurements. This means that PAI is a non-invasive approach that can be used to image small vascular structures.**

In addition, PAI can also be used for optical imaging and it is possible to image the haemoglobin oxygen saturation of the blood. This is calculated from measurements collected at two different wavelengths and was termed the “S-factor”. The oxygen saturation can also be translated to colour, resulting in a clear visual representation of the varying oxygen saturation levels of different blood vessels. Therefore, this imaging approach has the ability to provide detailed information about both vascular structure and function.

**VASCULAR IMAGING IN BREAST CANCER**

Breast cancer is the most common cancer in women worldwide. Angiogenesis is key to tumours metastasizing and spreading to other parts of the body, and also to supply oxygen and nutrition for tumour growth. In breast cancer, angiogenesis is also associated with a poor prognosis and transformation from mammary hyperplasia (increased cell division) to malignancy. Dr Masakazu Toi and Dr Yoshiaki Matsumoto at the Department of Breast Surgery, Kyoto University Graduate School of Medicine, have used PAI to visualise tumour-associated blood vessels in the human breast.

The PAI method involved a holding cup, in which the breast was placed. Water circulated underneath the holding cup, providing the material through which sound waves travel. Lasers, producing light waves at several different frequencies, were then used to irradiate the breast. A photoacoustic wave is produced, which is received by a probe and sent to the data acquisition unit, which processes the data. 3D images of vasculatures around the patient's breast tumour were acquired, as well as areas of the body in human subjects with and without breast cancer. The team were able to scan regions of the hands, legs and breast in an imaging region with 140mm diameter. Using additional information from ultrasound imaging, Dr Toi and Dr Matsumoto were able to build an accurate 3D picture of the smallest blood vessels, including arterioles (small blood vessels branching out from an artery) and venules (small blood vessels that unite to form a vein), within this area. The results also showed that the blood vessels around a breast tumour have different S-factors. This suggests that there are both veins leading away from the tumour, and arteries leading into it.
The work done by Dr Toi and Dr Matsumoto represents one of the first studies to report high-resolution imaging of blood vessels in live human cancer tissue.

In breast cancer imaging, it was possible to visualise small, tumour-related vessels using PAI. The work done by Dr Toi and Dr Matsumoto was able to image tumour-associated blood vessels in high resolution.

**FUTURE STUDIES**

In breast cancer imaging, it was possible to visualise small, tumour-related vessels using PAI. The work done by Dr Toi and Dr Matsumoto was able to image tumour-associated blood vessels in high resolution.

Dr Matsumoto represents one of the first studies to report high-resolution imaging of blood vessels in live human cancer tissue.

Dr Toi and Dr Matsumoto utilise photoacoustic imaging to visualise tumour-associated vessels in the human breast.

**Research Objectives**

Dr Toi and Dr Matsumoto utilise photoacoustic imaging to visualise tumour-associated vessels in the human breast in vivo.

**Detail**

Dr Yoshiaki Matsumoto is a professor at the Department of Breast Surgery, Kyoto University Graduate School of Medicine. Among his research contributions are the studies on cancer metabolism and the clinical application of the photoacoustic imaging technique. He has been working on the application of artificial intelligence to photoacoustic images of tumour vessels in breast cancer to study the normalisation of them induced by drug treatment.

**References**


**Personal Response**

In addition to breast cancer, do you have plans to explore the use of PAI for other diseases? Future studies will examine vascular disorders and damages caused by lifestyle-related diseases or infectious diseases.

**Collaborators**

- Luxonus Inc.
- Canon Inc.

**Funding**

- ImPACT programme, Cabinet Office, Japan

**Applications**

- Breast cancer, which is one of the most frequent causes of cancer-related mortality among women.
- Other cancers, such as melanoma and prostate cancer.
- Infectious diseases, such as sepsis and tuberculosis.
- Vascular diseases, such as atherosclerosis and peripheral artery disease.
- Dermatological diseases, such as psoriasis and vitiligo.

**Applications of Photoacoustic Imaging**

- Imaging of blood vessels in live human tissue.
- Contrast-enhanced imaging.
- 3D imaging.
- Multi-modality imaging.

**Applications of Artificial Intelligence**

- Drug development and clinical trials.
- Personalized medicine and precision healthcare.
- Imaging of tumour vessels in breast cancer.
- Imaging of blood vessels in peripheral artery disease.
- Imaging of vessels in dermatological diseases.

**Applications of Artificial Intelligence and Photoacoustic Imaging**

- Artificial intelligence can be used to optimise the laser irradiation method and sensor sensitivity.
- Artificial intelligence can be used to identify unusual characteristics of oxygen saturation patterns which are consistently associated with tumour-related blood vessels.
- Artificial intelligence can be used to study the normalisation of vessels induced by drug treatment.

**Applications of Artificial Intelligence and Photoacoustic Imaging in the Future**

- Artificial intelligence will aid in the development of novel drugs which target angiogenesis.
- Artificial intelligence will aid in the development of novel imaging techniques which can guide drug delivery.
- Artificial intelligence will aid in the development of novel imaging techniques which can guide surgical approaches.

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