Enhanced imaging solutions

Dimitra Darambara, PhD explains how she is using her expertise in physics to improve cancer diagnosis and treatment response through the development of more reliable and highly accurate innovative imaging systems

Could you outline your research on novel medical imaging technologies and techniques?

My research focuses on the development of novel imaging instrumentation and emerging medical imaging techniques, ranging from the creation of new detector technologies to the building of complete imaging systems for task-specific applications to better identify, visualise and quantify molecular and cellular characteristics of cancer. In particular, my research interests centre on the development of innovative photon-counting and pixelated semiconductor detectors to enhance molecular sensitivity, the realisation of single and multimodal molecular and spectral imaging systems for next-generation healthcare hardware; the development of sophisticated 3D computational anthropomorphic phantoms for dosimetric and imaging proof-of-concept studies; and the design and performance modelling of imaging systems by combining state-of-the-art Monte Carlo and Finite Element Analysis codes.

At present, much of my work is focused on significantly improving the diagnostic capability of cancer imaging detector technologies. The detector component is the heart of every detection system, either it is a medical imaging scanner or a sophisticated particle detector, that provides a wealth of quantifiable information for cell/tissue/organ/body or particle identity. A detector with the highest possible efficiency, spatial resolution and sensitivity leads to an imaging system with the best achievable image quality and quantitative accuracy, which supports early and reliable cancer diagnosis and effective treatment.

What are the greatest obstacles to the effective imaging of cancerous tumours?

Current challenges in cancer imaging include the volumetric assessment of tumour size, the identification of reliable and sensitive biomarkers for specific tumour diagnosis and early assessment of response to therapy, and the need for new concepts of translational bioinformatics platforms to analyse, visualise and interpret multi-layered datasets (big data) generated by the fusion of different imaging modalities. A further challenge is how best to utilise current imaging modalities to correlate as much information as possible and combine it with tumour biology to interpret the clinical imaging results for early, reliable and accurate tumour diagnosis. Additionally, the current assessment of cancer is based mainly on morphological changes and subjective qualitative estimations of tumour characteristics. As such, there is an urgent need for the development and implementation of quantitative imaging techniques, which will enable the tumour characteristics from clinical imaging to be matched with the biological heterogeneity within a tumour across a wide range of temporal and spatial scales, and identify reproducible and quantifiable imaging features that reflect specific aspects of the underlying tumour/tissue biology.

By what means can semiconductor and photon-counting pixelated detectors improve molecular sensitivity?

The detector performance is a key driver for diagnostic accuracy and quality. By taking advantage of some unique properties of direct conversion pixelated compound, semiconductor detectors can lead to a transformation in medical imaging diagnostics, offering a new generation of imaging systems with high resolution and clinical specificity, ultra-dose-efficient photon-counting detection and quantitative characterisation, and measurement of underlying biological processes at the molecular or cellular levels.

How can the capabilities of conventional and dual-energy X-ray imaging techniques for precise tissue identification, differentiation and characterisation be enhanced?

The dual-energy imaging currently used in clinical practice utilises two X-ray sources at different tube voltages and two detectors operating on the same rotational gantry. This technology has improved on conventional X-ray imaging by taking advantage of the energy-dependent absorption within tissues. However, it only examines two regions of the spectrum and only two types of materials can be separated. It does not fully exploit the energy dependence of attenuation coefficients of an object to enable multi-spectral signatures to enhance the intrinsic contrast from an atomic level. Furthermore, the major drawbacks of overlapping spectra and increased dose remain. The implementation of our novel photon-counting spectra and increased dose remain. The implementation of our novel photon-counting multi-spectral X-ray imaging (x-CSI) technology should allow detailed tissue/tumour characterisation (multi-energy) and assessment of phenotype prior to planning management.

What are the primary functions and benefits of x-CSI?

x-CSI is a novel, 3D, low-dose, high-resolution, non-invasive, specific and quantitative imaging technique capable of providing underlying molecular information of tissue structure superimposed on anatomy. It is a cutting-edge specialised imaging technique that can provide an innovative clinical solution for differentiating and characterising tumours. This will introduce a totally new way of imaging in oncology, and potentially improve diagnostic accuracy and result in more effective management strategies.

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**Molecular insights**

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**SIGNIFICANT PROGRESS HAS** been made in cancer imaging capabilities in recent years. High-resolution, multimodal, molecular and spectral imaging systems are enabling unsurpassed medical imaging through 3D disease detection, improved tumour characterisation, monitoring of tumour response to treatment, increased sensitivity and specificity, and the quantification of biological processes at the molecular and cellular levels. "These developments have triggered a shift from anatomical- to molecular-targeted imaging, generating a plethora of multidimensional datasets that have a significant impact on the fundamental understanding of cancer," explains Dr Dimitra Darambara, team leader of the multimodality molecular imaging team at The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research in London, UK.

Drawn to medical physics by the possibility of translating basic research into practical applications with significant real-world benefits, Darambara is working with her group on the development of novel technologies and techniques to improve cancer imaging. "Although it is a real challenge to bring new technologies and ideas from the basic physics lab into clinical practice with direct impact on the quality of cancer patients' lives, it is also fascinating, inspirational and rewarding," Darambara enthuses.

At present, Darambara’s research is largely driven by the desire to develop imaging techniques capable of detecting the myriad molecular mechanisms contained within tumours, in order to facilitate early, reliable and accurate diagnosis, as well as pave the way for more effective, personalised cancer treatments.

**CANCER IMAGING CHALLENGES**

Although imaging technologies and techniques have improved greatly, they are not without their limitations; for instance, current X-ray imaging systems seldom facilitate soft tissue differentiation. Although all tissues possess their own characteristic spectral properties that theoretically allow for their quantification, conventional technology is unable to differentiate between tissues with small spectral separations. This results in incomplete imaging with low soft-tissue contrast. "For example, conventional X-ray systems cannot differentiate between hepatoma, metastases and nodules in the liver; deduce water, lipid and protein content within the breast; or simultaneously separate soft tissue, bone, iodine and gold," Darambara elucidates.

It is for this reason that the multimodality molecular imaging team is working to improve molecular sensitivity through the use of photon-counting pixelated semiconductor detectors, which offer an array of advantages over existing technologies, from increased sensitivity and quantum efficiency to higher spatial, contrast and energy resolution.

In order to achieve its aims, the group employs its own unique ‘hardware-development’ approach: a dynamic system that combines a realistic multi-environment software platform with thorough experimentation. In this way, the technologies and techniques in development are tested and refined in an iterative exchange fashion, proof-of-concept...
To translate cutting-edge molecular imaging technologies and techniques for cancer applications. In addition to its work on advancing x-CSI, the group is also conducting investigations in the following areas by:

- Undertaking pre-clinical gold nanoparticle Cone-Beam Spectral Tomography imaging assessments for targeted dose enhancement and simultaneous, multi-agent and multimodality imaging
- Further developing an advanced 3D digital breast tomosynthesis system
- Estimating mean glandular dose and studying dosimetric effect of breast positioning in respect to the detector for 2D and 3D X-ray breast imaging
- Creating a multimodality breast imaging system that combines tomosynthesis with breast-specific molecular imaging
- Building a sophisticated 3D anthropomorphic computational voxelised breast phantom named DeBRa for imaging and dosimetric studies
- Conducting multiscale mathematical modelling of cell-based breast tumour growth, invasion and morphogenesis in the mammary gland
- Advancing a multimodal imaging system based on novel CZT detectors

In addition, x-CSI systems have the potential to empower clinicians to make more precise cancer diagnosis and better-informed predictions and treatment options, as the imaging system will support more reliable and in-depth diagnosis and more insightful monitoring of therapeutic response. As such, Darambara’s group is confident that the development of x-CSI will pave the way for the widespread implementation of precision medicine and personalised care.