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How imaging tech and liquid biopsy will play pivotal role in cancer care

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A core tenet of precision medicine is to simplify the delivery of the right treatment to the right patient at the right dose and at the right time. Precision Oncology is rapidly developing and currently includes molecular profiling of tumours to identify targetable alterations.



At the core of Precision Oncology is a patient-centric approach. 2023 marks the year of the 20th anniversary of the conclusion of the Human Genome Project. Today, the use of genotyping and genomics have become essentials in standards and researchers and the industry is looking into expanding to include big data, proteomics, transcriptomics, molecular imaging, and more, to translate that ideal into meaningful and equitable healthcare for patients.

Recent rapid developments within the liquid biopsy and medical imaging technologies should encourage radiologists to view it as an opportunity to find synergistic ways of combinational techniques to improve personalised medicine and optimise patient care.

Biomarkers and Digital Biomarkers

Biomarkers are molecules that have different expressions in tumour cells than in normal body cells, and can be used for diagnosis, prediction of sensitivity to treatment, and prognosis. Especially ctDNA (Circulating tumour DNA) which can be found in fluids has gained significant attention. This is especially because ctDNA can easily be obtained through a simple blood draw – a liquid biopsy – and is used as a non-invasive biomarker to identify tumour-specific abnormalities. As a less invasive technique as compared to solid biopsy, liquid biopsy has the potential to be used to detect and monitor the presence and progression of cancer.

In the first week of January, AstraZeneca and US-based C2i Genomics announced a partnership to utilise the C2i Genomics' whole-genome minimal residual disease assay and cancer-monitoring platform for use in clinical research and drug

development efforts. This announcement comes just a month after AstraZeneca and Guardant360 announced a collaboration for the Guardant360 CDx blood-based liquid biopsy assay as a companion diagnostic for a breast cancer drug being developed by AstraZeneca. Based on data provided by Digital Health venture analytics platform HealthTech Alpha, there were 146 partnerships announced between Digital Health omics-related solution providers and corporations and institutions in 2022, up 2.4x from the previous year.

Immuno-oncology

Immunotherapy is a formidable weapon against cancer as it has shown the potential to use the body's natural immune response against the infection. Compared to conventional therapy, immunotherapies have demonstrated longÃ¢â?¬Â•lasting and significantly better responses for cancer patients. For the immune context, biomarker discovery plays a pivotal role in the assessment of potential Immuno-oncology (I-O) therapies and therapy combinations. The appropriate identification of Biomarkers enables the adaptation of individual treatment approaches for each patient and can be used to monitor a therapy response. The efficient and successful development of I-O biomarkers requires utilisation of appropriate tools and, several aspiring studies have used artificial intelligence (AI) to facilitate the transitions from preclinical evaluation through clinical development.

Immune checkpoint inhibitors (ICIs) have shown a promising response for several cancer types with lung, bladder and head and neck as well as melanoma. In 2011, Bristol Myers Squibb (BMS) received the first FDA clearance of ipilimumab, an ICI employed against CTLAÃ¢â?¬Â•4, for the treatment of metastatic melanoma. Thereafter, another checkpoint protein, PD1, and its ligand PDÃ¢â?¬Â•L1 have been found to have a higher response and lower side effects relative to antiÃ¢â?¬Â• CTLAÃ¢â?¬Â•4.

While anti-CTLA-4 drugs are limited, at least six drugs are available against PD1 and PD-L1. These include Imfinzi (AstraZeneca), Bavencio (Pfizer), Tecentriq (Genentech / Roche), Libtayo (Sanofi / Genzyme), Opdivo (BMS) and Keytruda (Merck).

Keytruda was initially approved by the FDA in 2014 exclusively for the treatment of Advanced Melanoma. In the following years its application was extended to include a number of head and neck, lung, bladder, cervical, skin, kidney, colorectal, esophageal and breast cancers. In 2017, Keytruda was the first cancer drug to receive approval based on a common biomarker rather than the location in the body where the tumour originated which was extended in 2020 to include a second biomarker-based indication.

Innovative solutions in Digital Health and biotechnology are a key driver behind the continuous development of drugs like Keytruda.

Functional Imaging

Medical images have long been used to guarantee satisfying treatment planning and outcome management of radiation therapy. Recently, the use of functional images to extract quantifiable radiologic biomarkers has arisen. The application of functional images is used to strengthen and improve prognostication response to radiation therapies and to facilitate personalised treatment and clinical trial designs. Moreover, quantitative functional imaging can also be applied for heterogeneous dose painting, whereby radiation is delivered within the tumour volume by targeting radioresistant areas.

According to HealthTech Alpha, there are more than 220 Digital Health ventures active in the field of cancer medical imaging. Many of these ventures are employing artificial intelligence and machine learning capabilities to their product offerings. One example of how Digital Health is impacting the development of biomarkers is PathAI, a Cambridge, MA, based provider of AI-powered research tools and services for pathology. PathAI has developed AISight, a web-based digital pathology slide viewing platform that enables the management and review of whole slide images and will accelerate access to AI-powered algorithms' quantitative and visual outputs. In August 2022, the company received their FDA and the CE Mark from the EU for their AISight Dx digital pathology platform for primary diagnosis in clinical settings.

According to HealthTech Alpha PathAI has closed partnerships with numerous leading pharmaceutical companies, including BMS, GSK (both in 2022), Novo Nordisk, Roche, Merck, and Gilead Sciences.

Since 2021, more than 20 partnerships have been disclosed between medical imaging Digital Health ventures and leading pharmaceutical companies. Such partnerships are not entirely based on the latest developments in treatment options and

personalised medicine but also due to the advancements in the application of artificial intelligence in image processing. Its use in quantitative imaging is crucial to improve the quality of the images because of its traditionally worst signal-to-noise-ratio compared to other imaging techniques.

Artificial intelligence also helps to construct image-based biomarkers which can provide a comprehensive view of the tumour and its heterogeneity. And, because medical imaging techniques are largely non-invasive, its application for tumour phenotyping related to prognosis and monitoring the development and progression are favoured.

Moving Forward

Combining medical imaging technologies and liquid biopsy as complementary tools in cancer care at each step will play a pivotal role in the cancer care continuum.

As an example, a recent imaging study suggested correlations between a higher disease burden measurement on CT correlated with plasma ctDNA burden. Other results of a study on the detection of rising ctDNA levels also indicate that its monitoring may also prove to be helpful in detecting tumour progression in settings in which subtle imaging changes can be difficult to detect.

Through findings like this, radiologists should feel encouraged to better understand the potential of liquid biopsy and the development of new imaging algorithms for screening, diagnosis and prognosis, and cancer management. Through further collaborations all stakeholders, including radiologists, oncologists, researchers and big data scientists are needed to optimise combined technologies and improve the early cancer detection in real-world settings.

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