



LIQUID BIOPSY – AN EMERGING LIMELIGHT IN PRECISION ONCOLOGY

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ABSTRACT:

Liquid biopsies are different from other types of biopsies, such as core needle biopsies and fine needle aspiration biopsies, which are the main way doctors diagnose and treat most types of cancer. During a needle biopsy, a doctor surgically removes a small amount of tissue from a tumor or suspicious area. Then, a pathologist examines the tissue under a microscope for the presence of cancer cells. A liquid biopsy, however, is performed using a simple blood draw. The blood sample is then sent to a laboratory for analysis. Molecular cancer biomarkers are any measurable molecular indicator of risk of cancer, occurrence of cancer, or patient outcome. Most cancers have multiple genetic mutations and they may not have the same ones in all parts of the cancer. The tissue samples removed for biopsy may not show all mutations whereas liquid biopsies offer an improved chance of detecting these genetic changes.

“Liquid biopsies could be a game-changer in cancer testing,”

KEY WORDS: Precision oncology, next-generation sequencing, Molecular cancer biomarkers,

INTRODUCTION:

“Precision oncology is the evolving understanding of how cancers develop on a genomic level and our ability to develop drugs that hone in on those targets – ultimately leading to better patient outcomes.”

Because this field is so new, the scientific and medical communities have not yet decided upon a singular name for it. Here are some common names that all refer to precision oncology:

- Personalized cancer medicine
- Individualized cancer medicine
- Personalized medicine
- Genomic medicine
- Precision medicine
- Personalized cancer treatment
- Oncogenomics
- Personalized oncogenomics

In order to have the best chance of recovery from cancer, you need treatment that targets your specific mutations. And for that, you need precision oncology.

In recent years, the rapid development of next-generation sequencing (NGS) technologies has led to a significant reduction in sequencing cost with improved accuracy. In the area of liquid biopsy, NGS has been applied to sequence circulating tumor DNA (ctDNA). Since ctDNA is the DNA fragments released by tumor cells, it can provide a molecular profile of cancer. Liquid biopsy can be applied to all stages of cancer diagnosis and treatment, allowing non-invasive and real-time monitoring of disease development. The most promising aspects of liquid biopsy in cancer applications are cancer screening and early diagnosis because they can lead to better survival results and less disease burden. Although many ctDNA sequencing methods have enough sensitivity to detect extremely low levels of mutation frequency at the early stage of cancer, how to effectively implement them in population screening settings remains challenging.

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Liquid biopsies can be done in addition to a tumor biopsy to support an initial cancer diagnosis and provide more information. They can also be used multiple times throughout treatment to monitor a tumor and see how well a specific treatment is working.



Molecular cancer biomarkers are any measurable molecular indicator of risk of cancer, occurrence of cancer, or patient outcome. A cancer biomarker is a characteristic that is measured as an indicator of risk of cancer, occurrence of cancer, or patient outcome. These characteristics can be either molecular, cellular, physiologic, or imaging-based. They may include germline or somatic genetic variants, epigenetic signatures, transcriptional changes, and proteomic signatures. These indicators are based on biomolecules, such as nucleic acids and proteins, that can be detected in samples obtained from tissues through tumor biopsy or, more easily and non-invasively, from blood (or serum or plasma), saliva, buccal swabs, stool, urine, etc. Detection technologies have advanced tremendously over the last decades, including techniques such as next-generation sequencing, nanotechnology, or methods to study circulating tumor DNA/RNA or exosomes. Clinical applications of biomarkers are extensive. They can be used as tools for cancer risk assessment, screening and early detection of cancer, accurate diagnosis, patient prognosis, prediction of response to therapy, and cancer surveillance and monitoring response. Therefore, they can help to optimize making decisions in clinical practice. Moreover, precision oncology is needed for newly developed targeted therapies, as they are functional only in patients with specific cancer genetic mutations, and biomarkers are the tools used for the identification of these subsets of patients. Improvement in the field of cancer biomarkers is, however, needed to overcome the scientific challenge of developing new biomarkers with greater sensitivity, specificity, and positive predictive value.

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“Liquid biopsies could be a game-changer in cancer testing,” said Miro Venturi, Roche’s Global Head of Diagnostics Biomarkers. “In terms of patient acceptability and disease management, the benefits of non-invasive, quick and easily repeatable tests are clear. And in the longer term, liquid biopsies may ultimately be used to catch signs of cancer early, before symptoms arise. This could make a significant difference to the way we understand and treat cancer.”

“From a treatment perspective,” comments Lukas Amler Senior Director, Oncology Biomarker Development, Genentech, “the increased access to liquid biopsies, especially for patients that do not have tissue available or cannot undergo a new invasive biopsy, could significantly increase the number of patients who will benefit from powerful targeted medicines, particularly in lung cancer. Tissue could also be reserved for other novel testing for example for cancer immunotherapy where currently there are no blood tests available.”

A liquid biopsy is a simple and non-invasive alternative to surgical biopsies which enables doctors to discover a range of information about a tumour through a simple blood sample. Traces of the cancer’s DNA in the blood can give clues about which treatments are most likely to work for that patient.

A liquid biopsy test that can detect epidermal growth factor receptor (EGFR) gene mutations, which occur in 10-35 per cent of patients with non-small cell lung cancer (NSCLC), will help doctors to choose the right treatment for the right patient at the right time.

Much of the early research on liquid biopsies has been in lung, breast and prostate cancers but this technology is expected to have an impact on all types of cancer.

EVOLUTION OF LIQUID BIOPSY

As early as 1869, Thomas Ashworth first observed circulating tumor cells (CTCs) in a patient with metastasis and suggested that these tumor cells were shed into the bloodstream, leading to metastatic cancer. A long period of time passed before scientists began quantifying cell-free DNA (cfDNA), which describes DNA that is freely circulating in the bloodstream but is not necessarily of tumor origin. In 1948, researchers first detected and quantified cfDNA in both healthy and diseased patients. In 1966, researchers discovered high levels of cfDNA in lupus patients, and in the 1980s, cfDNA was first discovered in oncology patients. Unfortunately, at that time researchers were unable to differentiate between tumor and healthy cfDNA.

It was in 1994 that scientists were able to advance to the point where they could detect specific mutations in cfDNA. In 1997, Dennis Lo was able to detect fetal cfDNA in the blood, and in 2000, Veridex introduced the first commercially available liquid biopsy assay, the CELLSEARCH[®] CTC test.

In June 2016, the FDA approved the first liquid biopsy test, the cobas[®] EGFR Mutation Test, as a cfDNA test for the EGFR gene mutation in blood from lung cancer patients. Currently, there continues to be a growing interest in the liquid biopsy assay, including an increasing number of companies involved in the development of these tests for the diagnosis and stratification of cancer patients.

HOW BLOOD IS DRAWN FOR LIQUID BIOPSY:

To collect a sample for a liquid biopsy, a health care professional will use a needle to draw a small sample of blood from a vein, usually in your arm. This is the same type of blood draw you would receive if your doctor was doing other common tests, like a complete blood count. Then, your health care provider will send this to a laboratory for testing.

One advantage of a liquid biopsy is that it is a simple, noninvasive procedure. You do not need to take special precautions before or after your blood is drawn for a liquid biopsy, and your doctor will tell you if you need to stop taking any medications before having your blood drawn. While more and more public and private health insurance coverage includes liquid biopsies, you should always contact your insurance provider before getting a liquid biopsy to see whether your test will be covered under your plan.

CONCLUSION :

The liquid biopsy will not replace the tissue biopsy in the foreseeable future”, says Joakim Jagorstrand, Lifecycle Leader for Genomics and Oncology at Roche Diagnostics. “However, liquid biopsies will complement the tissue biopsy allowing more patients to be tested. The issue is that many times there is just not enough tissue to test on. This novel, minimally invasive technique has the potential to change the prognostic and predictive landscape for lung cancer genotyping and impact patient management. I think we are close, but we are not completely there yet.

More real world clinical studies and comparisons are needed to fully explore the potential of plasma based testing. It is an exciting opportunity, a win for the patient in many ways and Roche is one of the world leaders in developing such tests.”

More validation in clinical trials is required on the value of liquid biopsies in the medical setting. And, while liquid biopsy informs treatment decisions in lung cancer with an epidermal growth factor receptor (EGFR) mutation, targeted therapies do not exist for all cancers. Are liquid biopsies the best option in diagnosing and monitoring these cancers? What if any role do liquid biopsies play in informing treatment decisions in the emerging field of immune oncology? These are questions that scientists and clinicians continue to explore.

“Using a blood test rather than relying on tissue would be a breakthrough as sometimes a (surgical) biopsy doesn’t take enough tissue,” says Dr Jesme Fox, Medical Director of The Roy Castle Lung Cancer Foundation, a lung cancer charity. “The science isn’t quite there yet but there is hope for the future.”

However, as scientific knowledge advances, researchers are learning more about the potential of liquid biopsies to detect mutations, suggesting that the promise and power of this diagnostic technology could be truly game-changing.

Whatever name you prefer to use, it is indeed the future of cancer treatment: precision oncology will undoubtedly be the standard in health care, with time.

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