Needleless Blood Count

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Everyone would think it normal when doctors will order blood tests for diagnosis nowadays. Playing a vital role in human body, blood supplies oxygen and nutrients, removes wastes and delivers immune cells and platelets. An adult has a blood volume of more than five liters on average[1]. Blood cells, including red blood cells, white blood cells, platelets, etc., can reflect essential information in disease diagnosis. As a result, complete blood count (CBC), which provides information about cells in the blood, is a common practice at almost all stages of diseases. Though conventional blood tests are useful, they are invasive extractions that require drawing blood from the patient, which have a few major problems.

First, the invasive extraction itself could put some vulnerable patients at risk, such as immunocompromised patients and patients with coagulation disorders[2]. Even for healthy people, the invasive extraction hurts. Secondly, the invasive extraction may disturb the biological environment of cells and cause the changes of properties. And thirdly, drawing blood is a sampling process which could introduce errors to the number of cells. This could be worse when it comes to rare cells, such as circulating tumor cells (CTCs) which could flag cancer diagnosis and the risks of metastasis, causing either overestimation or underestimation of some specific cells that significantly affects the diagnosis of conditions. Sampling also introduces another problem that the sampling process can only get the transient result of blood flow instead of long-term real time monitoring.

Considering these major problems, non-invasive approaches have drawn interests of researchers around the world. And flow cytometry has been a technique to analyze cells and particles for decade. As a result, in vivo flow cytometry (IVFC) has been created and developed and has shown its potential of being an alternative to conventional blood tests. In this essay, some of the IVFC research results will be introduced.

IVFC allows noninvasive monitoring of cells. In general, when a cell flow through the

targeted area, a detectable response will be generated and collected, such as fluorescence, photoacoustic effect, photothermal effect, etc.[3] There have been many successful research applications that show the potential of IVFC as an approach to conducting noninvasive blood cell analysis and solving the problems of conventional blood tests.

In 2012, Golan et al. reported the successful in vivo imaging of red blood cells and white blood cells of a human volunteer's lower lip[4]. The vessels 70-200 microns below the surface were located and imaged. Then images of red blood cells and white blood cells were obtained, and the analysis results of both red blood cells and white blood cells match the in vitro results.

Metastasis is related to most of cancer deaths and caused by the dissemination of CTCs shed from the primary tumor[2]. As discussed above, CTCs are hard to quantify in conventional blood tests, mainly because there are usually less than 10 CTCs per mL blood[3]. IVFC has shown the capabilities in CTC observations. In 2012, Fan et al. reported the liver cancer CTC monitoring with 1.8-fold higher sensitivity than conventional whole blood analysis using IVFC[5]. In 2014, Aceto et al. proved that CTC clusters were from the primary tumor cells and greatly contributed to the breast cancer metastasis[6]. The IVFC was used to monitor and analyze single CTCs and CTC clusters.

The research applications have shown that IVFC can analyze white blood cells, red blood cells and CTCs, which presents the exciting potential for analysis of cells using IVFC, but there is still research work to be done. For example, some IVFC, such as photoacoustic or photothermal IVFC, can only be used to count/detect the presence of cells but not get the morphological information. Thus, the imaging capabilities become a focus of research on IVFC.

The morphological information is important because the shape and aggregation of certain cells can also reveal valuable information. Fox example, the aggregation of platelets can uncover the risk of thrombotic disorders, and thus, reduce the risks of related stroke and heart

attack. In 2017, Jiang et al. achieved images of single platelets and aggregated platelets using a self-designed in vitro flow cytometry with an artificial channel to flow the blood cells[7]. It is promising that the imaging of platelets can be achieved by in vivo approaches with the development of technology.

Furthermore, the morphological information can be used to develop image-based cells sorters that could help a lot in medical institutes by automatically counting different blood cells, flagging presence of rare cells, and monitoring the abnormal change of numbers of different blood cells over a prolonged period. Many studies have shown that with the help of machine learning, the sorting and counting of cells can be fully automated in real time based on the image data. With capability of detecting CTCs at early stages, IVFC will be the tool to save many people and provide invaluable information on the unknown mechanism and cure of cancer and metastasis.

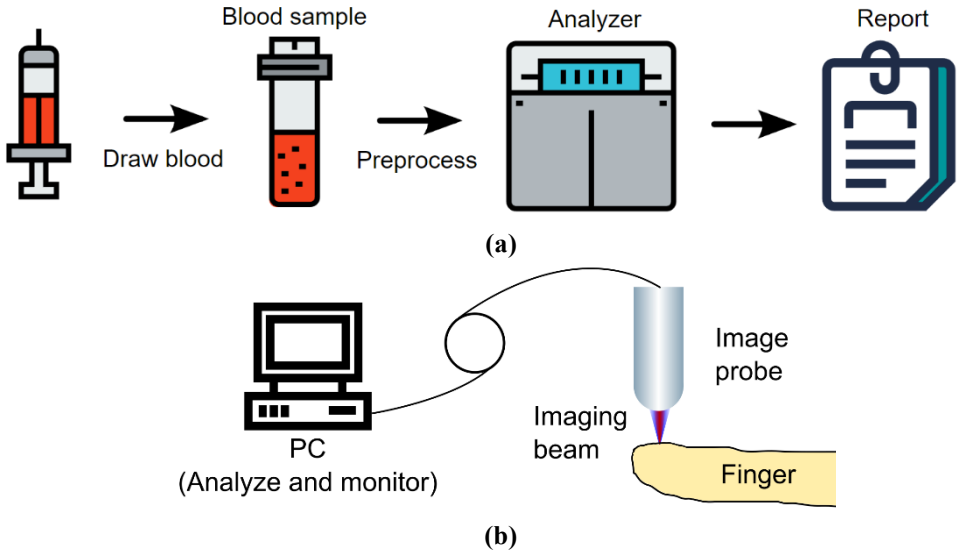

Fig. 1 (a) Conventional blood test workflow, and **(b)** potential application using IVFC to conduct blood test by imaging vessels in human fingers. (Icons by *svgrepo.com* are licensed under CC0.)

In summary, IVFC has already shown the capability of detecting and analyzing blood cells, including those are difficult for conventional blood tests to discover, in medical and biology related research. If the IVFC system can be further developed, a highly integrated bedside healthcare device that has the capabilities of imaging and sorting red blood cells, white blood cells, platelets, CTCs, and other rare cells will become a reality. Everyone would find it

fantastic if the patient only needs to put the finger against an optical probe, then the real-time data of blood cells can be displayed on the screen, and real-time long-term monitoring of blood cells can be provided by the same device on demand as well. By then, IVFC will be an alternative to the conventional blood test, which could certainly be useful to save people and contribute more to medical research.

References

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