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Perspective

In Vitro Cell Diagnostics Technique: Photo Acoustic Flow Cytometry (PAFC)

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ABOUT THE STUDY

Flow Cytometry (FC) is a well-known diagnostic technology that has transformed *invitro* cell diagnostics. In this method, cells are placed in an artificial flow and photo detectors are used to detect laser-induced scattering and/or fluorescent light from them. Modern multicolor FCs with sophisticated fluorescent probes are broadly applied in fundamental and clinical research for a variety of purposes, including quick study of huge populations of cells, detection of rare cancer cells, cell viability evaluation, and drug–cell interactions, among others. Photo Acoustic Flow Cytometry (PAFC) is a biological imaging technique that performs flow cytometry using photoacoustic imaging. Individual signal reactions are produced as a flow of cells passes through a photoacoustic device. To provide a quantitative evaluation of the input sample each signal is counted. The system can measure cellular size and complexity using various quantifications of light scattering from the cells, which may then be returned in a quantification of cell composition within a sample. Photo acoustic flow cytometry works on the same principles as conventional flow cytometry, but it uses a photo acoustic signal to distinguish cellular patterns. Flow cytometry also enables excellent *ex-vivo* analysis, but its penetration depth is limited due to its pure optical source limiting *in-vivo* study. Photo acoustics, on the other hand, may have an advantage over flow cytometry because it receives an acoustic signal rather than an optical one and can penetrate deeper. As PAFC is a new technology in biological cell research, it was combined with the well-known PTFC. The PA approach has a new issue in detecting fast moving absorbing micro- or nano-objects of various origins against the background of blood cell and surrounding tissue absorption. Existing approaches, such as improved Polymerase Chain Reaction (PCR) and immunochemistry assays, and even cell enrichment *invitro*, are unable to do this. Similar to standard *in vitro* FC, the PAFC could have a wide range of in *vivo* applications, including detection of various targets with intrinsic absorption or with PA labels targeting specific antigens and receptors (e.g., normal and abnormal cells, bacteria, viruses, conventional contrast agents, and advanced nanoparticles) in a variety of vessels. It may be particularly useful for early detection of infection during hematogenous spread of germs into various organs, vascular grafts, and stents. These infections, in particular, commonly result in death from sepsis, developed a quality therapy at the advanced stage of the disease. Using small, resilient, low-cost laser diode arrays with variable wavelengths, PAFC technology may allow us to construct portable "personal" flow cytometers for blood testing without a needle. High-pulse repetition-rate lasers, rapid signal acquisition methods, time-of-flight cell velocities measurement, and targeted lasers are among the technical advances made by PAFC. New advancement in PAFC include;

- Label-free monitoring of melanoma CTCs released during palpation, biopsy and conventional and laser surgery
- Multiplex targeting, magnetic enrichment, and detection of breast bulk and stem CTCs
- PA detection of CTCs (also known as disseminated tumour cells) in lymphatics as the earliest prognostic marker of metastasis compared to sentinel lymph node and blood assessment
- Targeted detection of pathogens within the bloodstream of single bacteria
- Identification of PA blood rheology, including real-time monitoring of RBC aggregation
- Diagnosis of sickle cells
- The study of cell death in the circulatory system
- The pharmacokinetics of NPs, liposomes, dyes, and other contrast agents, as well as their dynamic interactions with blood cells, are being studied
- Identification of cells and NPs based on their distinct blood flow velocities
- Theranostics as real-time, PAFC-guided, PT CTC and bacteria removal from circulation.

This method enables the detection of circulating bacteria (and cells) in real time with ultra-high sensitivity as a single bacteria (or cancer cell) in a background of normal blood cells. The development of portable devices attached to the wrist or lymph nodes for alarm control of bacterial infection dissemination, cancer recurrence, metastasis development, therapy assessment (by controlling the number of circulating bacteria or metastatic cells), or monitoring of circulating drugs using nanoparticle-based drug carries is expected to speed up the transition of thistechnology to humans (eg: liposomes). PAFC is in high demands for its various advantageous properties and low cost.

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