Electrochemical label-free pathogen identification for bloodstream infections diagnosis: towards a machine learning based smart blood culture bottle.

Résumé

Persistent bacteremia are most often associated with sepsis, some of the most urgent and life-threatening situations in medical practice, requiring a timely initiation of appropriate antibiotherapy. As the global sample-to-result time is affected by the consecutive steps in the workflow, efforts in sparing time during the blood culture may be wiped by long transport time, between sampling site and laboratory. Moreover, clinical laboratories currently employ a two-step strategy, with the detection of pathogen in blood culture bottle, followed by its identification once the microorganism is separated from the patient's blood.
In this report, we propose a breakthrough approach to address these two problems. Firstly, our smart blood culture bottles enable a continuous monitoring of blood culture with minimal instrumentation, away from the lab. Secondly, these instrumented bottles can yield identification without separating the pathogen from blood.

In our study, we have designed an instrumented blood culture bottle with a multi-material potentiometric sensor made of different conductive inks that incorporate either conducting polymers or metal oxides. Human blood from healthy patients was infected with reference bacterial strains: 31 reference strains (16 species) were tested, with various inoculums (between 5 and 300 cfu) to measure the variability of our results. Each culture led to a detection, we had no false negatives. Four experiments were conducted without the addition of bacteria, during 120h of incubation, to obtain the response of the system on sterile blood.

The detection times calculated with our device are comparable to those obtained by the latest generation of commercial optical automata (Bactec and BacT/ALERT). Moreover, the analysis of the measured potential evolutions reveals electrochemical profiles, allowing us to obtain information on the metabolome and thus the species present in the blood culture flask. Thanks to a machine learning programme, we are able to identify the Gram and genus of the microorganism in culture with more than 80% accuracy (99% for Gram) only a few hours after the positivity and without any manipulation or reagent.

This instrumented blood culture bottle eliminates the need for a costly and cumbersome automated system due to the simplicity and cost-effectiveness of the open circuit potential measurement electronics. Electrochemical metabolite analysis therefore allows for continuous monitoring of the blood culture but also for rapid initial identification.
Overall, this new blood culture method could therefore be a major step forward in microbiological diagnosis and management of sepsis. A faster (to obtain identification) and less expensive diagnostic system would be a significant advantage for the diagnosis of bloodstream infections in low- and middle-income countries, where antimicrobial resistance is most devastating and in low-density areas where transport time could be important. This concept also provides an opportunity to add value to the incubation time, which represents a blind period in the conventional diagnosis of bloodstream infections.

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Mots-Clés: Blood culture, Sepsis, Electrochemical sensor, Labelfree identification