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New microwave sensor arrays-for the rapid detection of pathogenic bacteria concentration and growth: Application to early diagnosis of sepsis

Nouveaux réseaux de capteurs microonde pour la détection rapide de la concentration et la croissance de bactéries pathogènes : Application au diagnostic précoce de la septicémie

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Boodstream bacterial infection is a medical emergency demanding early diagnosis and tailored antimicrobial therapy. Every hour of delay in the diagnosis of sepsis increases patient mortality[1]. Currently, clinical laboratories employ a two-step strategy: the first step involves the use of a blood culture system to detect the presence of growing organisms in blood culture. In the second step, positive cultures for species identification using phenotypic and genotypic assays. With the existing blood culture systems, the time to positive result typically ranges from 1 to 3 days, and an additional 1 to 2 days is needed for species identification with conventional methods, although MALDI-TOF MS and genotypic methods have shortened this time to hours instead of days[2,3]. Meanwhile, patients are treated empirically with broad-spectrum antibiotics. This approach puts the patient at risk for ineffective antimicrobial therapy and selection for antibiotic-resistant organisms. Other assays used to speed up the infection diagnosis include nucleic acid amplification tests (NAATs) for organisms and enzyme immunoassays for inflammatory biomarkers in whole blood and serum, respectively[2]. However, NAATs do not have sufficient sensitivity and specificity to replace microbial cultures, while biomarkers are nonspecific and unable to identify the etiology. Thus, there is still a crucial need of easy-to-use and low-cost devices with the capacity of both detecting the growing pathogenic bacteria and screening their antibiotic susceptibility in a very short time. In this context, biosensors and point-of-care devices are particularly attractive for a better handling of the patient. However, the proposed technologies (commercial or not) do not meet, for the moment, the whole requirements in terms of speed, cost and accuracy[4-5.]

In this work, we propose to tackle these challenges by combining the efficiency of microwave transduction technology with the specificity of biological molecules such as antibodies and the amplification/labelling capacities of biofunctionalized nanoparticles. Thanks to its intrinsic advantages, including simple and low-cost fabrication process, compatibility with other state-of-the-art technologies such as printed-circuit boards and microfluidic lab-on-a-chip systems, microwave-based transduction stands out as very promising for clinical diagnosis but has been rarely used in the field.

A microstrip patch RF sensor array configuration that works around 3.5 GHz frequency (inside the unlicensed spectrum defined by the FCC in USA and the ETSI in Europe)[6] will be designed for contactless detection of bacterial concentration and growth. The proposed RF sensor array will be engineered, optimized to improve existing resolutions and to detect the growing pathogenic bacteria with the highest possible sensitivity. Some design challenges to tackle are related to: (i) efficiency, (ii) compact size, and (iii) near sensor computing to become part of IoT system. Bacterial detection will be optimized on several representative microbial strains using different bioassay formats (microwells, microfluidic system). To achieve higher specificity and sensitivity of detection, cells will be captured from the sample-using nanoparticle functionalized with a suitable density of specific antibodies. The completely analytical system will be optimized to achieve the targeted microbial LOD (some cells/mL untreated blood) and detect bacterial growth in blood in less than 30 min. The sensor array will be validated to screen proliferation of bacteria in untreated blood samples in response to antibiotics.

References :

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