medGadget

MALDI-TOF MS and the Future of Rapid Testing: Five Questions for Dr. Nedal Safwat of bioMérieux

by Jan Sinnige on Oct 12, 2011 • 12:40 pm

Matrix-assisted laser desorption/ionization–time-of-flight mass spectrometry (MALDI-TOF MS) is one of the latest and most promising technologies being commercialized by bioMérieux, an international firm based in Marcy-l'Etoile, France. The technique relies on basic mass spectroscopy, but is designed to be used with large peptides and proteins of pathogens without breaking down molecules.It can provide very specific data about bacterial, viral, or fungal infections.

Medgadget editor Jan Sinnige, an MD MSc and resident in clinical microbiology and laboratory medicine at the University Medical Center in Utrecht (UMC Utrecht) in The Netherlands, had a chance to ask Nedal Safwat, Ph.D., Senior U.S. Clinical Marketing Manager from bioMérieux, Inc., about the company's technology, its impact on health care, and the future of bioMérieux.

Jan Sinnige, Medgadget: **What is the impact of this fast identification technology on the workflow of microbiologists? How should the classic microbiology laboratory adapt to this new rapid testing?**

Dr Nedal Safwat, bioMérieux: Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS) is a research-use only technology and is not yet available clinically. It allows lab scientists to profile the proteins of an organism and—based on that unique protein profile revealed in a spectra—can specifically and with great accuracy distinguish one organism from another. MALDI-TOF-MS can do this in just minutes, rather than days, which is the current standard. It also works on all species, including Gram-negative and Gram-positive bacteria, fungi, virus, and protozoan pathogens.

The accuracy and specify of this technology is like nothing that the clinical microbiology lab has ever seen before and it will have a profound impact on lab workflow and patient care.

The current state-of-the-art method to detect pathogen species is based on a biochemical process that detects unique metabolites produced by these species when they encounter various chemicals. The creation of these tell-tale metabolites results in a distinct color change that reveals the pathogen type. However, new molecular tests are hastening this process and MALDI-TOF-MS is one of the most promising.

Because of the speed of the technology, its greatest promise is helping labs quickly identify those infections that are the most difficult to treat and prone to being resistance, pathogens such as *Staphylococcus aureus Escheria coli and Klebsiella, Acinetobacter baumannii, Aspergillis, Enterococcus faecium), Pseudomonas aeruginosa, including some of the most difficult organisms like mycobacterium, filamentous fungi, and nocardia.* These organisms pose a great challenge within the hospital because they prey upon the most vulnerable, the very young and old, as well as those who are being treated for serious underlying conditions, such as cancer.

Currently, determining if a patient has one of these infections is a very time consuming process. Specimens (urine, blood, etc.) that are taken from patients with suspected infections are" streaked," or inoculated, onto media in culture plates. This media promotes the growth of the organism, which can take anywhere between 18 to 48 hours, depending on the organism.

Chores, such as plate streaking, take up a tremendous amount of time in the lab and divert laboratory expertise away from more important functions, such as susceptibility testing. Of course, waiting for enough growth on the culture plate is a major bottleneck in the workflow of the lab, as well. If something goes wrong, such as an insufficiently inoculated plate, the process must be repeated. This is not uncommon. All of this, unfortunately, makes the diagnosis process very slow.

Lab scientists have longed for faster technology which bypasses many of these labor-intensive chores. I think the microbiology lab community will adapt quite readily to technology that makes them faster and allows them to be stronger partners to treating physicians.

Medgadget: **What are the benefits of fast typing pathogens technology for patient care? Do you think that this technology might have an impact on the emerging antibiotic resistance problem?**

Dr Safwat: The clock is the enemy in treating a patient with an unidentified infectious disease. Standard plate inoculation and culturing can take between 24 and 72 hours, on average. If an error occurs or the plate is not properly inoculated, it's not uncommon for results to take 4-5 days. Providing treating physicians with results in minutes instead of days clearly benefits patients but also helps avoid or mitigate the use of an incorrect

antimicrobial. Depending upon how serious the infection is, physicians often rely on empiric antibiotics in order to treat what might be a deadly bacterial infection. If the infection turns out to be a virus, these antibiotics were unnecessary. Empiric antibiotics will always be used, but technology such as MALDI-TOF-MS can move us much closer to the goal of treating the right patient with the right antimicrobial.

For example, MALDI-TOF-MS could tell a physician very quickly that his or her patient is infected with *Escheria coli* , much more quickly than biochemical methods. However, there are many antibiotics that are effective against *e. coli*. Which should the doctor choose? The optimal antibiotic depends on the specific strain of *e. coli* that has infected the patient. By quickly identifying the pathogen as *e. coli*, the treating physician can rely on epidemiology data from the community, the hospital, or the specific location where the patient lives, such as a nursing home. This epidemiological data tells the doctor what strains of *e. coli* are most prevalent in the community, which is extremely helpful because it allows the the doctor to make a well-informed decision about the optimal antibiotic for that patient.

Another clear benefit of MALDI-TOF-MS is that it can take a great deal of time off of the current process of bacterial susceptibility testing. For example, if a patient tests positive for a blood infection, it typically takes 24 hours to culture this unknown infection in order to determine the species. In order to determine the optimal antibiotic to treat the infection, once the species is known, requires susceptibility testing, which usually takes 8 hours. So, MALDI-TOF-MS can reduce the time to precise treatment by 32 hours! That amount of time can not only save a life, but can also help decrease the misuse of the wrong antibiotic which is a major cause of antibiotic resistance.

Based on the data from our research partners, MALDI-TOF-MS provides accurate identification of 95 percent of the pathogens tested, which is much better than standard biochemical identification.

Medgadget: **Organisms need to be matched with a database of known protein sequences, shouldn't we be afraid to miss isolates that do not match the database when not culturing anymore?**

Dr Safwat: MALDI-TOF-MS will not eliminate pathogen culturing. In fact, culturing must continue in order to help develop the spectra of new and emerging infectious diseases. It is also likely that this technique will be used initially only when a highly infectious and deadly pathogen is suspected. For many microbiology lab tests and outpatient testing the standard culturing process is adequate and will remain state-of-the-art.

Medgadget: **How do you think the resolution of protein sequences will develop in the future? Will it be possible to recognize isolates of a single clonal line? Will it help us with rapid interventions in outbreak management?**

Dr Safwat: Researchers from Emory University School of Medicine and the Grady Memorial Hospital in Atlanta presented a poster at the 51st Interscience Conference on Antimicrobial Agents on September 19, 2011. They compared standard culturing to MALDI-TOF MS when linked to the bioMérieux microbial identification platform, VITEK, and the SARAMIS pathogen database

This database identifies gram-positive and gram-negative bacteria, yeast, fungi and spores based on their characteristic MALDI-TOF MS fingerprints with up to 98 percent recovery rate down to sub-species level. No pre-selection of analytical methods is required.

The Emory and Grady Memorial Hospital researchers concluded:

"(A) Total of 254 clinical isolates including 27 Candida species, 86 Gram-positive and 141 Gram-negative bacteria that were collected mostly from blood, respiratory, and urine cultures were used for validation. Of 27 Candida isolates that were identified correctly by using the Vitek-MS methods as by the conventional culture method, 14 were Candida albicans with the MS-likelihood index ranging from 78.3 to 98.9%, 10 were C. glabrata with MS-index from 89.3 to 99.9%, 2 C. parapsilosis and 1 C. tropicalis.

"Of 141 Gram-negative bacterial isolates that were identified correctly by the Vitek-MS as with the conventional culture methods, 27 were Acinetobacter baumannii, 23 Escherichia coli, 23 Klebsiella pneumoniae, 23 Pseudomonas aeruginosa, 18 Haemophilus influenzae, 11 Enterobacter cloacae, 9 Serratia marcescens, and 7 E. aerogenes; the MS-likelihood indexes ranges from 75.7 to 99.9%. Of 86 Gram-positive bacterial isolates that were identified correctly by using Vitek-MS method, 30 Staphylococcus aureus, 25 Streptococcus pneumoniae, 10 Enterococcus faecium, 9 S. agalactiae, 7 S. pyogenes, 3 E. faecalis, and 2 S. epidermidis; the MS-likelihood index ranges from 79.3 to 99.9%."

These pathogens include some of the most deadly and virulent microbes that plague hospital patients. Bacteria and yeast were included and the results were the same. MALDI-TOF-MS is as accurate as culturing, but remarkably faster.

Medgadget: **When can we expect approval of this technology by the FDA, and what news can we expect in the near future?**

Dr Safwat: We are still in the process of collecting data from various pilot study sites. ■