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Use of MALDI-TOF for diagnosis of microbial infections

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Guest:
Dr. Susan Poutanen is a Microbiologist & an Infectious Disease Physician at Mount Sinai Hospital in Toronto and an Associate Professor at the University of Toronto.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett.

The application of Matrix-Assisted Laser Desorption Ionization–Time of Flight Mass Spectrometry or MALDI-TOF MS, to microbial identification is revolutionizing clinical microbiology, providing rapid identification with minimal sample preparation and potential cost savings.

Worldwide the degree of implementation of Mass Spectrometry varies markedly. In a Q&A feature in the October 2013 issue of *Clinical Chemistry,* four experts from across the globe with firsthand experience in implementing mass spec in the microbiology laboratory provided insight into what this technology can and cannot offer, and what direction it will take us in the future.

One of the participants in that panel, Dr. Susan Poutanen, joins us in today's podcast. Dr. Poutanen is a Microbiologist & an Infectious Disease Physician at Mount Sinai Hospital in Toronto, and an Associate Professor at the University of Toronto. Dr. Poutanen, many clinical microbiology laboratories had implemented or are considering implementing MALDI-TOF MS as an identification tool for bacteria and yeasts. In addition to this identification tool, what other potential applications exist?

Dr. Susan Poutanen: It's a great question because right now MALDI-TOF is really recognized as a replacement for identification, and in fact, it is very exciting because just in the last few weeks, one of the systems that's available has now received FDA clearance, and so certainly lots of laboratories are going to be looking to this system as a potential replacement for their routine identification systems. And clearly the advantage of that is there are just lots of studies now -- not too many, but certainly more studies being published that are showing that the fast identifications that MALDI can provide are indeed advantageous as we discuss in our paper

with regard to reduce time to effective therapy, cost savings, and yet people who have looked at MALDI-TOF and understand that potential other applications realize that the benefits that could potentially be achieved are even more than that.

And certainly right now when you have identification you can change therapy and certainly we can see more optimal therapy quicker in patients because of it, yet we don't yet have a fast way to really determine resistance determinants, and trying to modify therapy even further.

And so the potential from MALDI-TOF to be expanded not only to help with fast identifications, but also to provide fast identifications of key resistance determinants such as ESBLs and/or carbapenemase production and/or methicillin resistance for example, is also there, and there are some preliminary data suggesting that it's promising that there very well maybe distinct applications down the road. They are not here just yet, but certainly in the future that looks very promising and that's not the only promising additional application.

The other is the issue in labs right now as well, most of us are doing quite a long extra work, trying to determine epidemiological relationships between bacteria, using something called pulsed-field gel electrophoresis or sequencing data and the like, and yet there is so much potential for MALDI-TOF to potentially also be used as a tool to allow for epidemiological comparisons of different strains to facilitate infection controlled investigations of possible outbreaks, and again, not there yet, but certainly the potential exists.

And finally in terms of other areas that labs often struggle with in terms of finding technologists who can continue to work in the area is our mycology labs. It's one area that required considerable expertise and experience and it's challenging to find replacement staff who have that experience when they are just coming out from graduation, to replace retiring technologists who have been there for many generations and years. So identifying fungi, filamentous fungi via the MALDI-TOF would be a hugely welcome tool and it's not there yet again, but there's certainly very promising preliminary data suggesting that it may very well be able to be applied in this area as well.

Bob Barrett: Now I understand that your laboratory is currently in the process of implementing MALDI-TOF. Based on your experience, do you have any practical advice about the implementation of this technology in a clinical microbiology laboratory?

Dr. Susan Poutanen: I sure do. We'd have actually done a very long stage implementation and it's been over the last year and a half or so which is extensive, in the sense that we combined our verification and our implementation and have been doing a very slow stage approach. And the reason for that is, the impact on both the laboratory as well as on the clinical wards and clinical clinic is not in substantial, and we wanted to make sure that we are doing it in a way that is going to be accepted by both our laboratory staff and by our wards and clinics.

So for example, in our lab what we have done is in addition to the initial verification study, we have been working on workflow analysis to see how we could best optimally bring it into our lab, in each section of the lab, to maximize the workflow and the elements of lean philosophy that we brought into our lab, to make sure that we are getting the biggest bang for our buck so to speak, in terms of the efficiency gain from workflow and time required to identify our organisms on our benches.

In addition to that, one of the major impacts as we have been waiting to develop an interface to facilitate the transfer of the identifications from the MALDI instruments to our laboratory information system and out towards our hospital information system. This has required a significant amount of time to, one, build the interface, but also to translate all of the new names that we are now seeing generated by the MALDI-TOF instruments, into names that our lab information system will recognize and that our hospital information system will accept, and also to discuss and make sure that those names make sense to the end user and aren't potentially confusing.

Further, of course, the training of all staff both day and night is an element, which is not that onerous, because it is actually a very simple task to do, but nonetheless, you must take that into consideration. And finally, we have been delaying that and doing it piecemeal in our lab so that we have staff buy-in and we are really going to use our staff to be part of the working team to determine how best to do this.

And ultimately, what we have been doing is stage wise implementing it bench-by-bench, but at the same time we have been working with the wards and clinics and our key stakeholders, like our infectious disease team, our antibiotic stewardship team, our infection control team, department heads early on, to make sure that we have their buy-in and how we are going to be doing this. For example, the names that we are going to be reporting out, to make sure that they are acceptable and not confusing. The times of day that we will be reporting out, given that it's so easy to use and

so fast in terms of providing a turnaround time of an identification, we are no longer reporting out our identifications once a day, we are doing it multiple times throughout the day, and obviously it's not useful to do so, if you don't have the end users available and ready to act on those results at the times that you are reporting it out.

That dialog was certainly important for us, and we are just now on the final phases of fine tuning all that with our interface, literally just to ready to get it up and running, and so our plan in terms of implementation now, is to do it as we discussed, bench-by-bench slowly to make sure that everyone indeed is using it as we expected it to be, and that there are no problems in our actual implementation.

Having said all that, since we have done this as a very long phased project, the amazing utility of the MALDI and the attractiveness of doing identifications on this piece of equipment was so attractive to most of our technologists that even though we haven't formally implemented the full plan of how we are going to be maximizing the benefits of this instrument, our technologists have asked; since it is now verified, to start using it where they have trouble bugs, and so in fact, our lab has been using it unofficially, while we have been staging our formal implementation which will be eminent now.

Bob Barrett: Doctor, are you planning to have MALDI-TOF MS replace the standard identification assays currently used in your laboratory, and if so, what has your lab done to plan for a backup identification system in the event if there is an equipment failure with the mass spec instrumentation?

Dr. Susan Poutanen: Well, that's an excellent question. We actually are quite a large lab, we serve at least ten institutions, both acute care hospitals, long-term care facilities, rehab facilities, and our total number of identifications a week are in a spectrum of thousands or so, and certainly we don't want to have our lab go to a full stop in the event that there is an equipment failure.

We considered this long and hard and initially when we were looking at incorporating the MALDI-TOF into our laboratory and look at our business case and our potential for our cost return of purchasing in the upfront cost of the purchasing of the equipment, we had to take into consideration this exact question is, are we okay with having one MALDI-TOF instrument and then what do we do if it fails? Can we in fact incorporate going back to our old system or with our large load of organism identifications that occur, will we be able to stop and have enough potential automated biochemical type identification systems that we are using now as our backup, and we didn't feel that that was possible.

So what we opted to do and what we realized as well is that a huge benefit to do this, is to purchase two instruments. And why it was a benefit is, one, we have that redundancy in the event that when there is an equipment failure with one of them, but in fact two, it allows us to be even more efficient in how we use the MALDI-TOF in the lab, because we have now two different instruments for the benches to use, and so in the morning we have our blood culture and sterile bench for example, using our MALDI-TOF number one, whereas we have a respiratory bench and our miscellaneous bench is using our MALDI-TOF number two.

So our identifications are going out as fast as possible as soon as the technologist come in, and so there are benefits gained by not just the ability to have the equipment failure backup, but also in terms of maximizing our turnaround time to identifications by having purchased two instruments. And that was a decision that we looked into our lab as being the best decision which was still cost effective in terms of our ultimate cost return of investment.

Bob Barrett: Microbiology laboratories seemed to be in the midst of a paradigm shift with increased opportunities to incorporate automation and robotics, how do you see MALDI-TOF MS fitting into this new era?

Dr. Susan Poutanen: It was really an exciting time to be in microbiology, and indeed, not only do we have wonderful new instruments like the MALDI-TOF MS, but we also have automation and robotics as you alluded to. In fact, this is really the first time you can see a lot of change happening in microbiology, and it's really in response to the fact that microbiology, as well as other laboratories, are seeing increasing workloads due to our increasingly aged population, more intense interventions with increased immunocompromised persons with transplants, and with chemotherapy, and cancer, our treatments are improving, and unfortunately all in the era of having reduced budgets, and so, we are at that standstill where, if we don't change how we are actually doing things, we are not going to be able to cope with this increased number of specimens coming through our lab.

And so automation, which primarily right now focuses on front end specimen processing has really changed the whole field in terms of saying, hang on, we have got a way to make it a little more efficient in the front end there, and there are promising further utilities of automation through the use of what are called smart incubators, whereby specimens which are automatically processed by robotics are then put into incubators that are automatically screened by cameras, so that technologists who are remote can verify

negative cultures and get them out without ever touching the plates, and can look at positive cultures and use touch screen commands to indicate which actual colonies need further identification, and if they weren't with the MALDI, it wouldn't have been able to be done as efficiently.

Indeed these automated systems are expecting labs to incorporate the MALDI-TOF instrument to be able to ultimately maximize the benefit of this full automated lab, so to speak. And so the ultimate goal would be that labs would now be having automated front,end processors, smart incubators, touch screen commands from technologists, remote from the actual specimen plate, to be able to indicate to the robot which colony needs to be identified and then for the MALDI-TOF instrument to be accessed via the robotics and for identifications to ultimately be done without potentially ever having even touch the actual plate.

And indeed, in term of trying to maximize the benefit of that in our laboratory, we have moved forward with automated front end specimen processing, we have budgeted for smart incubators this year, and our ultimate goal is to facilitate the ultimate, a max benefit of this, by incorporating our MALDI-TOF identifications as well in that context.

So I think for all that right now, it is a very exciting time for the potential to really maximize our efficiencies and to incorporate all these new technologies into the laboratory.

Bob Barrett: Well, finally doctor, I will just open it up to you, do you have any additional comments or suggestions you would like to share?

Dr. Susan Poutanen: Well, certainly I think just following up on that last question, I mean it's really an exciting time to be part of clinical microbiology. To date, microbiology has really been rooted, and deeply rooted, in traditional methodologies, and in a relatively short window of time in the last few years, MALDI-TOF, automation, robotics, and other emerging technologies like sequencing and the like, have all been introduced and are really leading to substantial changes in traditional microbiology labs, as we know them today, and I think it is incredibly an exciting time and certainly right now with MALDI-TOF as the real first step to be easily incorporated, I think that the laboratories who are in the process of considering this, should seriously consider it and certainly look to labs that have already incorporated it, in terms of all the benefits that it has to each laboratory.

Bob Barrett: Dr. Susan Poutanen is a Microbiologist & an Infectious Disease Physician at Mount Sinai Hospital in Toronto and an Associate Professor at the University of Toronto. She has

been our guest in today's podcast examining mass spec in the microbiology laboratory.

I am Bob Barrett. Thanks for listening!