The art and science of positive blood cultures

Karen Titus

October 2022—It might be possible to tot up, using only the number of toes on an ordinary foot, how many labs are feeling full of vim and vigor these days, open to concepts like *creative destruction* and *get those creative juices flowing* and *have fun with it*—slogans once easily uttered but now tiring to enact.

Nevertheless, Margie Morgan, PhD, D(ABMM), would like her colleagues to at least consider the possibility of inspiration in the microbiology laboratory. In particular, Dr. Morgan, medical director of microbiology and professor of pathology and laboratory medicine, Cedars-Sinai Medical Center, Los Angeles, has some thoughts about using a new automated system to facilitate rapid microbial identification from positive blood cultures.

The Arc system, from Accelerate Diagnostics, is composed of the Arc module and blood culture kit and concentrates organisms recovered in positive blood cultures for direct testing on MALDI-TOF mass spectrometry.

Dr. Morgan and colleagues have been using the system since February. Initially, they performed comparative studies against a manual extraction method the laboratory had been using, she says.

Interest in making a change was considerable, especially among overworked laboratory staff. Prior to bringing on the Arc system, she notes, the laboratory was exploring using Bruker's MBT Sepsityper, which uses a standardized, multistep manual protocol for the concentration of positive blood cultures to identify organisms, she says.

Ultimately, however, "We thought an automated instrument could do it in a much more time-efficient manner for our staff." Manual methods typically require about 30 minutes of hands-on time, she says, while Arc decreases hands-on time to two to three minutes.

Unlike many labs, Dr. Morgan's isn't experiencing staffing shortages. Nonetheless, "We're really busy these days," she says, and the manual method absorbed too much of her staff's time. "So they were wanting to try the Arc to see if it could make the process simpler with less disruption of workflow."

As Dr. Morgan explains it, the Arc automates the concentration of a positive blood culture, making multiple manual pipetting and extraction steps unnecessary. The user vortexes the positive blood bottle, then extracts about 1.8 mLs of the blood culture, putting it into a processing capsule. The capsule and Arc test cartridge are placed in the module. About an hour and 10 minutes later, a concentrated sample is prepared for placement on the MALDI target plate for testing.

"So it's basically hands-off," she says, "and it does all the concentration for you."

Another advantage: When manual pipetting and processing steps are required, it's most efficient for labs to batch tests. With the Arc system, she says, "it is reasonable to do one specimen at a time. You don't have to wait for specimens to accumulate."

So far, she says, the Arc has met the lab's efficiency goals. Some 99 percent of the time, she says, the system supplies a usable nonviable liquid pellet. "The instrument functions without problems; we've not had any operational issues.

"You always wish something was faster," she continues with a laugh. "It would be great if it was five minutes instead of an hour and 10 minutes. But other than that, it has lived up to our expectations."

Dr. Margie Morgan in her office at Cedars-Sinai, where she and colleagues are using the Arc–MALDI-TOF mass spectrometry combination to facilitate rapid microbial identification from positive blood cultures. [Photo by: Roland DeCrescent]

It works particularly well for Gram-negative rods, with more than 95 percent identified successfully, Dr. Morgan says. The lab has also had good results with Gram-positive organisms, with identification of 80 percent.

Yeast, on the other hand, has been more problematic, though that's not necessarily tied to issues specific to Arc, she says. "More likely due to the biomass of yeast in the positive blood culture." Nevertheless, it has proved useful for yeast. She reports that the laboratory obtains direct identification 50 to 60 percent of the time. The remaining 40 or so percent are cultured and identified using MALDI after colony growth.

"We're still trying to investigate methods to increase the yeast identification percentage," Dr. Morgan says.

Yeasts can be difficult to identify on MALDI, given the potential for variability based on technique, agrees Jennifer Dien Bard, PhD, D(ABMM), director of clinical microbiology and virology, Children's Hospital Los Angeles (CHLA). But now, "MALDI is our first and primary choice when it comes to identifying yeast. And we were able to discontinue all of our other traditional methods that we use for yeast identification."

Dr. Dien Bard was a member of an advisory panel for the Arc system's development. From her perspective, any new system would need to minimize hands-on time for it to pass muster in a laboratory. Turnaround times would need to be quick as well, "especially since you're competing against molecular samples and/or technology, which can provide identification within an hour or less." Ideally, such attributes could also help with staffing shortages.

Dr. Dien Bard's laboratory does not use the Arc system. About nine years ago, "We developed our own lysis procedure directly from positive blood cultures that we're still using," says Dr. Dien Bard, who is also chief of academic and faculty development at CHLA and professor of pathology (clinical scholar), Department of Pathology, Keck School of Medicine of USC. This approach allows them to identify Gram-negative and Gram-positive organisms directly from a positive blood culture using MALDI.

Dr. Dien Bard

But she sees the advantages to the Arc, especially since it allows labs to use the MALDI database. “Which is much more comprehensive than any molecular PCR system that’s out there,” she says. “Instead of, let’s say, 18 or so targets, you have hundreds of thousands of organisms that can be identified on a MALDI-TOF database.” That’s one of the reasons, she says, her lab developed its simplified lysis protocol rather than opt for PCR.

The real learning curve, Dr. Morgan says, has less to do with implementation or processing than answering the question of how best to use the Arc.

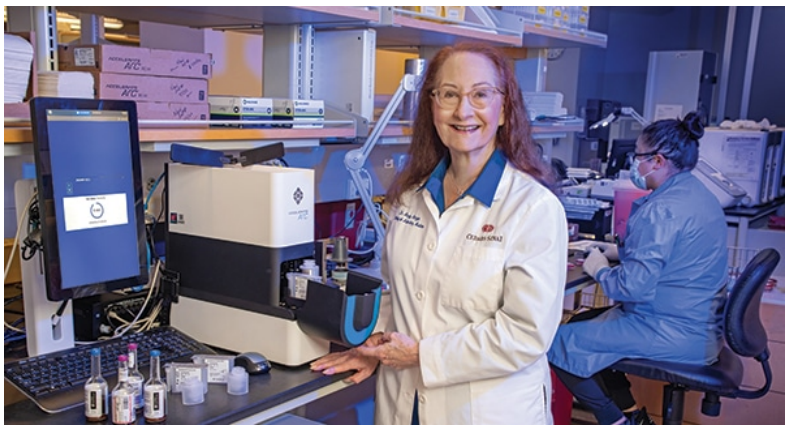
That’s been the focus of much of the lab’s energy, she says—thinking through the potential applications. “How could we make the best use of this? Is it every positive blood culture? Is it just certain blood cultures? Do you want to extend into possibly doing sterile body fluid that’s also growing in the blood culture media?”

All such questions were part of what Dr. Morgan calls the fascination, fun, and intrigue of using the Arc.

Naturally, other questions came into play as well. Could the lab perform its testing at lower cost? Using the Arc-MALDI combination, could it replace the front-line use of multiplex molecular panels?

Gazing beyond the usual questions, however, might enable laboratories to spring some fresh ideas, Dr. Morgan suggests. Like one’s taste in art, it will vary from user to user. “I think it’s going to be up to each individual laboratory to see how they can best use it,” Dr. Morgan says. “And in their particular hospital setting, how they can create an algorithm to make it most useful. I think that’s one of the nice things about the Arc—you can use it in variable ways.”

When she and her colleagues began using it in their own lab, she recalls, “we were thinking narrow-range thoughts.” That included testing organisms that didn’t identify on another Accelerate system—the Pheno—the lab was using, as well as organisms that weren’t identified with molecular panels.



Dr. Morgan and her team are thinking through the potential applications of the Arc (pictured above). “I think it’s going to be up to each individual laboratory to see how they can best use it,” she says.

“Then we thought: Well, why do that? Do we need to use that molecular system at all? Let’s just go directly to Arc.” In other words, they decided to turn it around. Rather than do molecular panels upfront, these panels became the reflex option for organisms such as *Staphylococcus* and *Enterococcus* for which detection of resistance genes could

help optimize patient therapy.

Dr. Dien Bard, too, is a fan of innovative thinking, noting that MALDI has shaken things up in laboratories for the better. “It’s really changed the way we have worked up organisms and identified organisms for patient care. Broadening how we use that system is important.” That could include not only implementing it for other organisms, such as molds and mycobacteria, but also looking at other types of specimens in addition to blood. “Thinking outside the box,” she says.

She notes that interest is growing in using MALDI for resistance and susceptibility testing. “We’re not there yet, to the point where we can use it on a routine basis. But it would be exciting and great to use if it were simplified enough so that labs could use it that way.”

Dr. Morgan considers her laboratory to be in the early stages of using the Arc-MALDI combination. “I’m not sure we’ve even reached our full potential yet.” She and colleagues continue to accumulate data and present it to their stewardship group.

Further down the road, she expects to see the field accelerate—move toward more systems for rapid susceptibility testing. “Now we can offer Arc with MALDI for rapid IDs for positive blood cultures and work toward incorporating this information into rapid susceptibility systems when they are available.”

That’s one leg of the three-legged stool that underpins most decisions in the lab, says Dr. Dien Bard. “You want something that’s going to be better than your existing system. Is it going to be faster? Is the performance of the test going to be improved? Will it be lower cost? Those are typically the three rules we tend to look at when making a decision about new tests—better, faster, or cheaper—or *and* cheaper. If you can get all three, that’s great.”

(Although faster isn’t always better. If the result isn’t immediately actionable, it may not justify the need to speed things up further. “That could help determine what kind of approach you want to pursue,” Dr. Dien Bard says.)

Dr. Morgan also sees costs driving how laboratories maneuver. “Quality is always your first thought in any endeavor,” she says, “but let’s be honest that cost isn’t far behind.” If the lab could use a method such as Arc with MALDI to replace a more expensive system, with similar turnaround times, or to identify truly unusual organisms that can’t be identified with a molecular panel, “it could be a very nice addition, long term, to our laboratory,” Dr. Morgan says, noting that her experience to date has been promising.

“It’s not 100 percent—it’s not going to solve all your problems,” she says. “But I think it’s going to be at least the start of some great things.”

For that to happen, imagination needs to be the fastest out of the starting blocks. “A lot of labs have gotten stale,” Dr. Morgan observes, “just sending everything to a very expensive molecular panel.” Not that she’s pointing fingers. “We have been on that road a little bit ourselves.” So when a new option comes along, such as Arc plus MALDI, with its interesting possibilities, she says, “Keep an open mind and continue to be creative.”

Thinking big can be hard, particularly for labs that are busy and short of staff. “And we’re all worn out from COVID,” she says. “Let’s just face it—it’s been a horrible couple of years.” All of which have stifled creativity.

She suggests starting with a basic question: What can we do with this system? The flexibility and ease of use make it worth considering for labs looking to improve turnaround times on their blood culture bench or for sterile body fluids, she says. “It could provide some alternatives to costly molecular amplification systems.”

Not that everyone will appreciate the creativity itself, Dr. Morgan concedes. Cedars-Sinai’s infection control and stewardship group appreciates that the microbiology lab is continually looking to improve technologies. But not all physicians will understand the advancements, though they are appreciative of the rapid organism identification from positive blood cultures, she says. Her business manager and administration will definitely take note of lower costs.

The effort has been worth it. Dr. Morgan has found that developing ways to use Arc plus MALDI for positive blood culture organism identification provided much-needed respite from the daily grind. “It was fun to think about something a little creative that could also benefit our patients.”

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