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On the Path from Materials Chemistry to Clinical Use

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Over the last 2 decades, a plethora of new diagnostic methods have been proposed in the academic literature, but few have made it to end users *(1)*. A hurdle is that for a new diagnostic method to take hold, vastly different facets of the technology, including sample handling, assay chemistry, and device hardware, must be considered from the outset to function together seamlessly in the final implementation. For example, to develop a faster test, improved chemical reagents alone are insufficient; rather, the reagents must also work with equipment easily accessible to the end users.

In this issue of *Clinical Chemistry*, Sakamoto et al. *(2)* present the use of novel materials that can be detected with equipment accessible to clinical laboratories. The heart of their technology is the synthesis of multifunctional nanoscale beads. The beads, 140 nm in diameter, were composed of a copolymer of styrene and glycidyl methacrylate. The polymers were chemically functionalized to attach to antibodies and encapsulated both fluorescent europium complexes and iron oxide nanoparticles. The combination of these properties enabled the beads to serve multiple functions at once: the beads could be pulled toward or away from certain surfaces, could bind to target molecules, and could serve directly as reporters.

This materials chemistry should ideally be usable with equipment accessible to the end users. Here, the sandwich immunoassay worked in a standard 96-well plastic plate, but placed on top of an additional 96-well magnetic plate. The magnetic plates are commercially available and normally used for transfection of cells. They magnetized the beads in solution and formed a magnetic gradient to attract the antibody-coated beads to the surface in contact with any bound targets.

The authors believe the collection of beads to the surface helped speed up the assay. The mechanism would presumably involve an increase in mass transfer (and hence the on-rate of the binding kinetics). Because the beads themselves were fluorescent, the assay was also sped up by eliminating a signal-amplification step. A time-resolved fluorescence measurement of each well showed a discernable signal within 5 min after adding sample to the well. The authors reported limit-of-quantification values of 10 pg/mL for brain natriuretic peptide and 0.02 ng/mL for prostate-specific antigen. The authors also reported the use of such beads for immunohistochemical staining, with a signal appearing within 20 min of initial treatment of specimens.

Will this method ever take hold in the market? After all, many different novel assay chemistries, reporters, and chemical reagents have been proposed for improving sandwich immunoassays. The answer must lie in additional future testing with clinical specimens. For promising technologies, it is imperative that analytical and materials chemists work quickly with clinicians to establish such testing procedures.

Another clue lies in recent implementations of new diagnostic technologies, where automation, including sample processing, has been a critical driver for adoption. The successful rollout of Cepheid GeneXpert for diagnosing tuberculosis *(3)* was driven largely by the ability of minimally trained workers to use the device. In our experience at Claros Diagnostics (now OPKO Diagnostics), we noticed that previous prostate-cancer diagnostic devices failed for use in physicians' offices, even if their analytical performances were satisfactory, primarily because they were insufficiently automated. In the work of Sakamoto et al. *(2)*, the reduction of assay steps is likewise an attractive feature.

Another interesting element is the use of magnetic force to enhance the detection of targets. Currently, the authors use fluorescence plate readers to detect the beads; this strategy is logical because such equipment is prevalent in clinical laboratories. Nevertheless, magnetic particles could in the future be detected directly using a magnetometer or via giant magnetoresistance *(4)*.

Indeed, the clinical end-use case must be considered carefully. If the intended use is at the point of care, it must be possible to build such detection hardware with a portable form factor. If the intended use is clinical laboratories, the hardware can be larger, but another question arises: what would be the tangible advantage for laboratory technicians? Current laboratories already have established equipment for automating immunoassays, while the overall turnaround time of clinical tests is limited less by the speed of the assay and more by batched workflow.

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Overall, Sakamoto et al. *(2)* present a clever adaptation of synthesizing multifunctional beads for automating and speeding up immunoassays. Like other promising novel assay chemistries and materials, the path to clinical success must involve usability with accessible equipment, validation with clinical specimens, and matching of the advantages to real needs of clinical uses.

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