Bremerhaven, Germany) permit the analysis of ALK and ROS1 using a single FISH slide, with good performance. On the basis of a combination of 4 fluorochromes as used previously in some commercially available FISH probes, such as the Vysis Melanoma FISH probe kit (Abbott Molecular), it is feasible to design a multiplex probe that would concurrently analyze up to 3 oncogenes on a single FISH slide (eg, ALK, ROS1, and RET; see Figure, A, for a probe design and Figure, B, for a proposal of an interpretation algorithm).

In this manner, even if the NanoString system reviewed by Ali et al 1 is a very promising tool to analyze concurrently several genes in cytology NSCLC samples, in our opinion multiplex FISH could also not only be a valuable method in this field, it may also be easier to implement in histopathology laboratories at this time.

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The purpose of our article 1 was to evaluate the role of the NanoString system in the analysis of gene fusions in lung cytology. We never assessed whether NanoString system is cheaper than fluorescence in situ hybridization (FISH). Indeed, to compare the cost of a 1-gene test with that of an entire gene panel can be misleading. It is not appropriate to refer to NanoString “transcriptomic analysis” and to report costs without specifying the exact number of genes included in the panel. It is generally accepted that NanoString can be more cost-effective than FISH, particularly in terms of assessable targets and data interpretation. FISH is considered a quite expensive and laboratory-intensive technique, with a low power of multiplexing. Currently, multiplex FISH assays for lung cancer are commercially available only for the simultaneous analysis of 2 fusion genes, ALK and ROS1. However, we agree on the possibility to design and develop a multiplex probe to concurrently analyze up to 3 oncogenes, but we have some concerns about the interpretation of data.

Problems related to FISH interpretation have been widely reported and discussed over the years. Undoubtedly, FISH is considered the gold standard for the analysis of gene fusions, but literature data indicate that it is prone both to false-negative and false-positive results and to a significant interobserver variability. FISH analyses are evaluated by pathologists and can suffer from some degree of subjectivity. Moreover, in cases with nuclear overlapping, crush artifact, or technical limitations, FISH analysis may be uninterpretable. In this way, the interpretation of multiplex FISH could be even more complex. So, in our opinion, a few minutes are not always sufficient to interpret FISH even for highly skilled pathologists.

On the other hand, NanoString data interpretation is fully automatized and objective thanks to dedicated analysis software. In addition, concerning the analysis of gene fusions, in comparison to FISH, NanoString system also allows us to recognize the most frequent and known fusion variants, which can influence the response to tyrosine kinase inhibitors. We also agree with the fact that the detection of low percentages of re-arranged alleles could be challenging, but it was reported that a tumor cell content of 10% can be sufficient to detect gene fusions by NanoString.

In conclusion, we believe that FISH is a valuable technique with a crucial role in the clinical practice of lung cancer, but the introduction of new diagnostic systems could be advantageous. Particularly, NanoString can provide an alternative molecular diagnostic approach that can help to control costs, eliminate unnecessary testing, and improve turnaround time. Anyway, it always has to be considered that the adoption of a specific technique depends on local resources, expertise of the laboratory, number of cases per year, and local reimbursement policy.

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Accepted for publication July 17, 2018.

The authors have no relevant financial interest in the products or companies described in this article.


In Reply.—We thank the authors for their interest in our review 1 and for their comments.

In conclusion, we believe that FISH is a valuable technique with a crucial role in the clinical practice of lung cancer, but the introduction of new diagnostic systems could be advantageous. Particularly, NanoString can provide an alternative molecular diagnostic approach that can help to control costs, eliminate unnecessary testing, and improve turnaround time. Anyway, it always has to be considered that the adoption of a specific technique depends on local resources, expertise of the laboratory, number of cases per year, and local reimbursement policy.

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Accepted for publication July 19, 2018.


Updates and Customizations in Synoptic Reporting

To the Editor—Synoptic reporting is required by the College of American
Pathologists (CAP) and employs checklists to improve reporting in surgical pathology. The CAP provides these checklists as written documents in both Microsoft Word (Microsoft Corporation) and PDF format, as well as a set of XML files for use with the electronic Cancer Checklist (eCC).1 However, the value of checklists extends beyond the specific content defined by CAP; checklists can aid in ancillary test ordering and billing compliance,2–4 and sites may make local customizations to satisfy their clinicians. Although the CAP provides a list of optional questions in their products, the use of a noncustomizable list of optional elements leads to incomplete and inconsistent reporting.5 As a result, the use of the CAP-provided products without customizations fails to fulfill the potential offered by the CAP tools.

We have been using a Web-based product with extensive customizations for nearly 2 years.3 Even with our reflex ancillary studies rapidly changing, this site has kept a widely dispersed group of pathologists on the same standard while incorporating customized questions, customized formats to improve the speed and accuracy of data extraction by the clinician from the report,4 billing data, ancillary studies, and additional instructions on the site for the pathologist (including staging criteria and immunohistochemical evaluation) that do not appear on the report. This has led to significantly improved reporting performance for our group as well as others who use similar methods.2,3 Prior to these customizations, 2.1% (32 of 1043) of cases with synoptic reports had addendums with additional clinical information requested by the clinicians. After the inclusion of these additional customized questions, only 0.08% (3 of 3973) of cases with synoptic reports had addendums for additional requested information (Fisher exact test, P < .001). Each of these addendums represents an unnecessary phone call, and this likely underrepresents the true incidence, because only cases with addendums were included.

Despite these advantages, most pathologists are reluctant to customize their synoptic reports because updating these CAP products is extremely burdensome, and the updates usually override and remove any customizations. Although CAP releases a set of paper documents and XML files for each update, by design these products must replace rather than integrate with what pathologists are already using, and local pathologists, not the CAP, are responsible for incorporating and maintaining updates. This entails either significant manual effort to edit written local versions of these documents, or working with the local Information Technology departments and the particular vendor of the eCC. Given that CAP considers the protocols “living documents that get updated...not infrequently,” it is no surprise that many sites are unwilling to devote any additional resources to customize their checklists above and beyond what they already must do to simply keep them updated. Indeed, as a manager from Epic Corporation has said in CAP Today, “customization comes with a big maintenance burden...shouldn’t be taken lightly...and you [the local pathologist] will have to figure out who is responsible for making sure the new forms...are maintained.”

Fortunately, it does not have to be this way. There is no technical reason that updates need to delete all customizations. In 2018, Web-based tools can easily solve this problem and are usually taken for granted. No one loses his or her customized contact list simply because his or her cell phone operating system is updated. Pathologists, who are quick to not only embrace but demand the latest molecular techniques for their patients’ care, should do the same for their synoptic reporting. A Web-based product that includes either a Web site with local pathologist access, an application programming interface that works with specific vendor laboratory information systems or the local pathologist’s Web site, or a combination of these options would solve this problem. This would allow sites to easily maintain customized question and answer sets during the update process. The CAP should be responsible for keeping the required elements up to date and available in a method that local pathologists can easily integrate into whatever method they are already using, local pathologists should be responsible for customizing it to meet their local needs, and updates and customizations should not interfere with each other. Unleashing the full potential of checklists by incorporating Web-based technology would be a clear “win-win-win” for pathologists, clinicians, patients, and the CAP.

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Accepted for publication July 31, 2018.


In Reply.—The electronic cancer checklists (eCCs) produced by the College of American Pathologists (CAP) enable pathologists to complete the synoptic report within the routine workflow of the anatomic pathology laboratory information system (AP-LIS), and most AP-LIS vendors offer an eCC synoptic reporting module. About one-third of eCC users customize their synoptics by including additional data elements that local pathologists or clinicians want in their reports. These customizations can align the synoptic report with individual practices and help improve report completeness, but also add complexity and work for the pathology department. As noted by Renshaw and Gould, these locally determined elements are not included in protocol or eCC updates and therefore must be