DNA Ploidy Cytometry Testing for Cervical Cancer Screening in China – Letter

We read the article of Tong et al. (1) with great interest. However, on closer analysis, we found several points that need clarification.

Although the authors call this a “randomized controlled trial,” both tests were done on almost all of the study subjects and the data presented in Table 2 is pooled from both arms of the trial. Nowhere, including in the supplementary data, are the results for each separate arm of the trial reported. We believe that it should be possible to check the values for “Crude estimates” in Table 3 for cancer cases from the data presented, but we have not been able to do this. In fact, it is unclear to us how many cancer cases were found in this study.

Table 2 reports that DNA gave positive results for ∼6,000 of 21,500 cases, and yet the “crude” specificity reported in Table 3 is <60% rather than >70% as implied by these numbers. This enormous false-positive rate is not commented on, and yet, apparently, the positive predictive value of DNA is higher than that for cytometry, which has half as many false positives. The true positive rate is unclear, but at most is only 100—or much less than 6,000.

In the abstract, it states that: “The sensitivity of both tests used together was 100%, and the specificity was 91.8%.” We could not find this calculation anywhere in the article itself and think it unusual to report a result only in the abstract. It can be shown that there are only two ways by which test results such as this can be combined: as a logical “or” of positive tests results (that is, the combined test result is positive if either test is positive) or as a logical “and” of test results (that is, the combined test result is positive only if both tests are positive). It can be shown that the “or” will increase sensitivity and decrease specificity whereas the “and” will decrease sensitivity and increase specificity. Yet these authors claim to improve both sensitivity and specificity simultaneously.

The “100%” sensitivity obtained by combining the tests is by construction of the experimental design. Pap screening studies rarely have an independent and reliable reference diagnosis (for example, biopsy tests on all subjects), but only compare the results of two tests. There is no way to know how many positive cases actually exist in the study population. Such studies only measure a kind of relative sensitivity and specificity that compares one test with the other—absolute sensitivity and specificity is not determined. Because only DNA and cytology were used to discover cancer cases, the logical or of their positive results must be 100% sensitive, by experimental design.

Finally, given that the results reported by these authors seem to be pooled from both arms of the trial, we fail to understand what makes this a randomized controlled trial.

We respectfully ask for careful clarification of these points.

David M. Garner
Martial D. Guillaud
Integrative Oncology, Imaging Unit, BC Cancer Agency/Research Centre, Vancouver, British Columbia, Canada

Calum E. MacAulay
Integrative Oncology, Imaging, Genetics and Radiation Biology Units, BC Cancer Agency/Research Centre, Vancouver, British Columbia, Canada

Disclosure of Potential Conflicts of Interest
D. Garner: consultant, Motic Medical Diagnostic Systems; M. Guillaud: minor consultant, Novacyt.

References
Clinical Cancer Research

DNA Ploidy Cytometry Testing for Cervical Cancer Screening in China – Letter

David M. Garner, Martial D. Guillaud and Calum E. MacAulay

Clin Cancer Res  Published OnlineFirst June 22, 2010.

Updated version  Access the most recent version of this article at:
doi:10.1158/1078-0432.CCR-10-1058

E-mail alerts  Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions  To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions  To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.