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NEWS

In this issue

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Standardization of methods of analysis and assurance of the quality of the obtained results have become more than ever crucial in this era of molecular pathology, and this issue of the journal, there is once again a strong emphasis on this aspect of our daily trade. The issue opens with a review by Roi-Chaudhuri et al. (https://doi.org/10.1007/s00428-019-02559-z) on the application of molecular analysis to cytology samples. In many different settings, a cytology sample may be the only biospecimen available and methods have been developed to perform reliable molecular analysis on such samples. An obvious advantage of a fresh cytology sample over formalin-fixed paraffin embedded tissue is the much more natural state of the material. A disadvantage can be the paucity of lesional cells. The sensitivity of next-generation (deep) sequencing, however, has largely overcome this limitation. Molecular analyses can even be performed on microdissected cytology smears. The authors discuss a range of applications along with pitfalls and limitations. Their overall conclusion is that today's cytopathologist cannot provide adequate care if not supported by ancillary molecular tests.

The methods and quality-assurance papers in this issue include the study performed by Keppens et al. (https://doi.org/10.1007/s00428-019-02525-9) on causes of errors observed during quality-assurance rounds of molecular testing, actions undertaken to alleviate observed shortcomings, and the effect of such actions on assay quality. In one quality-assurance testing round, one in four of the observed shortcomings was due to pre- and post-analytical errors, associated with insufficient quality of the tissue sample for molecular analysis. In a follow-up round, this had shifted, as half of the observed errors were due to methodology problems. Follow-up measures taken were retrieved through a survey sent around to the participants of the test rounds and a workshop. Follow-up measures often included protocol revisions and occasionally additional training of involved staff. While these led to improved performance, the experience gained re-emphasizes the importance of continuous attention to quality improvement through all phases of the test process.

In the study by Lucas et al. (https://doi.org/10.1007/s00428-019-02582-0), quality assurance of the used assay platform is the primary aim. The authors compared two different platforms for immunohistochemical assessment of PD-L1 expression in non-small cell lung cancer. One of the platforms, a combination of an immuno-stainer and a monoclonal antibody, is FDA approved but the particular immuno-stainer is not widely available in Europe. The other is not FDA approved but both antibody and immuno-stainer are widely available and the question was how these two platforms compare and, in addition, whether the antibody of the FDA approved test would work also on the alternative (more widely available) immuno-stainer. It turns out that both assays provide satisfactory results in most centers, confirming the validity of the non-FDA-approved assay. Interestingly, the antibody from the FDA-approved assay did not perform well on the alternative immuno-stainer. These results emphasize the need for local protocol development during the phase of implementation, in addition to careful validation of each new molecular test. It also confirms that for molecular testing (which includes immunohistochemistry), validation of the test results is at least as important as formal (e.g., FDA) approval of the test.

The cover image is from this paper and shows membranous PD-L1 staining in a non-small cell lung cancer case.

A third aspect of quality assurance concerns inter-observer variability in the assessment of histological characteristics. This is a notorious issue in grading of prostate cancer using Gleason patterns. Savic Prince et al. (https://doi.org/10.1007/s00428-019-02577-x) address this in a study focusing on the application of deep learning using a convolutional neural network approach. Digitized whole sections of prostate biopsies were subjected to this approach with the intention to get to automated recognition of areas of cancer and subsequently their grading as either Gleason pattern 3 vs. 4 or more. For the distinction between benign and malignant glands, accuracy of over 90% was obtained. The same level of accuracy was obtained for recognition of the Gleason pattern, but with somewhat lower specificity and sensitivity. Finally, substantial agreement was found between automated Gleason pattern grading and that performed by an experienced pathologist. The paper makes an important point. As yet, there

is little evidence supporting the contention that deep learning–based artificial intelligence can make complex pathological diagnoses. However, when it comes to quantification of elements in microscopical images or recognition of well-defined patterns, artificial intelligence can provide important support to the pathologist.

As important as quality assurance is, much of what pathologists do and what our journal publishes focuses on original observations on important questions in diagnostic pathology, which includes description of new (purported) entities. In this vein, Taskin et al. (https://doi.org/10.1007/s00428-019-02583-z) report on sarcomatoid carcinomas of the gallbladder. These appear to be rare at less than 2% of all cases of gall bladder carcinoma. Interestingly, most appeared to arise from pre-existing surface epithelial dysplasia while they may also be associated with intracholecystic papillary-tubular neoplasm. Histological patterns varied from pleomorphic-sarcomatoid, to more spindle cell morphology to an angiosarcomatoid pattern with occasionally heterologous elements, including osteoclast-like giant cells. Prognosis was overall poor but when matched according to grade and stage comparable with that of conventional adenocarcinomas of the gall bladder.