In this issue

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Methods are important in pathology. They are often essential for new discoveries, but evaluation and refining of existing methods and new ones that can improve diagnostic accuracy are drivers in advancing our discipline. This issue of our journal has a little series of methods oriented papers.

Loughrey and collaborators (DOI [10.1007/s00428-015-1780-1](https://doi.org/10.1007/s00428-015-1780-1)) evaluated primary digital pathology reporting in gastrointestinal pathology. The study compared 100 glass slide diagnoses and 100 digital diagnoses from three study pathologists. A very high intra-observer concordance rate was observed. There were only 14 discordant pairs, with most often preference for the glass slide diagnosis but, most importantly, only discordances of minor clinical significance. Inter-observer concordance, viewing-modality independent, was even higher, comparable to any second viewing of pathology material. Digital pathology in primary diagnostic reporting appears to be robust. Will we abandon our microscopes in the near future?

Chenard et al. (DOI [10.1007/s00428-015-1781-0](https://doi.org/10.1007/s00428-015-1781-0)) assessed the reliability of combining the tests for HER2 status of breast cancer on a single slide by sequential immunohistochemical staining for HER2 protein and silver in situ hybridization for assessment of gene amplification. They obtained 93 % concordance between HER2 protein staining obtained during diagnostic histopathological work-up and the combined test. Discordances had no bearing on therapy decisions. The concordance between ISH results in single staining versus double staining mode was even higher. Reading a single slide

with the two signals was about 25 % faster than sequential reading of two single stained slides. The authors contend that the double staining approach is a real improvement which might facilitate more rapid clinical decision making for breast cancer management.

Aitken et al. (DOI [10.1007/s00428-015-1765-0](https://doi.org/10.1007/s00428-015-1765-0)) compared sensitivity and specificity of next generation sequencing (NGS) with mutation-specific restriction enzyme digestion followed by polymerase chain reaction amplification to detect *CTNNB1* mutations in desmoid-type fibromatoses. On formalin-fixed paraffin-embedded tissue specimen NGS had a sensitivity of over 92 % with a specificity of 100 % for the detection of *CTNNB1* mutations. Not only were all mutations detected by conventional methods also identified by NGS but it also identified additional mutations, in part not previously described. NGS has high sensitivity for the detection of *CTNNB1* mutations, requires a minimal amount of DNA, and appears to be time and cost efficient. It seems on the way to become a standard in molecular testing.

Thway and collaborators (DOI [10.1007/s00428-015-1777-9](https://doi.org/10.1007/s00428-015-1777-9)) assessed performance of fluorescence in situ hybridization (FISH) and reverse transcription-polymerase chain reaction (RT-PCR) for detection of characteristic *FOXO1* gene rearrangements in the diagnosis of alveolar rhabdomyosarcoma. FISH was more often technically successful than RT-PCR. When both tests were technically successful, their results were highly concordant. In supporting a diagnosis of alveolar rhabdomyosarcoma, sensitivity of RT-PCR was similar to that of FISH but specificity was better. Notwithstanding their similar sensitivity, the authors recommend performing both RT-PCR and FISH because FISH provides additional information when RT-PCR is not successful, while PCR allows detection of specific fusion transcripts identifying subgroups which might differ in behavior. The cover image comes from this paper and illustrates dual-color break-apart probes with split red and green signals indicating a *FOXO1* gene rearrangement.

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