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Laboratory methods, including reliable reagents, remain a key element in the work-up of tissue specimens for diagnostic purposes. In this context Forest et al. (<https://doi.org/10.1007/s00428-019-02613-w>) address the question how expression of PD-L1 can be reliably assessed in bone specimens, as these require decalcification before any further histological processing can be undertaken. The authors exposed bone metastases as well as control placental tissues to an acid and a chelating agent decalcification protocol and tested immunoreactivity using two different anti-PD-L1 antibodies. One antibody showed a significant decrease in the number of immunoreactive cells in both protocols whereas the other antibody was less affected by either decalcification protocol. Delayed fixation had no effect on PD-L1 immunoreactivity with either antibody. The paper underlines the importance of careful fine-tuning of immunohistochemistry staining protocols prior to introducing them into daily diagnostic practice.

In the study reported by MacColl et al. (<https://doi.org/10.1007/s00428-019-02626-5>) the question was asked if any combination of characteristics of a benign breast papilloma at biopsy might be predictive of the occurrence of in situ or invasive carcinoma in a subsequent resection specimen. The authors reasoned that absence of ‘high-risk’ characteristics might spare the patient unnecessary breast surgery. In their cohort of cases the authors found a (pre) malignant lesion in about one in eight patients who underwent surgical resection of the lesion after a biopsy diagnosis of papilloma. The presence of radiologically detected calcifications, advanced patient age and tumor size were found to be associated with an increased risk of the presence of a (pre) malignant lesion in the resection specimen. The authors reason that with this relatively low risk, and stratification of patients according to these risk factors, resection of biopsied benign papillomas should be limited to high risk patients. A second paper on breast cancer is that by Tan et al. (<https://doi.org/10.1007/s00428-019-02635-4>), who revisit the importance of Ki-67 expression in triple-negative breast cancer. The authors applied multiplex

immunofluorescence labeling together with image analysis to quantify proliferative activity in both the (tumor)epithelial and the stromal/immune cell compartments in order to assess their association with outcome. Surprisingly, high (tumor) epithelial Ki-67 labeling index was associated with better prognosis, which is somewhat counterintuitive and brings up the question which molecular mechanisms might be involved. Also, high proliferative activity in the immune-cell compartment was associated with better prognosis, which is less surprising. The cover image is from this paper and shows multiplex immunofluorescence labeling of a case of triple negative breast cancer, with Ki-67 nuclear staining in green.

Bosch et al. (<https://doi.org/10.1007/s00428-019-02670-1>) report on the effect of different modalities of neo-adjuvant pre-operative treatment approaches of rectal carcinoma on pathological staging and prognosis. In the TNM classification the ‘y’ prefix is used to indicate that the patient received pre-operative treatment. Problem is that different modalities are used: full preoperative chemoradiation therapy but also short-course radiation therapy. The chemoradiation regimen usually leads to downstaging (the ypTNM stage is lower than the clinical pretherapeutic TNM). This is not the case for short-course radiotherapy, presumably because the time frame of this regimen is too short for tumor-regression to fully proceed. The authors argue convincingly that it would be important in TNM staging of rectal carcinoma to differentiate between these different treatment modalities. Other important findings are the large discrepancies between clinical and pathological stage after surgery only, the excellent prognosis of Stage I disease after chemoradiation therapy as well as short-course radiotherapy, the latter regardless of the lack of signs of tumor regression, and the less favorable outcome of stage II and III patients after chemoradiation therapy relative to patients treated with short course radiation therapy.

Finally, Agostinelli et al. (<https://doi.org/10.1007/s00428-019-02681-y>) review the pathological characteristics of pediatric-type follicular lymphoma in order to further clarify

the differential diagnosis with follicular hyperplasia. The characteristic morphology, follicular growth pattern with irregular lymphoid follicles with numerous blastoid cell containing germinal centers in a starry-sky pattern, the pattern of marker expression and the clonal immunoglobulin gene rearrangements provided the usual diagnostic criteria. As new marker the group proposes FOXP-1, as this was expressed in almost

all cases of pediatric-type follicular lymphoma but not in follicular hyperplasia.

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