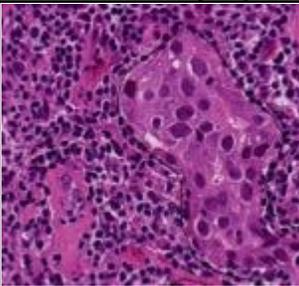
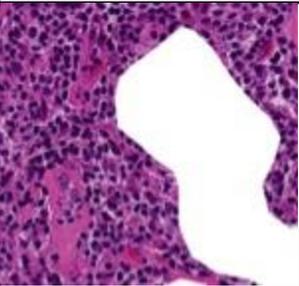
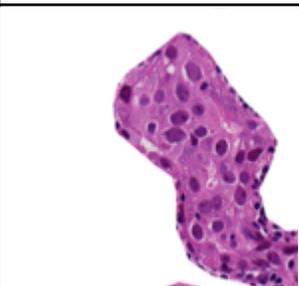
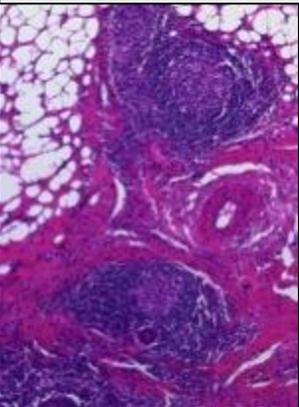


## Morphology and definition of immune infiltrates in breast cancer – biological and diagnostic relevance

	Biological relevance	Diagnostic relevance
<b>Lymphocyte-predominant breast cancer (LPBC)</b>		
	Working category to describe tumors with “more lymphocytes than tumor cells”.	Definitions vary across studies with stromal TILs of 50-60% used as a cutpoint. LPBC be used for predefined subgroup analyses and for description of tumors with a particularly high immune infiltrate, however, keep in mind that TIL are a continuous parameter and the cutpoint for LPBC is still arbitrary.
<b>Stromal TIL</b>		
	Indicator of increased accumulation of immune-cells in tumor tissue	Stromal TIL have been shown to be predictive for increased response to neoadjuvant chemotherapy as well as improved outcome after adjuvant chemotherapy. <b>Based on current data, this parameter is the best parameter for characterization of TIL for diagnostic purposes.</b>
<b>Intratumoral TIL</b>		
	TIL with direct cell-cell contact with tumor cells, might be an indicator of direct cell-based anti-tumor effects.	Several studies have shown that intratumoral TIL are more difficult to evaluate and do not provide additional predictive / prognostic information compared to stromal TIL.
<b>TIL at the invasive margin</b>		
The localization of TIL at the invasive edge is included in the evaluation approach presented in this guideline.		For breast cancer there are no studies with a separate evaluation of TIL at the invasive edge. For practical purposes, the reliable evaluation of the invasive edge might be difficult when using core biopsies in the neoadjuvant setting.
<b>Tertiary lymphoid structures (TLS)</b>		
	Typically localized in the surrounding area of the tumor, TLS might be localized in normal tissue directly adjacent to the tumor, consisting of a T cell zone next to a B cell follicle, often with germinal centers.	While these structures may be important for the biology of tumor-immune reactions, they are not yet optimized for diagnostic assessment. The main problem is that TLS have a spatial heterogeneity and are principally localized in areas surrounding the tumor. They might not be in the plane of the tissue section that is being evaluated, in particular when using core biopsies. Furthermore, it might be difficult to distinguish lymphoid aggregates from true TLS, in particular when the germinal center is not in the plane of the section.