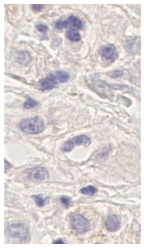
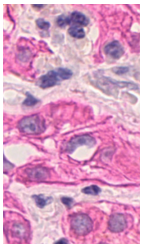
Introducing our new pioneering PD-L1 Analysis APP for enhanced precision in pathology

For scoring PD-L1 positive tumor cells for NSCLC, various studies report a low inter-observer agreement [1] for pathologists, which gives rise to the concern, that the decision of immunotherapy treatment eligibility depends on the lab the sample is evaluated in. Visiopharm's PD-L1 (NSCLC) algorithm reliably detects invasive tissue and quantifies the positive tumor cells. In the integrated workflow, the analysis is triggered and done fully-automated, delivering the results for the pathologist's review once ready.

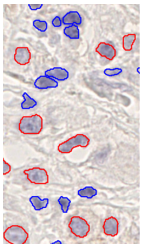
Our clinical validation study with three European sites directly compared manual assessments (as ground truth) with the APP's stand-alone analysis and pathologist's APP-assisted interpretations.



Stain & scan PD-L1



Double stain with PCK



Transfer regions to primary PD-L1 image

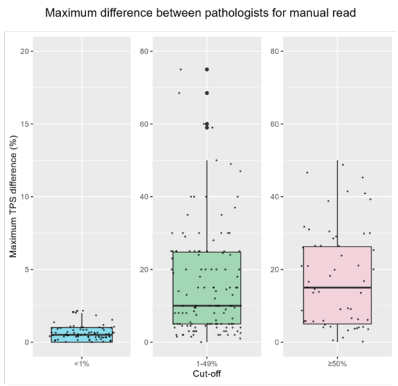
Patented approach for automatic annotation

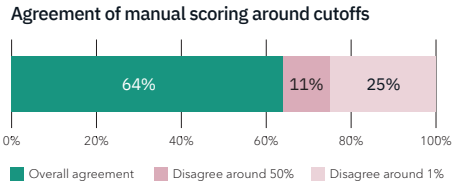
A known challenge for PD-L1 evaluation is the accurate distinction of tumor cells from inflammatory cells. We used our patented technique to ensure a highly accurate and objective ground truth for tumor and non-tumor cell identification to train the algorithm.

> "I did spend less time with scoring using the APP, especially because the APP was able to make a good distinction between tumor cells and inflammatory cells.
>
> Tri Q. Nguyen, pathologist,
> UMC Utrecht, The Netherlands

[1] Troncone G, Gridelli C; doi: 10.21037/tlcr.2017.10.05

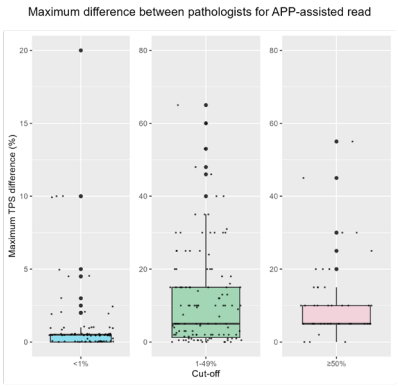
Low agreement between pathologists

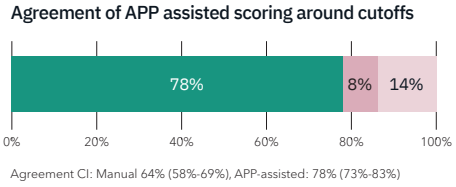




In our study we could reproduce the high interobserver variance of manually assessed TPS scores. This results in low agreement of the category scores (pos/neg) between the pathologists. Most of the discordant cases were around the 1% cutoff, indicating a higher risk of misclassification for this cutoff.

Increasing agreement using the APP as support

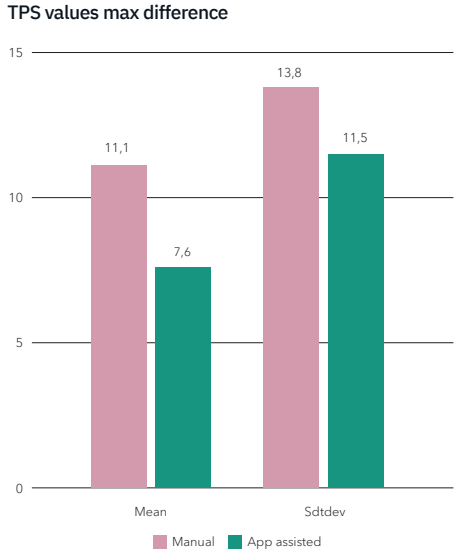




Agreement CI: Manual 64% (58%-69%), APP-assisted: 78% (73%-83%)

When using the App results as a support, the variance decreased clearly, catching outliers. The higher variation for the <1% cases is caused by reducing previously false negative cases, which were now identified as >1% by the pathologists. Overall agreement increased significantly, especially around the 1% cutoff, demonstrating that the APP supports an increased consistency in those difficult to score cases.

Decreasing the variability in TPS scoring using the APP



Using the APP the pathologist's differences in TPS decreased, catching outliers. This causes the agreement of the overall category score to increase.

High agreement for APP only results

The APP results were quite impressive, confirming that the APP result offers an accurate and reliable support for the pathologist.

1% cut-off:
0.91
(0.87 - 0.94)
agreement
(95% CI interval)

50% cut-off:
0.96
(0.93 - 0.98)
agreement
(95% CI interval)

While the APP was validated on 22C3, we also tested a small set with SP263 against one pathologist, again with excellent results.

1% cut-off:
0.87
(0.80 – 0.94)
agreement
(95% CI interval)

50% cut-off:
0.94
(0.89 – 0.99)
agreement
(95% CI interval)