# From Qualitative to Quantitative Histopathology Analysis

In recent years molecular pathology has emerged as an imperative tool in treating cancer. Molecular pathology is used primarily to diagnose disease and guide the prevention and treatment of disease and is typically coupled with anatomic pathology. The most important molecular pathology test is Immunohistochemistry (IHC). Treatment of breast cancer, for example, relies primarily on analysis of a panel of IHC slides of different molecular targets.

Contrary to classic histopathology, which is based on qualitative assessment of the morphology of cells within a tumor, molecular pathology techniques are intrinsically quantitative and give statistically-based results. IHC uses special antibodies to label target compounds, typically proteins, which are then visualized in specific parts within cells and are counted one-by-one.

Despite the inherent quantitative nature of IHC tests, these still rely on manual counting by the pathologist and are thus, once again, dependent on human subjectivity. Computer-aided (CA) systems are ideal in such cases, because a computer is fundamentally "good at counting". Such systems analyze and count IHC-labeled cells within captured frames of defined tumor regions, with high precision and accuracy.

A good example of the benefits of using a computer assisted system for quantitative analysis is the Ki67 IHC test. This is a cell proliferation marker that is used to stratify good and poor prognostic categories in invasive breast cancer. The CAP guideline for Ki67 is to score at least 1000 tumor cells and calculate the percentage of positive cells within the tumor region[1]. This is inherently difficult and time consuming for the pathologist and leads to lack of standardization and consistency in results. Computer-aided systems, on the other hand, can very efficiently perform this type of analysis. In *Figure 1*, image analysis was performed on a Ki67 slide using ASI's HiPath™ system. For this specific frame, 480 nuclei were captured and analyzed within seconds with a final score of 18.7% positivity for the slide, placing this case in the category of high proliferation for Ki67. In other words, based on a 15% threshold, this sample is positive for Ki67. The yellow rectangle is a zoom-in into a defined region within this frame. Note the accuracy of the system in counting each individual cell.

Figure 1
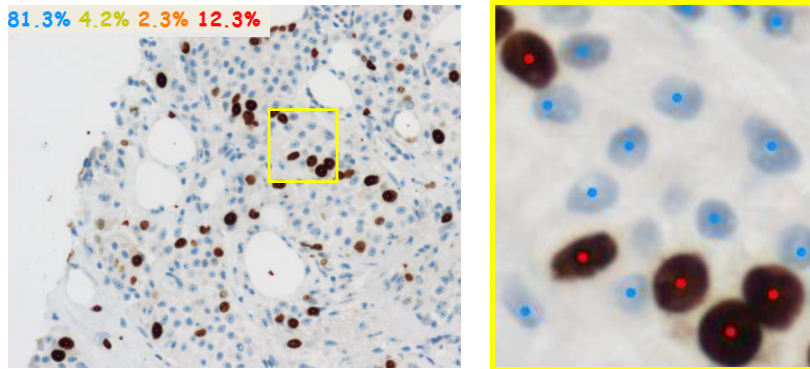
HER2/neu represents an additional challenging IHC test. Scoring in this case depends on precise identification and classification of cell-membrane. In *Figure 2* below, a HER2/neu test was performed using HiPath™. Here CA analysis was used to accurately separate between membranes and nuclei and then classify and count each individual cell within the selected tumor region. Note the clear visualization of membrane in each individual cell. This is imperative for scoring of HER2/neu samples and is related directly to treatment with Herceptin (Roche).

Figure 2
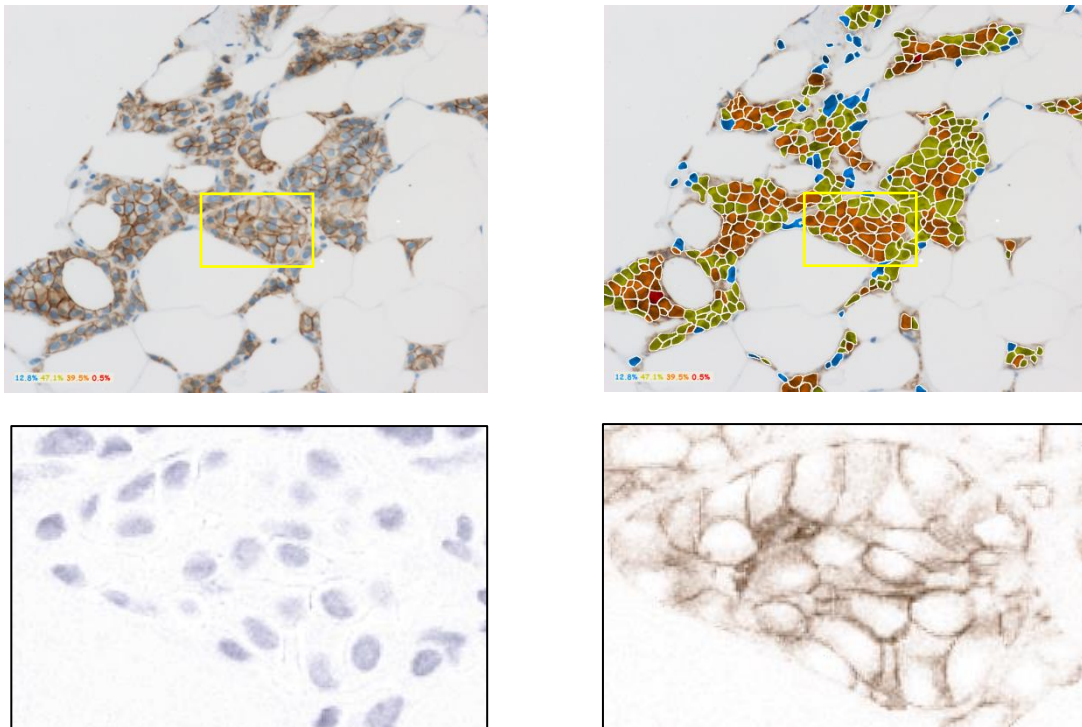
The benefits of using computer-aided analysis in molecular pathology are beyond question. New IHC targets, such as PD-L1, are becoming an imperative part in treating cancer. Many of these new assays are difficult to analyze and require the aid of a computer. Slowly but surely computer-aided systems will inevitably become an integral part of the daily work for pathologists and beyond.

[1] J Natl Cancer Inst. 2011; 103: 1656–1664