## Novel imaging technique within tissue diagnostics has interesting properties for breast-cancer classification

Based on upconverting nanoparticles protein expression in tissue samples can be highlighted in a new way, separating cell morphology and protein expression. The technology, developed by Lumito AB, potentially facilitates automated tissue classification of breast cancer samples without the need for introducing AI.

Upconverting nanoparticles have the ability to upconvert low-energy light to high energy light. Illuminating these particles with infra-red laser results in emission of light in the visible spectra. These particles could be attached on tissue samples to study protein expressions. The particles are bound to anti-bodies that in its turn bind to protein expressions such as receptors. A typical expression of interest is the HER2-expression, a protein that occurs in cancerous cells in breast cancer tissue. The HER2-protein signals the cells to grow and divide in an abnormal pace and causes the formation of an increasing amount of HER2-receptors on the cell membrane. The HER2-expression is used for assessing whether an individual with breast cancer can be subject to targeted therapy. The HER2-score is divided into four different categories, 3+, 2+, 1+ and 0. If the HER2-expression is classified as a 3+ the antibodies can be used to attack the cancer cells. This method stands in contrast to traditional cancer-treatment options such as chemotherapy, radiation and, in the case with breast cancer, mastectomy. Using the novel imaging technique, 47 images of breast cancer tissue were acquired with the purpose to evaluate their different HER2-scores. The images were evaluated and labelled by three different pathologists. An investigation was made comparing the performance of algorithms derived from pathology guidelines to the performance of the pathologists. Additionally the algorithms were developed with the purpose to make them interpretable from the medical perspective to gain confidence from experts in the field.

The algorithms were developed following two regimes. The first algorithm was based on a regional level. Each region was divided into quadratic patches and each patch was from its statistical properties classified as one of the HER2-scores. From the amount of patches in each HER2-score, the score for the tissue sample was decided. The second algorithm derived a typical intensity profile for a cell belonging in each HER2-score. For each cell in a region a mathematical similarity to each of the intensity profiles were calculated where the most similar decided the score of the cell. From the amount of cells within a score a score for the tissue sample was decided.

Both algorithms performed comparably to a pathologist and would work well as a screening tool. It is difficult to say how well the algorithms performed in reality due to the, from the pathologists, inconsistent labelling and the relatively small data set. The conclusion is that, via interpretable algorithms one could classify these novel images with sufficient accuracy in such way that they could work as a screening tool. This would free up time for pathologist to spend more time on difficult assessments and potentially save lives. To further validate the results a larger dataset is required but the investigative report showed that imaging via upconvertning nanoparticles possesses promising attributes for automated breast cancer, and more specifically HER2, classification.