

LS19-018 - Deciphering breast cancer heterogeneity and tumor microenvironment with correlative imaging

Abstract

Breast cancer is especially difficult to treat because it's not a uniform disease. Even within the same tumor, different areas can behave and respond to treatment in very different ways. This complexity is called breast cancer heterogeneity, and it happens because cancer cells constantly change in response to stress from their surroundings—particularly when they don't get enough oxygen (a condition known as hypoxia). When breast tumors are exposed to low oxygen, they adapt by forming abnormal blood vessels and changing how they use energy and grow. These changes are a big part of what makes breast cancer more dangerous. Our goal was to find new ways to detect these changes using advanced imaging, so that we don't need to rely on invasive tissue biopsies. To this end, we combined powerful imaging techniques—like PET/MRI scans—with detailed maps of the tumor's molecular makeup. These maps were created using technologies like MALDI mass spectrometry, Imaging Mass Cytometry (CYTOF), and multispectral imaging, and analyzed using artificial intelligence (AI). This combination allows us to “see” what's happening in the tumor without needing to cut into it. We developed a new type of PET/MRI scan that doesn't require contrast agents. This scan can detect key features of the tumor's environment, such as how it processes sugar (glucose), how fast it's growing, how much oxygen it receives, and how well it's supplied by blood vessels. These are all factors linked to how fast the cancer spreads. For example, we used [18F]FDG-PET and glucoCEST-MRI to measure how much sugar the tumor uses and how acidic it is—both signs of aggressive cancer. We also used [18F]FMISO-PET to look at how much oxygen is getting to the tumor and how well the blood vessels are working. Our scans revealed that all types of breast cancer—even within one tumor—contain different “neighborhoods” or habitats with unique characteristics. Compared to less aggressive forms like luminal A breast cancer, more aggressive types (like HER2-positive and triple-negative breast cancers) had areas with abnormal sugar use, low oxygen, and poor blood flow. In the lab (ex-vivo), we examined slices of the same tumors that had been scanned, using technologies that show what proteins and markers are present in each cell. This helped us understand how different types of cancer cells—well-oxygenated, low-oxygen, and fast-growing—differ in their biology. Finally, we used AI to combine all our imaging and lab data. We built a deep learning model that could accurately predict what type of breast cancer a patient had based only on imaging. The model worked better when we combined multiple types of imaging, showing the power of an integrated approach. We also discovered strong links between what we saw on the scans and the tumor's actual biology. These findings open the door to better, non-invasive tools for diagnosing and treating breast cancer, and may help personalize treatment in the future. Our work has been shared in scientific talks, posters, and five peer-reviewed publications (n=5).

Scientific disciplines:

Molecular biology (34%) | Machine learning (33%) | Magnetic resonance imaging [MRI] (33%)

Keywords:

Cancer biology, positron emission tomography, magnetic resonance imaging, mass spectrometry imaging, computational sciences

Principal Investigator: Katja Pinker-Domenig
Institution: Medical University of Vienna
Co-Principal Investigator(s): Goran Mitulovic (Medical University of Vienna)
Lukas Kenner (University of Veterinary Medicine Vienna)

Status: Completed (01.05.2020 - 30.04.2025)
GrantID: 10.47379/LS19018

Further links to the persons involved and to the project can be found under
<https://www.gmbh.wwtf.at/funding/programmes/ls/LS19-018/>