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Breast cancer metastasis progress based on the 3D collagen fibril orientation map

Breast cancer is the leading cause of cancer death in women worldwide [1]. In these patients, more than 90% of breast cancer-related deaths are caused not by the primary tumor, but by their metastases at distant sites. Metastasis is an extraordinarily complex process, entailing tumor cells to acquire a set of features that allow them to develop new foci of the disease. Systemic changes in the microenvironment between the cancer cells and the host stroma play an important role in supporting the growth and progression of the tumor by degrading, re-depositing, cross-linking and stiffening collagen fibrils. Although the knowledge of breast carcinogenesis is being progressively elucidated with 2D cell-culture experiments, they are not able to reproduce the real physiological pattern of the tumor microenvironment where the surrounding cells are equally as important as the tumor cell itself. Small-angle X-ray scattering has been successfully exploited to observe the organization of collagen fibrils in breast tissues [3]. To probe the remodeling of collagen fibrils in breast tumors in a volume-resolved way, it was exploited the potential of Small-angle X-ray Scattering Tensor Tomography (SASTT) in providing six-dimension images. Therefore, this study aimed to provide the basis to help in deciphering the mystery organ-specific metastasis.

The SASTT experiment was carried out at the SAXSMAT P62 beamline at the PETRA III storage ring in Hamburg, Germany. The SAXSMAT beamline has dedicated instrumentation to perform such an experiment. It used a 12.4 keV monochromatic beam focused to have 20 x 20 μm2 at the sample position to scan horizontally and vertically at several rotations and tilt angles with 50 ms exposure time. The region of interest of the freeze-dried breast tumor samples was selected and cut in a cylindrical shape with 1mm diameter and 1.5 mm height and placed on top of the tomographic stage system. A two-dimensional single-photon counting detector, Eiger2-9M ®DECTRIS, positioned at 3854 mm from the sample was used to record the photons scattered at small-angle, covering a q-range between 0.06 nm-1 and 1.95 nm-1. An in-house python-based pipeline data processing and reconstruction was used to average each of the 2,034,900 SAXS patterns and further reconstruct it.

A higher degree of content and orientation of the collagen fibrils was observed in the SASTT images at the tumor region previously indicated by an expert breast pathologist as a metastatic area. The orientation of the collagen fibrils to the tumor boundary can be an important sign of how the invasion of tumor cells into the stroma and migration toward the blood or lymphatic stream to a secondary organ is triggered.

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