

Scientists around the world are conducting advanced research to improve the monitoring and treatment of cancer patients. Soft tissue sarcomas are very rare and diverse cancers. Sarcomas require a personalized approach, especially in cases of large tumors with a high degree of malignancy. Treatment often involves a multidisciplinary approach including chemotherapy, radiation therapy and surgery. There is therefore a need for a detailed understanding of the genomes of different types of sarcomas, in order to understand their genesis and to incorporate personalized therapeutic management to treat patients more effectively.

Among the relatively new molecular tests that allow a more detailed understanding of the tumor's response to treatment and an assessment of the risk of recurrence or progression during the patient's follow-up after treatment is liquid biopsy. Liquid biopsy is a test that analyzes free-circulating tumor DNA (ctDNA) isolated from a patient's peripheral blood. Changes in the amount of ctDNA observed over time allow appropriate therapeutic and diagnostic decisions to be made.

The main goals of the project revolve around monitoring genetic, transcriptomic and epigenetic changes specific to sarcomas. In the proposed approach, we will use liquid biopsy to monitor:

- (1) response to preoperative radio-chemotherapy treatment,
 - (2) tumor recurrence or appearance of metastases clinically and/or on imaging studies at 2year follow-up.
- The study will also profile the sarcoma genome, allowing the selection of biomarkers that will serve to predict and monitor a patient's response to therapy, detect early recurrence and advance our knowledge of sarcoma development.

By analyzing ctDNA during and after treatment, we will provide information regarding the effectiveness of chemotherapy and radiotherapy in real time. This approach could revolutionize the way we assess treatment response and potentially lead to better outcomes for patients diagnosed with sarcoma. Another major goal of the study is early detection of disease recurrence. Analysis of ctDNA will provide tracking of biomarkers of recurrence before there are visible changes on imaging. By monitoring ctDNA levels during follow-up, we will establish a correlation between the ctDNA profile and the risk of recurrence or spread of the disease.

The ultimate goal of the project is to provide clinicians with valuable tools to make personalized treatment decisions for patients diagnosed with sarcoma. By analyzing genetic, transcriptomic, and epigenetic variations/abnormalities, monitoring ctDNA, and correlating ctDNA levels with clinical presentation, the proposed results will contribute to early detection and targeted treatment of patients diagnosed with sarcoma, and thus significantly improve patient outcomes.

We propose a pioneering approach that holds great promise for the future of sarcoma patient treatment, offering new insights into the molecular characteristics of the disease and providing clinicians with powerful tools to tailor therapy based on individual patient needs.