Whole genome sequencing of cell-free dna from metastatic breast cancer patients: a study of accuracy and response

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Abstract

Background

Breast cancer is the most common form of cancer in women. Though the primary breast tumor is not itself life threatening, metastasis usually is. The MESTAR project has proved that we can improve current clinical practices of detecting and monitoring metastatic breast cancer significantly by implementing FDG-PET/CT scans.

Objective

This project studies the genomic part of MESTAR and aims to examine the use of circulating tumor DNA analysis as a tool to detect and monitor metastatic breast cancer progression, and compare it to the imaging modules.

Methods

We will apply whole-genome sequencing on blood samples from patients with suspected recurrence, or with confirmed metastasis undergoing treatment. By using whole-genome sequencing, we can increase sensitivity by utilizing the breadth of the whole genome, as opposed to sequencing very deep only in targeted areas of the genome. Our approach towards estimating tumor content in patient plasma consist of a tumor-informed approach, in which we first discover which somatic point mutations characterize the tumor, and then look for the presence of these in the plasma. We also attempt to approach tumor-fraction estimation in the plasma without prior information about the solid tumor. This estimation is based on copy-number analyses.

Results

Preliminary results indicate that ctDNA analysis can detect progression as early as the best scanning modules, using both the tumor-informed approach, but also tumor-agnostically. Through algorithmic monitoring of copy-number alteration patterns, preliminary results suggest that we are able to detect early metastatic progression, using plasma samples only.

Conclusion

The MESTAR project includes more than 4000 blood samples from 328 patients, which have all been evaluated by both traditional CT- and PET-scans. We expect that we can compete with both scanning modules, and potentially detect metastatic progression even earlier. This project has the potential to affect clinical practices, and allow earlier detection and more accurate treatment response monitoring of a life-threatening disease.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.