Is lean soft tissue (i.e., skeletal muscle) a potentially modifiable biomarker predictive of prognosis, treatment tolerance and quality of life in women with estrogen receptor negative metastatic breast cancer?

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The community of women with metastatic breast cancer is growing as a result of more treatment options. Unfortunately women with estrogen receptor negative (ER-) metastatic breast cancer do not have as many therapies to choose from, which requires us to develop methods to optimize treatment tolerance and response. Current breast cancer models focus on the negative relationship between increasing body fat and breast cancer growth. However, there are now numerous studies in other cancer populations showing a strong relationship between good levels of skeletal muscle with improved treatment tolerance and better survival. We also know that skeletal muscle varies greatly from person to person, regardless of body mass index. This cannot be seen with the naked eye and occurs often in persons who are overweight or obese. Because skeletal muscle mass is often a target tissue for cancer drug metabolism, ***low*** levels of skeletal muscle can lead to higher levels of toxicity, such as nausea, vomiting, hair loss, and decreased blood counts. This results in dose reductions, dose delays or worse, stopping the drug altogether.

Fortunately, skeletal muscle mass is easily measurable using CT scans and skeletal muscle is potentially modifiable via lifestyle behaviors, such as diet and exercise. However, before we can test scientifically based methods to improve skeletal muscle mass, we need to understand if skeletal muscle mass is related to treatment tolerance and prognosis in these women, like it is in persons with kidney, colon and thyroid cancer. We also need to understand how skeletal mass changes from initial metastatic diagnosis throughout treatment.

For this study, we will be using information contained within the electronic medical records of 55 women with ER- metastatic breast cancer at two medical centers. We will get the names and medical records of these participants from institution's cancer registries and/or the medical oncologists who treat them. Similar to other studies, we will use archived CT images of the abdomen completed for diagnostic or routine surveillance purposes. These images are conducted ~ every 3 months and include the third lumbar vertebrae (L3) and the 8 muscles in this area, which reflect total body skeletal muscle mass. We will measure the amount and quality of these muscles using the CT image prior to treatment for metastatic disease, and at least 2 other times within 12 months of diagnosis. The information gathered from these scans, along with other data from the electronic medical record (e.g., medications, doses, radiology reports, weight, height, etc.) will be used to see if there is a relationship between low levels of skeletal muscle (quantity and quality) and treatment tolerance (dose-reductions) and prognosis (shorter time to disease progression and overall survival.) In addition, we will be asking 15 women with ER- metastatic breast cancer who are on their first or second anti-cancer treatment to complete questionnaires to see if skeletal muscle ***quality*** and/or ***quantity*** are related to symptom burden and quality of life.

Our study team reflects a highly qualified group of scientists and clinicians with expertise in nutrition, radiology, body composition and medical oncology and years of research experience. We have a united passion for improving the lives of women with metastatic breast cancer and have intentionally focused this application on those with ER- disease. Many reviewers perceive women with metastatic BC as "emaciated," nearing the end of their life, or frankly, not interested in research. Through our work, we know this is simply not true for the majority of these women. Thus, the data from the proposed work is crucial to support our hypotheses and to move our work, informed by women with metastatic BC, forward. While we recognize that interventions targeting muscle mass will not cure metastatic BC, the goal of this research trajectory is to identify methods to improve treatment tolerance, prognosis and the quality of survivorship for these amazing women.