

## **Public/Lay Abstract**

### **Rationale:**

Patients with stage IV breast cancer have 5-year survival rates of less than 25% despite considerable innovations in breast cancer therapy. Breast cancer cells have the tendency to spread to other organs in the body to form metastases, and these cells may remain undetected for years. Bone is the most common location for metastasis as up to 75% of stage IV breast cancer patients develop metastasis at this site. The cues that cause these cells to grow into metastatic lesions after arriving to the bone marrow are unknown. It is known that physical properties, including how soft or stiff the surroundings of a cell are, greatly influence tumor cell behavior. However, current models to study metastasis do not account for the diverse physical properties of the bone marrow, where breast cancer cells can travel and eventually thrive. In addition, the bone marrow is a primary home to the immune system. How macrophages, a type of white blood cell that plays a versatile role in the bone marrow, interact with tumor cells to stimulate their growth has not been studied extensively. To begin to answer important questions about how bone marrow stiffness influences metastatic progression, this research will analyze the environment in the bone marrow that promotes the growth of breast cancer metastases.

### **Goal:**

We will design a model that more accurately represents the physical properties of the bone marrow in order to 1) evaluate how tumor cells grow in environments that mimic stiffnesses they would encounter in the bone marrow and 2) determine how macrophages influence the growth of tumor cells in this model.

### **Interim Outcomes:**

The proposed research is an early-stage project that will establish how and why the environment of the bone marrow, where breast cancer cells can travel, causes the growth of metastases. The results from these studies will be crucial for understanding the reasons behind the progression of breast cancer metastasis, which will lead to a direct patient impact in the future. Successful completion of these studies will (a) yield the development of a realistic model of the bone marrow; (b) identify how soft or stiff environments influence the tumor cell response; and (c) reveal the role of immune cells in metastasis.

### **Significance:**

Each of the above outcomes has the potential to affect how patients are treated in the future as we will discover novel ways to inhibit tumor metastatic growth. This project is highly interdisciplinary and combines engineering, imaging, and cancer biology to analyze how different cell types interact with their surroundings in a tunable, 3D biomimetic bone marrow model. Overall, this research will be crucial in determining what type of environment can lead to the growth of metastatic lesions and how we can stop this growth. This study will considerably enhance our understanding of how stiffness in the bone marrow, ranging from softer in the center to harder closer to the bone, supports breast cancer metastasis. This work will help us discover new ways to improve outcomes for patients living with stage IV metastatic breast cancer.