Bone metastasis remains the leading cause of death in patients with advanced breast cancer. However, the underlying mechanisms remain unclear. Most previous studies of bone metastasis have focused on the role of bone cells in regulating tumor cell behavior in the skeletal microenvironment, but tumor cell interactions with the mineralized bone extracellular matrix (ECM) may be similarly important. This talk will discuss how a combination of high-resolution X-ray scattering analysis with large-area Raman imaging, backscattered electron microscopy, histopathology, and microcomputed tomography can be used to characterize bone mineral properties in mouse models of advanced breast cancer. Furthermore, it will describe how physiologically mineralized collagen may be used as a biomimetic platform to study how the mineralization state of skeletal collagen type I may regulate tumor cell interactions with bone and which functional consequences may emerge for the pathogenesis and therapy of breast cancer bone metastasis.