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3D printed biomimetic bone model with micronetwork and nanohydroxyapatite for breast cancer metastasis study

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ABSTRACT

Currently, metastatic breast cancer (BrCa) provides a crucial clinical challenge. Metastasis occurs as part of a cascade of BrCa evolution, after vascular remodeling and extravasation at the tumor site occur. BrCa tumors commonly metastasize into bone; therefore, it is important to develop a working bone model that accurately simulates the metastasis, arrival, and eventual invasion of BrCa into bone. Here, we propose to use a 3D printing system and nanomaterial to recreate a biomimetic and tunable bone model suitable for the effective simulation and study of metastatic BrCa invading and colonizing a bone environment. For this purpose, we designed and 3D printed a series of scaffolds, comprised of a bone microstructure and nanohydroxyapatites (nHA, inorganic nanocomponents in bone). The size and geometry of the bone microstructure was varied with 250- and 150-μm pores, in repeating square and hexagon patterns, for a total of four different pore geometries. 3D printed scaffolds were subsequently conjugated with nHA, using an acetylation chemical functionalization process and then characterized by scanning electron microscope (SEM). The SEM imaging showed that our designed microfeatures were printable with the predesigned resolutions described earlier. Imaging further confirmed that acetylation effectively attached nHA to the surface of scaffolds and induced a nanoroughness. Metastatic BrCa cell 4 h adhesion and 1-, 3-, and 5-day proliferation was investigated in the bone model in vitro. The cell adhesion and proliferation results showed that all scaffolds are cytocompatible for BrCa cell growth; in particular, the nHA scaffolds with small hexagonal pores had the highest cell density. Given this data, it can be stipulated that our 3D printed nHA scaffolds may make effective biomimetic environments for studying BrCa bone metastasis.