Biofabrication of a vascularized 3D tissue in vitro model

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Abstract:
One of the biggest limitations in the field of regenerative medicine is the lack of vascularization. The vascular system is primarily responsible for transporting blood to the different tissues of the human body; its function is not only to transport nutrients and gases, but also to remove metabolic waste and provide chemical signals to ensure proper function and maintain cellular homeostasis.
However, due to oxygen and nutrient diffusion limits (about 150-200 μm), thicker tissues are often not properly vascularized, leading to the formation of hypoxic and necrotic areas which is the main cause of graft rejection but also can increase the metastatic predisposition of certain cells types.

In this context, we understand the importance of developing technologies and methods to encourage the growth of new vessels (vasculogenesis) and the repair or replacement of native vessels (angiogenesis). Therefore, the physiological vascularization of tissues, in particular tumor neoangiogenesis, has been deepened to imitate the complexity of the phenomenon *in vitro* and develop a 3D model that is able to mimic the process of spontaneous bone metastases in breast cancer.

The ultimate goal of the project is to study the complexity of the metastatic process and thus enhance the screening of highperformance drugs against this type of cancer. In order to recreate a physiologically relevant vascularized tissue, two main aspects must be taken into account: first of all the heterogeneity of micro-environments within a specific tissue; second the fact that the biological environment is subject to a continuous remodeling based on the adaptation of physiological and pathological conditions.

With the purpose of facilitate the connection between the main circulation and the relevant tissue, a vascularized tissue model was created by the additive manufacturing of leaching templates within a fibrin hydrogel. The artificial vascular network (from 1 mm to 200 μm diameter) was produced by Extrusion-based 3D printing of leachable carbohydrate glass.