Recent studies on using alginate gels as a 3D cell culture substrate, which gives insight to cancer biology, are growing. Integrin encapsulation in RGD alginate gels can give an idea about how cancer cells signal to recruit blood vessels, and this can lead to the development of new anti-angiogenic cancer therapies [39].

An important limitation of most 3D cell culture systems is the difficulty in analyzing and quantifying cell matrix interactions. However, this problem can be now solved by various fluorescence resonance energy transfer (more commonly referred to by the acronym FRET) techniques, which enable an ability to quantitatively probe the relation between cell adhesion and decision making. These types of analysis now help one to predict cell behavior, particularly in 3D culture, and to design proper 3D cell culture substrates for a number of applications.

4.2.3 Tissue Regeneration with Protein and Cell Delivery

For the past few decades, alginate gels are used as vehicles for the delivery of proteins or cell population which can direct the regeneration or engineering of various tissues and organs in the body. There exist some limits to the size of a regenerative agent that can be released from an alginate gel because the pore size is ≈5 nm. Most of the proteins can be delivered even without degradation, whereas larger molecules such as DNA can be released via degradation. Further studies are ongoing in this area.

4.2.3.1 Blood Vessels

Blood vessels are critical for the transport of oxygen and nutrients to all parts of tissues, removal of metabolic waste, and trafficking of stem and progenitor cells, which are important for the growth of organs in an embryo and wound repair in adults [40]. New blood vessel formation is crucial in tissue engineering, and it provides treatment to patients suffering from coronary and arterial diseases. Blood vessel formation is exploiting the sustained and localized realizing of heparin from alginate gels. Differential binding of various growth factors to alginate gels leads to sequential delivery of factors in the early and late stages of angiogenesis, which supports the maturation of new vessels and better functionality. Those growth factors that promote initiation of angiogenesis and maturation of capillaries are VEGF and platelet-derived growth factor (PDGF), respectively [41]. When host cells that are capable of responding to delivered proteins are lacking or dysfunctional, transplantation of cells is more attractive for the formation of new blood vessels. The delivery of VEGF from alginate–PLG