5 min (Nair et al. 2007). Injectable Chitin-PCL-nanohydroxyapatite microgels have been prepared through simple regeneration chemistry without crosslinkers. This microgel system demonstrated an early osteodifferentiation and mineralisation *in vitro* (Kumar et al. 2015). The use of growth factors such as VEGF, TGF-β (Park et al. 2007), FGF (Dyondi et al. 2013) were loaded in the gels and showed significantly improve in the neovascularisation and bone formation. For example, silk hydrogel was used for the delivery of VEGF and BMP-2 into maxillary sinus floor. This system demonstrated the potential of using such a delivery system for deeper and irregular bony defect regeneration (Zhang et al. 2011). Chitosan-alginate injectable hydrogels have also been used successfully to deliver BMP-2 along with MSCs for bone regeneration (Park et al. 2005).

Challenges and Future Directions

Currently the TERM field is growing and focusing on novel delivery systems. The key to success is designing the construct or scaffold based on specific application. For example, when one desires to engineer bone or cartilage, load bearing capacity of new tissue plays an important role. Also, delivery of bioactive molecules to the target and rate of delivery will play important role in regeneration. Hydrogels have many different functions in the field of TERM. They are applied as space filling agents, as delivery vehicles for bioactive molecules and 3D structures that organize cells and present stimuli to direct the formation of a desired tissue. Many hydrogels (natural, synthetic or combination of both) have been developed and patented with different properties to address bone regeneration but only handful are commercially available. Most of them fulfill one or two requirements (e.g., biocompatibility, controlled delivery) without considering other design parameters (e.g., degradation profile, mechanical properties and method of delivery). Many studies so far have shown promising results at the pre-clinical phase. However, unable to overcome controlled release of growth factors and/or cells, batch-to-batch variation of natural polymers, production of growth factors for human use have hindered clinical translation. As our understanding of biological process of tissue regeneration expands, this information must be incorporated into the design of new hydrogel where target oriented delivery system with appropriate bio-chemical properties. It is vital to understand the interactions occurring at the cell surface and material interface to develop clinical applications. By using different synthetic methods, many new hydrogel systems are already underway. For example, controlled degradation of hydrogels, cell adhesion ligands have been attached to these material and growth factors have been incorporated into them to specifically regulate cell fate. Also, different synthetic protocols enhance the material biocompatibility as well as mechanical properties. Similarly, these methods have been developed to control porosity, improve diffusion and gently incorporate cells into the scaffold. These advances have the potential to improve materials properties and support the development of more natural and functional tissue. It is noteworthy to mention briefly about new type of hydrogels such as three dimensional printed hydrogels, memory shaped hydrogels and the advent four dimensional/active printed materials that could change their shape and under various stimuli. With further research in this field, hydrogels for bone regeneration will have better patient compliance.