

## Research Information

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### Cutting Edge Medicine: New Frontiers for Physiotherapy Interventions

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Imagine a paraplegic being able to walk and run! A number of us who saw the movie 'AVATAR' a couple of years ago saw exactly that – or was it just virtual reality – a mind game where the brain of protagonist playing the part of a paraplegic perceives walking, running, jumping etc. via a simulated computer program.

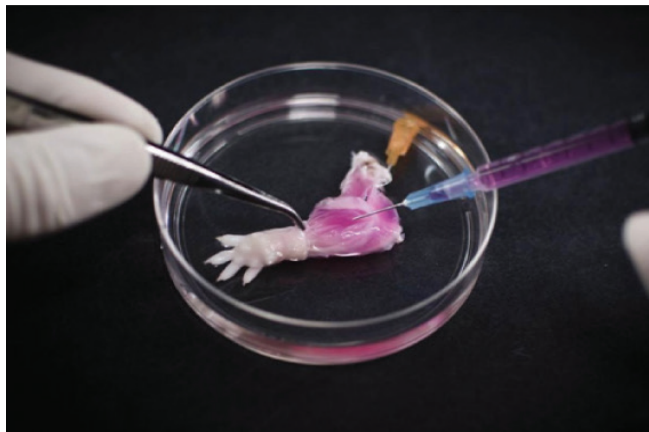
Could this be a reality in the future? Absolutely – the question one needs to ask is not if, but when? Current evidence suggests that not too far in the future, advances in technology and biological sciences will take us beyond a simulated perception of movement to an experience of a real movement of body parts and the body'. Currently, robotic science and artificial intelligence has already moved (no pun intended) humans to experience the benefits of technology assisted (robotic) arm and leg movements. At the same time, in parallel, scientist have made some significant advances in biological tissue repair or regenerative medicine. Given that the fundamentals underlying Physiotherapy practise are based on the facilitation of repair at the tissue level, the purpose of this brief manuscript is the significant role that physiotherapy can play in this frontier of medicine.

Wikipedia ([https://en.wikipedia.org/wiki/Regenerativ\\_medicine](https://en.wikipedia.org/wiki/Regenerativ_medicine)) defines regenerative medicine simply as the process of creating biologically compatible new cells and/or organs, which are used to replace diseased or injured tissue. In contrast to repair with scar tissue, this field of medicine engineers repair by stimulating the body's own biological processes to repair the damaged tissue by producing healthy tissue. A popular intervention of regenerative medicine

that a number of us are probably familiar with is the injection of stem cells into areas of damaged tissues and stimulating them to repair tissue that has been damaged – also known as –stem cell function enhancement.

Stem cells are cells that can differentiate into specialized cells and which take up function of the damaged or diseased tissue – they are of two broad types – embryonic and adult. In adults naturally occurring stem cells in the body are found in the bone marrow etc., while embryonic cells are harvested from the umbilical cord blood right after birth. Both act as a repair system for the body – replenishing adult tissue as needed, such as the blood, skin, bone, liver etc.

A common technique used in regenerative medicine is to infuse harvested stem cells directly into the site of an injury in an attempt to regenerate the damaged tissue and repair it. This technique has been used effectively to some degree to heal degenerated joint cartilage and tendons that do not regenerate by themselves and heal with the formation of scar tissue. Another technique that has been used effectively is by the infusion of stem cells into collagenous scaffolds placed within a nutrient rich environment of growth factors to create body parts, such as skin, bone, muscle etc. These parts are then implanted back into the donor host to replace diseased tissues/organs without the fear of immunological rejection. A scaffold is used primarily to provide shape and a space for the cells to be infused. The stem cells multiply, differentiate and fill up the scaffold to grow into a 3-dimensional body part. Eventually the scaffold dissolves and the regenerated tissue gets infused with blood vessels



**Figure 1:** A regenerated rat upper limb

and blends in with the surrounding tissue.

Figure 1 shows a regenerated rat forelimb which was created in a Petri dish. To begin with the researchers took a rat forelimb scaffold from a dead rat and seeded it with stem cells and nurtured it in an environment rich with nutrients, oxygen and electric stimulation. This process after several weeks allowed muscles and blood vessels to regenerate, cover the scaffold and acquire the form a rat forearm. After 2-3 weeks the researchers applied skin grafts to the limb. Please note that an important and significant aspect of this regenerative process was the electrical stimulus that was required to grow muscle tissue. Thus regenerating muscle tissue necessitate contractions using electrical impulses, blood vessels require metabolic activity, bone requires shear forces etc. (<http://www.theverge.com/2015/6/4/8730453/rat-limb-biolimb-regeneration-decellularization>) Regenerative medicine thus, has opened up a panorama of new possibilities in repairing biological tissue by regenerating the original tissue. This leads to full healing of the injured tissue instead of repair by scar tissue, which is inherently weak and leads to a cycle of injury/re-injury. This vicious cycle of damage to the tissues ultimately results in degeneration – particularly of tissues that have limited recovery potential – such as muscle, tendons, ligaments etc. Some common musculoskeletal conditions that could benefit from full healing or healing via the regeneration of

tissues are: muscle strains, ligament injuries, tendon injuries, cartilage injuries, joint degenerative disease etc.

It is important to note that physiotherapists can play a significant role in optimizing the results of regenerative medicine - both during the healing/tissue regeneration period as a facilitator, as well as post tissue regeneration as a consolidator to maximize the results of regeneration through a rehabilitation process.<sup>(1)</sup>

During the tissue regeneration period it is important to recreate the exact physical environment at the molecular level for the stem cells to re-engineer themselves and form functionally relevant tissue. Thus, for optimal musculoskeletal tissue repair the regenerating tissue (stem cells and scaffolding) need to be subjected to a combination of contractile, compressive, shear, tension and hydrostatic and vibratory forces, as muscles and bones are routinely subjected to these forces during movement. These stimuli help perfuse the collagenous scaffolding with increasingly more cells as well as determine cellular differentiation and consequently result in the formation of functionally relevant musculoskeletal tissue.<sup>(2)</sup> Tissue regeneration has been reported to happen within six months in patients who were implanted with a biologic scaffold infused with stem cells at the site of injury. In addition, it was reported that there was an increase in muscle strength in the implanted muscles and a consequent improvement in function.<sup>(3)</sup> Similarly, Han et al<sup>(4)</sup> reported improvements in muscle physiology and strength of damaged muscles that were implanted with regenerated muscle tissue in a series of patients suffering from different degrees of volumetric muscle loss. All patients were implanted with an extracellular matrix scaffold infused with stem cells into the damaged muscle (s), which in some cases spanned several muscles and physiotherapy was started within 48 hours. Therapy consisted of a strength based program that was based on a preoperative program.

### Conclusion

Regenerative medicine is still in its initial stages of development and the associated role of physiotherapy practice within this branch of medicine, at best in its nascent stage. However, initial results and trends are promising. Research studies are increasingly providing evidence in support of this emerging branch of medicine and rehabilitation.

In the context of physiotherapy, what is important is that optimal mechanical stimulation using tissue specific stimuli have been shown to facilitate this regenerative process during the initial regenerative stage as well as later during the rehabilitation stage. Physiotherapy consisting of therapeutic exercises and manual mobilization techniques produce beneficial torsional forces to facilitate tissue regeneration. However, physiotherapy also consists of several electrical modalities that produce mechanical stimuli that stimulate a variety of mechanical receptors at a cellular as well as a molecular level – such as ultrasound, electrical stimulation etc. Accordingly, a judicious application of these modalities during the regenerative process may be of value. Several

studies have reported desirable results using low intensity pulsed ultrasound in the healing of bone tissue in patients with fractures.<sup>(2)</sup>

Physiotherapists are ideally positioned to become important members of a regenerative rehabilitation team. I predict that not very far in the future physiotherapists will be zapping their patients to heal them by tissue regeneration techniques instead of scar tissue formation!

### References

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