Applied Biomechanics and Bioinformatics for Analysis of Limb Lengthening Research

Heba M.Afify
Department of Biomedical Engineering, MTI University, Egypt

Abstract—Biomechanics demonstrated by the variety of topics associated with physical therapy such as exercise, sports, neuromuscular control, energetics, and locomotor apparatus. Biomechanical treatment related to physical and mechanical components of the patient. Physical therapists are educated in the bio aspect of treatment, whereas prosthetists/orthotists are educated in the mechanical aspect. Physical therapy need to become more familiar with mechanical treatment and learn how to integrate this into their physical treatment program. Orthotics must become more familiar with the importance of physical treatment and the internal corrective forces necessary for efficient ambulation. In order to develop biomechanical treatment, an understanding of genetic factors that based on responsible genes for bone formation, is needed. Limb lengthening is used increasingly for children who have unequal lengths. It is critical for maintenance of joint motion that can be difficult to achieve. The National Institute for Health and Care Excellence (NICE) recommends human growth hormone treatment (HGH) as an option for children whose is associated with poor growth. Also, it can sometimes help prevent problems such as weak bones (osteoporosis). Recently, HGH can reduce muscle damage during limb lengthening by enhancing myogenesis and decreasing fibrogenesis. Improved limb-lengthening strategies in terms of tissue engineering and gene therapy, or enhancement of bone repair, are under intense investigation. This article illustrates how bioinformatics and physical therapy can improve a patient's status by assistance of biomechanical treatment.

Index Terms— Biomechanics; Bioinformatics; Physical Therapy; Limb Lengthening; HGH.

1 INTRODUCATION

Biomechanics began to flourish in the 1960s, but interventions on the human body through artifacts have a long history that originated with prehistoric supports for fractured bones and skin treatments. Daedalus with his mythical wings and the Tailor from UIm with his arm-extending wings for gliding [1] were precursors of biomechanics, one in legend and other in reality. After medieval times this process progressed to encompass artificial teem, and rudimentary artificial limbs. Eventually, the interventions on the human body fulfilled other needs through diagnostic and curative tools and processes, which based on the application of biomechanics. It starting in the 1960s [2] by using X-ray visualization through computed tomography, ultrasound scans, and magnetic resonance imaging, to hearing aids, surgical robots, tissue engineering, and the application of engineering knowledge to the understanding of biological [3] and therapeutic processes. Most of these developments were strongly interdisciplinary, blending engineering, physiology, physics and mathematics. Interdisciplinary continues to characterize the field.

Other biomechanics milestones include the first artificial organs. Some researchers [4] related biomechanics to analysis of motion. Because of the many different interpretations of biomechanics [5], controversy still exists in 1984 on which biomechanics should be used to represent the study of human statics and dynamics. Almost any topic related to musculoskeletal function is a part of biomechanics including exercise analysis, injury mechanisms, growth and development, methods of treatment, operative techniques, tissue properties, orthotics and prosthetics, design and performance of implants, and functions of the handicapped [6]. Additionally, certain implements and devices apply forces to the human body. Therefore, biomechanics is also considered to involve work-place design, man-equipment interface, the structure and design of tools and implements [7]. Biomechanics must be considered an inherent part of physical therapy, which purports the distinctive characteristics of prevention, evaluation, and treatment of movement dysfunction [8]. In fact, isolating physical therapy from biomechanics appears impossible.

The abnormal body movements may be caused by using internal or external forces [9]. Internal forces produced by biological changes may cause the abnormal body movements. For example, body movement may be too slow because of insufficient coronary blood flow, movement may be too fast because a portion of the brain is damaged, or movement may be excessive because edema has reduced the capability of the musculotendinous unit to produce force. Abnormal movement may also result from forces external to the body. Examples are abrupt foot contact with an unexpected elevation in the sidewalk or reduced spinal rotation because of an orthotic device worn about the torso. Therefore, Biomechanical treatment requires the direct interaction and integration of the two disciplines, physical therapy and orthotics that need each other [10].

Limb lengthening reasons are divided into three groups: congenital (from birth), developmental (from a childhood disease or injury that slows or damages the growth plates), and posttraumatic (from a fracture that leads to shortening of the bone ends). There are many ways to solve this problem such as lengthen the short limb by surgery, or control in gene that responsible on bone growth restriction.

Limb-lengthening technology has progressed significantly from the early 1950s when a handful of doctors first began the practice. Gavriil Ilizarov [11] invented the external fixator in Russia, a device he modeled after a horse harness. Now, many surgeons in the U.S. perform limb-lengthening procedures, and a new internal approach [12] offers patients expanded mobility and promises fewer complications. The device, called "Precice," received U.S. Food and Drug Administration approval for consumer use but is still relatively unknown within the greater medical community. A move to lengthen limbs internally rather than via an external scaffold could reduce the effects of painful treatments, especially among younger patients. However, there were many risks associated with limb lengthening surgery [13] that may result in further bone or skin infections (osteomyelitis, cellulitis, staph infections). Genetic researches of bone introduced the solution of limb lengthening without surgery. In the past, there was overlapping between biomechanics and physical therapy as in fig.1. Currently, there is overlapping between biomechanics and bioinformatics research.

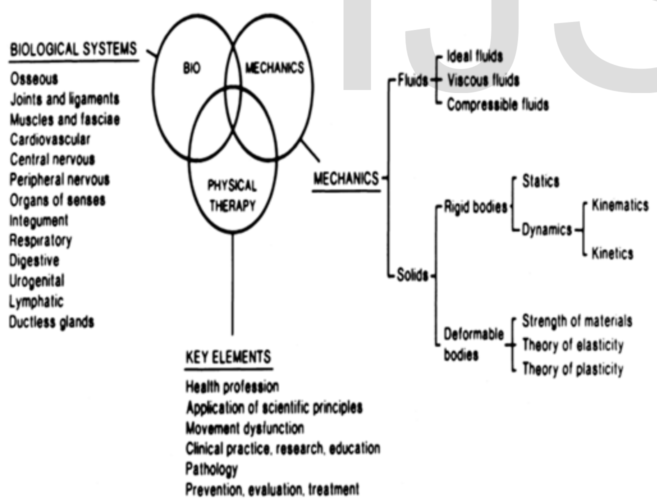

Fig.1. Illustration of overlap between biomechanics and physical therapy

2 IMPORTANCE PHYSICAL THERAPY IN LIMB LENGTHENING SURGERY

If a person has particularly short limbs, a limb-lengthening process, known as distraction, may be an option. This involves dividing the limb bone and fixing it to a special frame. This is gradually adjusted every day to encourage the bone to grow over time. Limb lengthening is a process that takes advantage of bone's ability to heal itself by generating more bone. An operation is carried out during which limb is broken or short limbs, and then, while supported by a frame or a fixator, their limb is stretched. This allows extra bone to form in the gap between the ends of the bone, and this grows stronger over time so that it can support patient's movement fully.

There are two phases of lengthening until the bone is fully healed: the distraction phase and the consolidation phase. The distraction phase is the lengthening phase. After the desired length is obtained, the newly regenerated bone is still very weak because of lack of calcium within it. The hardening and calcification of this new bone is called the consolidation phase.

As restricted growth can be associated with several related conditions and, affected children and adults are likely to be cared for by a team of different healthcare professionals. These may include:

1. a paediatrician (child health specialist)
2. a nurse specialists
3. a physiotherapist
4. an occupational therapist
5. a dietician
6. an audiologist (hearing specialists)
7. a speech and language therapist
8. a neurologist (specialist in nervous system disorders)
9. an orthopaedic surgeon
10. a geneticist

In this part, we focus on role of physical therapy to understand the integration between biomechanics and physical therapy [8]. Although biomechanical computations, physical therapy play a critical role in limb lengthening and skeletal deformity correction. Physical therapists needed to prevent the loss of joint motion [14]. The following modalities help in the management of new growth and tissue regeneration.

a. Programs of progressive weight bearing are important during all phases of limb lengthening rehabilitation. During the lengthening phase, patient should be encouraged to perform weight bearing as prescribed. Some patients may experience pain from increased weight bearing, and the increased weight bearing can cause undue stress on the pins or wires.

b. Hydrotherapy helps patient avoid significant muscle weakness, especially when both limbs are being lengthened. It promotes active range of motion. The natural buoyancy allows simulated weight bearing. The higher the level of the water, it achieves the more weightless one feels. Hydrotherapy also helps in keeping pin sites clean.

c. Electrical stimulation can be used as an adjunct to a strengthening program and to augment voluntary muscle contraction.

In physical therapists' quest to become more independent or interdependent with other disciplines, they are obliged to practice clinically and educate with a solid understanding of biomechanics. Furthermore, physical therapists need to make scholarly contributions in the areas of biomechanics and creatively apply biomechanical principles in their clinical practice.

Biomechanical treatment includes orthotics and prosthetics services. Therefore, biomechanical treatment and physical therapy are need to be in the same place at the same time and work together consistently to provide total treatment. By working together, they can expand their present knowledge and skills to act as the guiding force for a new generation of rehabilitation specialists.

Limb lengthening surgery can sometimes result in a significant increase in height, but it's a lengthy treatment and has a risk of complications, so it's not always recommended. NICE says there is uncertainty about the safety and effectiveness of this procedure, so they recommend making sure to understand exactly what it involves and to talk to doctor about the risks if it's suggested as a treatment. Some patient have pain after the limb-lengthening procedure. Other possible complications include poor bone formation, infection, bone lengthening at an inappropriate rate, and blood clots. To avoid these complications, open new directions for limb lengthening research may have broad relevance in growth regulation without surgery pains.

3 LIMB LENGTHENING GENE CONTROLLED BY BIOINFORMATICS ANALYSIS

Genetic factors play roles in many diseases. Often these factors are ill defined and unpredictable. Other diseases are caused by specific single gene mutations and are passed to offspring in Mendelian inheritance patterns. There are over 5000 documented Mendelian disorders; over 500 of these affect bones and joints. The most common dysplasias are osteogenesis imperfecta, achondroplasia, and osteopetrosis [15]. The surgical pathologist usually does not play a good role in the diagnosis of skeletal dysplasias.

There are major genetically determined differences in relative growth rates of individual bones. Differences in growth patterns are controlled by genetics component. According to heritability studies, 50-85% of the variance in bone mineral density is controlled by genetic factors which are mostly polygenic [16]. Recent article [17] examined the multifunctional roles of prominent nuclear proteins, cytokines, hormones, and paracrine factors that control osteogenesis. With an ever expanding list of new regulatory factors, the complexities of the molecular mechanisms that control gene expression in skeletal cells are being further appreciated. Technological developments made it possible to study increasing numbers of genetic control of bone remodeling.

Osteogenesis imperfecta (OI) is a group of genetic disorders that mainly affect the bones [18]. The term "osteogenesis imperfecta" means imperfect bone formation. Genetic factors are used to define the different forms of osteogenesis imperfecta. Mutations in the COL1A1, COL1A2, CRTAP, and P3H1 genes cause osteogenesis imperfecta. Several treatments are being explored for their potential use to treat OI. The OI Foundation provides current information on research studies, as well as information about participating in clinical trials that based on HGH treatment and gene therapies.

On the other hand, genes associated with cellular growth and proliferation, cell cycle, cell death, and tissue development were highly regulated in limb lengthening. HGH is a major promoter of postnatal longitudinal growth [19]. In addition, HGH antagonizes insulin action as part of the coordinated mechanisms by which multiple hormones maintain metabolic homeostasis. Park SE, and Park PK [20] suggested that HGH can reduce muscle damage during limb lengthening by enhancing myogenesis and decreasing fibrogenesis. Gene played a central role in regulating bone density [21].

A genetic variant that regulating a gene responsible for bone mineral density and fracture risk has been identified by researchers. Another promising method of growth-factor delivery in the field of limb lengthening is the application of gene therapy. Gene therapy for bone regeneration has already produced promising results in animal studies [22].

Much attention has been focused on the study of bioinformatics [23] due to important role of HGH in bone turnover. In addition to its well-documented influences on stature, muscle mass, lipid and carbohydrate metabolism and postnatal growth [24]. Pandey A.V [25] introduced an overview of some basic bioinformatics resources that are needed to analysis of HGH gene. Research is ongoing within all relevant fields and it is hoped that sequence analysis of limb lengthening gene will be successfully treated with genetic skeletal disorders to optimize outcome.

Although, the biomechanical treatment of patients is related to physical therapy, we believe that bioinformatics analysis demonstrated uniformly good trial of bone regeneration following by biomechanical treatment. Using the bioinformatics tools on genetic data of bone will revolutionize in limb lengthening without surgery. Moreover, gene prediction that based on restricted growth will be acts as a distinctive characteristic for healthcare. We suggest two streams for activating the role of bioinformatics in limb lengthening. Frist, exploiting principles of bioinformatics to improve the postnatal growth by changing the genetic data disorder. Second, exploiting principles of bioinformatics to improve the prenatal growth by predicating the hereditary factor at an early stage through family disease history. The issues of cost, efficacy and biological safety are need to be answered before this strategy of growth factors delivery is applied in humans.

4 CONCLUSIONS

Finally, elimination of pains form limb lengthening surgery remains elusive. Future studies should investigate the extent of bioinformatics for control of genes that responsible of bone regeneration. We found that investigation regarding the use of bioinformatics researches in biomechanical program is still lacking. There is still surprisingly little information available about limb lengthening gene for bone regeneration in vivo in humans.

Bioinformatics is a fertile area with open-ended opportunities and challenges to manage limb-lengthening gene by improvement of movement dysfunction. In addition, development of genetic testing on bone is more essential to reduce risks of limb lengthening. Determining how integrally a role bioinformatics principles play for limb lengthening is long overdue.

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