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Abstract:

BACKGROUND: Bones are exposed to different injuries as well as chronic diseases, which can affect the health of them. Different variables affect healing method, as timing, quality, recurrence, and long-term effect.

METHODOLOGY: This article is adopting the qualitative method as it is reviewing other researches; it is a scientific survey which is demonstrating the bullet points of each research, such as conclusions, methods, obstacles, and other future studies.

RESULTS: The effect was found to be very promising as a quality of osteoblast and timing of healing with precipitating effects among long and short terms.

DISCUSSION: The main objective of this study is to introduce the role of implants and grafts in orthopedic. The interventions are made based on the knowledge of the physiology of the bones, their injuries, and the response of the body toward it. Different metals were studied to be used in the implants, and advantages of their use were found. In addition to developing grafts from different tissues such as animal tissue, platelets, and others.

CONCLUSION: It can be concluded from the previous studies that future interventions can be made from using different materials to develop grafts and implants which shall aid in the healing process.

Keywords:

Early healing, fractures, grafts, implants

Introduction

Tumerous variables, including Compound and confused fractures, bone tumors (e.g., osteosarcoma), rot, extreme osteomyelitis, propelled osteoarthritis, high vitality injury, and other pathologic illnesses, can be the underlying reason for bone defects.^[1-3] In many cases, it is frequently important to balance out the stayed suitable hard sections and expel the sick hard parts that have no appropriate vascular stockpile from the patient's body.^[4] Following orthopedic careful mediations, all things considered, huge bone imperfections are developed. Moreover, broad fibrocartilage tissue arrangement following self-healing response may prompt the advancement of deferred associations or nonunions in 5%-10% of cases.^[5]

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Objectives

The main objective of this study is to introduce the role of implants and grafts in orthopedics, and these subobjectives arise:

- Discuss the modern methods of developing grafts and implants
- Reviewing the effects of adopting these methods on fractures and healing
- Comparing between different experiences and types of grafts and implants.

Methodology

This article is adopting the qualitative method as it is reviewing other researches; it is a scientific survey which is demonstrating the bullet points of each research, such as conclusions, methods, obstacles, and other future studies.

Overview

Bone is a perplexing organ with various capacities, including hematopoiesis,

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guideline and capacity of key minerals, the security of imperative life-continuing organs, assistance of movement, and so on. At the point, when bone is exposed to harmful, professional fiery improvements (injury, disease, etc.), the equivalent natural procedures managed by the inborn safe framework follow, similarly as with different tissues and organ frameworks, to impact neighborhood fix and bone healing. These occasions require continuous correspondence between cells of the monocyte-macrophage-osteoclast heredity, which legitimately faces the culpable boost, (e.g., with disease), yet then starts fix through the procedure of macrophage change (polarization) into an ace healing phenotype, and through the freedom of cytokines, chemokines, and different variables that advance angiogenesis and the homing of cells of the mesenchymal undifferentiated organism osteoblast genealogy. Likewise, mesenchymal-determined cells balance fiery cells to advance goals of master incendiary exercises and reconstitution of ordinary tissue.

Bone is a profoundly powerful tissue that experiences a steady procedure of rebuilding to oblige changing mechanical anxieties, and to fix creating weariness fractures. Notwithstanding, this procedure of renovating, bone has a wonderful potential for recovery. For sure, under ideal conditions, bone can recuperate totally without stringy scar arrangement into a structure and capacity that is indistinct from the state before the damage. The procedure of fracture healing is exceptionally intricate, and in numerous regards, inadequately comprehended. A few key standards overseeing bone recovery have, nonetheless, been entrenched as have a few key factors that fundamentally impact the result of healing. To be sure, upgrading the conditions for healing is the premise and the objective of all fracture treatment.

Outstanding among other perceived elements that impact result and furthermore the kind of bone fix is the level of relocation between the fractured bone finishes just as the mechanical solidness of the fracture condition.^[6-8]

Grafting in orthopedics

Bone grafting is a usually performed technique and is the second generally normal transplantation tissue, with blood being by a long shot the most common.^[9] It is assessed that in excess of 500,000 bone-grafting systems are performed every year in the United States and 2.2 million worldwide so as to fix bone deformities in orthopedics, neurosurgery, and dentistry.^[10] Today, bone grafting is utilized to upgrade healing in deferred associations, nonassociations, ostoectomies, arthrodesis, multifragmentary fractures, and to supplant hard misfortune coming about because of neoplasia or blisters.^[11] Osteogenesis, osteoinduction, and osteoconduction are the three fundamental components of bone recovery alongside the last holding between host bone and grafting material, which is called osteointegration. Osteoprogenitor cells living inside the giver graft may get by during transplantation, could possibly multiply and separate to osteblasts, and in the long run to osteocytes. These cells speak to the "osteogenic" capability of the graft.^[12] "Osteoinduction" then again is the incitement and initiation of host mesenchymal immature microorganisms from the encompassing tissue, which separate into bone-shaping osteoblasts. This procedure is intervened by a course of sign and enactments of a few extra- and intra-cellular receptors, the most significant of which have a place with the transforming growth factor- β superfamily.^[12] Osteoconduction is a trademark whereby the graft goes about as a changeless or resorbable platform, precisely supporting ingrowth of vessels and new bone from the fringes of the deformity into and onto its surfaces. This trademark starts or instigates new bone development.^[13] At last, "osteointegration" portrays the surface holding between the host bone and the grafting material.^[13]

Autografts that are collected from one site and implanted into another site inside a similar individual are named autografts, autologous, or autogenous bone grafts.^[14] Obviously, paying little respect to the source or structure (autograft or allograft), all transplanted bone grafts continue through five phases: aggravation, revascularization (slender buds attack the graft), osteoinduction (separation of multipotent cells into osteoblasts), osteoconduction (ingrowth into the graft by methods for the host), and finally renovating.^[15] The early incendiary reaction is fundamental in fracture healing as the provocative cytokines animate osteogenic separation of nearby or transplanted mesenchymal undeveloped cells.^[16] During the aggravation, invulnerable cells are among the primary cells to be available at the fracture site, and these impact flagging atoms control the healing course by pulling in cells from the encompassing tissue to the harmed site. The master provocative cytokines related with the natural tissue reaction to damage are interleukin-1, interleukin-6, and tumor necrosis factor- α . They assume a significant job in the enlistment of endogenous mesenchymal cells and incitement of angiogenesis.^[17] In addition, nearby corrosiveness and cytokines, contained in the exudate aggregating in the harmed zone, supplement this impact. To be sure, fiery go-betweens, for example, prostaglandins E1 and E2 may invigorate angiogenesis, and may likewise be in charge of flagging early bone resorption by osteoclasts and expansion of osteoprogenitor cells.^[18] At long last, pole cells containing vasoactive substances are plenteous during this stage and add to the arrangement of new vessels.^[19] Inside hours, a transient extraosseous

blood supply rises up out of the encompassing delicate tissues, revascularizing the hypoxic fracture site.^[20] As a graft, autogenous bone is perfect, yet the gather of autografts might be related with extreme contributor site torment and grimness even with new trapdoor collecting systems (with the trapdoor method, cancellous bone is reaped from the iliac tubercle, which falsehoods 3 cm back to the anterior superior iliac spine (ASIS). The connections of the sash and the abs to the iliac peak are kept unblemished). In techniques requiring a lot of graft, there may not be satisfactory amounts of autogenous bone accessible.^[21] As a result of the noteworthy deficiencies of autogenous bone graft, a present comprehension of accessible grafting choices is fundamental.

Allografts are collected from one individual and implanted into another of similar species.^[22] In a quest for a sufficient substitute for autogenous bone, cadaveric allograft has been a choice. Basic and morselized structures are accessible and arranged as either new solidified or solidify dried.^[21] These grafts give an auxiliary structure or platform for host tissue to develop, subsequently making allograft osteoconductive. Then again, its osteoinductive properties are unremarkable, best case scenario. On implantation, the host is required to encounter an intricate resistant reaction.^[21] Solidifying or stop drying the allograft is critical in limiting this response; nonetheless, the central properties of the material might be adjusted.

The technique for arrangement is intended to limit the host's safe reaction; hence, in many allografts, there are no suitable cells to offer osteogenic properties. The more forceful the allograft preparing, the less serious immunologic reactions will happen. One of the most significant strides in decreasing immunogenicity and malady transmission is liquid pressurization to maximally dispose of bone marrow and cell flotsam and jetsam. Crisp allograft has the most elevated danger of infection transmission, fuses ineffectively because of immunogenicity, and is not typically utilized. New allografts are never again utilized clinically therefore. Solidified allografts initiate more grounded invulnerable reactions than stop dried allografts.^[23] Allografts are handled by two essential methods, solidifying, and demineralizing, the two procedures of which guarantee demise of the host cells. Stop dried (lyophilized) allografts are washed in antitoxin twice, solidified at -70°C, and evaporated to 5% of water. These new solidified allografts are more osteoinductive and more grounded than stop dried grafts. Human immunodeficiency virus (HIV) has been transmitted in new solidified allograft, however not in stop dried bone.^[23] Stop dried allograft is the least immunogenic however has subpar osteoinductive and mechanical properties and quality

contrasted with crisp solidified graft. Further sanitization of the stop dried bone by ethylene oxide or gamma illumination may likewise reduce osteoinductivity properties.^[24] Rehydration of the stop dried bone can bring about longitudinal minuscule and naturally visible splits, which may represent up to half decrease in the biomechanical properties.^[24] The timeframe of realistic usability of the new solidified bone put away at 20°C is 1 year, and 5 years whenever put away at –70°C. The time span of the usability of stop dried bone is uncertain.^[23]

Deadly bacterial disease with Clostridium species after utilization of a femoral condyle allograft for reconstructive knee medical procedure has recently been accounted for.^[25] Hematogenous seeding from gut greenery before collecting likely taints the contributor tissue. After an intensive examination, an aggregate of 26 patients with allograft-related contaminations: 13 with Clostridium species diseases and 14 with contaminations related with a specific tissue handling office. Variables that may contribute in sullying with gut vegetation incorporate the time interim between death of the benefactor and tissue recovery, delays in refrigeration, and system of death (e.g., injury). The Clostridium case features the issue of bacteriostasis; societies acquired when preparing in anti-infection/ antifungal arrangement by the tissue processor were negative.[25]

Another potential disappointment related with allograft is related with its inability to suitably revascularize. Revascularization of regular solidified allografts is constrained. Histologic investigations of host-graft intersections depicted deficient vascular ingrowth, arriving at close to 10 mm from the graft-have intersection and 2 mm underneath the periosteal surface.^[26]

Tissue role in implants development

Nonunions are a difficult clinical issue and a noteworthy reason for constant torment and inability. In spite of the low occurrence of inconveniences in bone fractures, arriving at 10% when deferred associations are incorporated, their effect is as yet significant because of the high commonness of fractures in the all-inclusive community.^[27] Furthermore, huge bone imperfections and atrophic nonunion can be seen optional to arthroplasty, spinal arthrodesis, or bone tumor resection with destroying results. In the treatment for enormous bone imperfections, autografts are the highest quality level, despite the fact that their inventory is restricted, and there are comorbidities identified with the graft contributor site. Allografts are a significant option in contrast to autografts; however, they just give osteoconductive properties, being inclined to graft disappointment and nonunion appearance.^[28] At last, the osteogenic properties of bone morphogenetic

proteins (BMPs) (particularly BMP-2 and BMP-7) have been broke down in a few creature models, showing productivity like autografts in the treatment for nonunions. In any case, ectopic hardening and expanded bone resorption are portrayed as potential BMP-related reactions related with supraphysiological levels applied during clinical use.^[29]

Tissue building techniques have been proposed as an appealing alternative to bone grafts by joining autologous mesenchymal ancestor cells (MSCs) and osteoconductive biomaterials^[30] or by preconditioned MSCs separated through an endochondral pathway.^[31] The fundamental capacity of tissue-designed frameworks is to give a physical help to the forebear cells filling the rigid imperfection. Moreover, biomaterials can be functionalized to discharge osteogenic or osteoinductive variables that animate the separation of cells.^[32]

Randomized clinical examinations for cell-based treatments applied to fracture nonunion are hard to set up. To begin with, nonunion appearance is exceptionally subject to the kind of bone fracture and anatomical area.^[33] What is more, factors that instigate the presence of fracture nonunion have not yet been resolved, and the careful procedures applied may fluctuate contingent on patient needs.^[34] In this manner, to all the more likely decide the osteogenic properties of MSCs, preclinical creature models where the cause of the nonunion is controlled are attractive. In one of the examinations, researchers have created and approved a model of fracture nonunion so as to test the helpful capability of two noteworthy wellsprings of MSCs, bone marrow and periosteum, present at bone autografts and with a perceived job during bone recovery and fix.[35]

The purpose behind the low productivity of the cell-based treatments presently cannot seem to be resolved. A significant rot was watched in the exogenous cells in all gatherings. Indeed, even in live bone grafts, where contributor cells incorporate, it was hard to follow the cells in the main week postimplantation, and there were just a couple of cells present following 10 weeks, demonstrating that the vast majority of the implanted cells had passed on. It has been recommended that the unforgiving physiological condition created by the surgery, or by injury, is unsafe for cell endurance, particularly because of the incendiary condition and the diminished oxygen and supplement supply.^[36]

In any case, it was found that countless rat bone marrow mesenchymal stem cells rBMSCs were available following multi-week of implantation, when expert fiery sign was a long way from its greatest pinnacle detailed at 24 h following the damage.^[37] Then again, rBMSCs numbers appeared to decay when 3 days postimplantation, and

the numbers stayed low or imperceptible as the fix advanced. Different creators have exhibited cell rot in comparative basic size deformity models, in spite of the fact that utilizing xenotransplantation approaches with resistant advantaged cells. Regardless, the impacts saw in healing are like those seen here, and trophic elements may clarify these results.^[38]

The use of metals in orthopedics

Musculoskeletal issue is the most predominant medical issues in human that truly influence the quality existence of the patients. Because of statistic changes, the quantity of older experienced musculoskeletal issue is developing quickly, and this marvel will continue.^[39] Biomaterials are usually utilized in orthopedic medical procedures as bone substitutes, fixatives, and adjustment gadgets for fractured bones, tendon, and ligament fix and total hip arthroplasty.^[40] All the more significantly, a subsequent medical procedure will be frequently required to evacuate the implanted equipment to maintain a strategic distance from potential unfavorable impacts after fracture healing.^[41] To look for novel biomaterials for orthopedic gadgets, biodegradable polymers, for example, polylactide, polyglycolide, and co-polymers, have increased expanding consideration. These polymers have reasonable mechanical properties near cancellous bone, degradable conduct in the human body, and perfect analytic imaging for healing evaluations.^[42] Be that as it may, medical procedure disappointment may happen when utilizing these polymer-based gadgets because of their inadequate mechanical quality or fragility. All the more truly, the side-effects of these polymers can actuate long haul fiery reactions in peri-implant tissue.^[43] Moreover, the total corruption of polymer gadgets may not support bony ingrowth from long haul clinical perceptions.^[44] Subsequently, it is urgent to build up another age of medicinal metallic materials that are biodegradable, biocompatible and does not influence bone ingrowth after careful implantation.

One of the fundamental preferences of magnesium (Mg)-based implants over standard lasting metal implants is its biodegradability. Mg can corrupt by means of consumption, which starts from its standard cathode capability of - 2.372 V versus typical hydrogen anode (NHE). A metal with such a low standard cathode potential can erode in watery arrangements through the development of Mg hydroxide and equal mole of hydrogen gas.^[45] The middle of the road erosion items can either be consumed or used as Mg2+ by responding with Cl - ions in the body liquid or processed by macrophages. Notwithstanding, its biochemical highlights and capacities, Mg has fitting mechanical quality that is near cortical bone, which may address worries on refracture or inadmissible healing result at the fracture site by decreasing pressure protecting.^[46] All the more significantly, Mg implants have been broadly answered to decidedly animate new bone development, which is valuable to bone fracture healing.^[46] All in all, Mg-based orthopedic gadgets appear to be conceivable from the mechanical and natural perspectives, given the erosion of the gadget can be controlled *in vivo*.^[47,48]

Conclusion

It can be concluded from the previous studies that future interventions can be made from using different materials to develop grafts and implants which shall aid in the healing process. The interventions are made based on the knowledge of the physiology of the bones, their injuries, and the response of the body toward it. Different metals were studied to be used in the implants, and advantages of their use were found. In addition to developing grafts from different tissues such as animal tissue, platelets, and others, and the effect was found to be very promising as a quality of osteoblast and timing of healing with precipitating effects among long term and short term.

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Conflicts of interest

There are no conflicts of interest.

References

- Oryan A, Bigham-Sadegh A, Abbasi-Teshnizi F. Effects of osteogenic medium on healing of the experimental critical bone defect in a rabbit model. Bone 2014;63:53-60.
- Oryan A, Moshiri A, Raayat AR. Novel application of theranekron®enhanced the structural and functional performance of the tenotomized tendon in rabbits. Cells Tissues Organs 2012;196:442-55.
- Bigham Sadegh A, Mirshokraei P, Karimi I, Oryan A, Aparviz A, Shafiei Sarvestani Z. Effects of adipose tissue stem cell concurrent with greater omentum on experimental long-bone healing in dog. Connect Tissue Res 2012;53:334-42.
- Oryan A, Alidadi S, Moshiri A. Osteosarcoma: Current concepts, challenges and future directions. Curr Orthopaedic Pract 2015;26:181-98.
- Malhotra A, Pelletier MH, Yu Y, Walsh WR. Can platelet-rich plasma (PRP) improve bone healing? A comparison between the theory and experimental outcomes. Arch Orthop Trauma Surg 2013;133:153-65.
- Claes L, Recknagel S, Ignatius A. Fracture healing under healthy and inflammatory conditions. Nat Rev Rheumatol 2012;8:133-43.
- Jagodzinski M, Krettek C. Effect of mechanical stability on fracture healing – An update. Injury 2007;38 Suppl 1:S3-10.
- Giannoudis PV, Einhorn TA, Marsh D. Fracture healing: The diamond concept. Injury 2007;38 Suppl 4:S3-6.
- 9. Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: An update. Injury 2005;36 Suppl 3:S20-7.
- Greenwald AS, Boden SD, Goldberg VM, Khan Y, Laurencin CT, Rosier RN, *et al.* Bone-graft substitutes: Facts, fictions, and applications. J Bone Joint Surg Am 2001;83-A Suppl 2(Pt 2):98-103.
- 11. Van Heest A, Swiontkowski M. Bone-graft substitutes. Lancet 1999;353 Suppl 1:SI28-9.

- Cypher TJ, Grossman JP. Biological principles of bone graft healing. J Foot Ankle Surg 1996;35:413-7.
- Costantino PD, Friedman CD. Synthetic bone graft substitutes. Otolaryngol Clin North Am 1994;27:1037-74.
- 14. Zimmermann G, Moghaddam A. Allograft bone matrix versus synthetic bone graft substitutes. Injury 2011;42 Suppl 2:S16-21.
- Oryan A, Alidadi S, Moshiri A, Maffulli N. Bone regenerative medicine: Classic options, novel strategies, and future directions. J Orthop Surg Res 2014;9:18.
- Rifas L. T-cell cytokine induction of BMP-2 regulates human mesenchymal stromal cell differentiation and mineralization. J Cell Biochem 2006;98:706-14.
- Schmidt Bleek K, Schell H, Lienau J, Schulz N, Hoff P, Pfaff M, et al. Initial immune reaction and angiogenesis in bone healing. J Tissue Eng Regen Med 2014;8:120-30.
- Simonds RJ, Holmberg SD, Hurwitz RL, Coleman TR, Bottenfield S, Conley LJ, *et al.* Transmission of human immunodeficiency virus type 1 from a seronegative organ and tissue donor. N Engl J Med 1992;326:726-32.
- 19. Parikh SN. Bone graft substitutes: Past, present, future. J Postgrad Med 2002;48:142-8.
- Gomes KU, Carlini JL, Biron C, Rapoport A, Dedivitis RA. Use of allogeneic bone graft in maxillary reconstruction for installation of dental implants. J Oral Maxillofac Surg 2008;66:2335-8.
- Keating JF, McQueen MM. Substitutes for autologous bone graft in orthopaedic trauma. J Bone Joint Surg Br 2001;83:3-8.
- Bauer TW, Muschler GF. Bone graft materials. An overview of the basic science. Clin Orthop Relat Res 2000 Feb;(371):10-27.
- Ehrler DM, Vaccaro AR. The use of allograft bone in lumbar spine surgery. Clin Orthop Relat Res 2000 Feb;(371):38-45.
- 24. Sandhu HS, Grewal HS, Parvataneni H. Bone grafting for spinal fusion. Orthop Clin North Am 1999;30:685-98.
- Centers for Disease Control and Prevention (CDC). Update: Allograft-associated bacterial infections – United States, 2002. MMWR Morb Mortal Wkly Rep 2002;51:207-10.
- 26. Davy DT. Biomechanical issues in bone transplantation. Orthop Clin North Am 1999;30:553-63.
- Praemer A, Furner S, Rice D. Musculoskeletal injuries. Musculoskeletal conditions in the United States. Park Ridge, Ill.: American Academy of Orthopaedic Surgeons, c1992.p. 85-124.
- Hornicek FJ, Gebhardt MC, Tomford WW, Sorger JI, Zavatta M, Menzner JP, *et al*. Factors affecting nonunion of the allograft-host junction. Clin Orthop Relat Res, 01 Jan 2001, (382):87-98
- Angle SR, Sena K, Sumner DR, Virkus WW, Virdi AS. Healing of rat femoral segmental defect with bone morphogenetic protein-2: A dose response study. J Musculoskelet Neuronal Interact 2012;12:28-37.
- Scarduelli C, Ambrosino N, Confalonieri M, Gorini M, Sturani C, Mollica C, *et al.* Prevalence and prognostic role of cardiovascular complications in patients with exacerbation of chronic obstructive pulmonary disease admitted to Italian respiratory intensive care units. Ital Heart J 2004;5:932-8.
- Bahney CS, Hu DP, Taylor AJ, Ferro F, Britz HM, Hallgrimsson B, et al. Stem cell-derived endochondral cartilage stimulates bone healing by tissue transformation. J Bone Miner Res 2014;29:1269-82.
- 32. Geiger M, Li RH, Friess W. Collagen sponges for bone regeneration with rhBMP-2. Adv Drug Deliv Rev 2003;55:1613-29.
- Bishop JA, Palanca AA, Bellino MJ, Lowenberg DW. Assessment of compromised fracture healing. J Am Acad Orthop Surg 2012;20:273-82.
- Cuomo AV, Virk M, Petrigliano F, Morgan EF, Lieberman JR. Mesenchymal stem cell concentration and bone repair: Potential pitfalls from bench to bedside. J Bone Joint Surg Am 2009;91:1073-83.
- 35. Colnot C. Skeletal cell fate decisions within periosteum and bone marrow during bone regeneration. J Bone Miner Res

2009;24:274-82.

- Berner A, Henkel J, Woodruff MA, Steck R, Nerlich M, Schuetz MA, *et al.* Delayed minimally invasive injection of allogenic bone marrow stromal cell sheets regenerates large bone defects in an ovine preclinical animal model. Stem Cells Transl Med 2015;4:503-12.
- 37. Morgan EF, De Giacomo A, Gerstenfeld LC. Overview of skeletal repair (fracture healing and its assessment). Skeletal Development and Repair. Part of the Methods in Molecular Biology book series (MIMB, volume 1130) Springer; 2014. p. 13-31.
- Zhang ZY, Teoh SH, Chong MS, Lee ES, Tan LG, Mattar CN, et al. Neo-vascularization and bone formation mediated by fetal mesenchymal stem cell tissue-engineered bone grafts in critical-size femoral defects. Biomaterials 2010;31:608-20.
- Geetha M, Singh AK, Asokamani R, Gogia AK. Ti based biomaterials, the ultimate choice for orthopaedic implants – A review. Prog Mater Sci 2009;54:397-425.
- Farraro KF, Kim KE, Woo SL, Flowers JR, McCullough MB. Revolutionizing orthopaedic biomaterials: The potential of biodegradable and bioresorbable magnesium-based materials for functional tissue engineering. J Biomech 2014;47:1979-86.
- 41. Minkowitz RB, Bhadsavle S, Walsh M, Egol KA. Removal of

painful orthopaedic implants after fracture union. J Bone Joint Surg Am 2007;89:1906-12.

- 42. Ibrahim AM, Koolen PG, Kim K, Perrone GS, Kaplan DL, Lin SJ. Absorbable biologically based internal fixation. Clin Podiatr Med Surg 2015;32:61-72.
- Amini AR, Wallace JS, Nukavarapu SP. Short-term and long-term effects of orthopedic biodegradable implants. J Long Term Eff Med Implants 2011;21:93-122.
- Barber FA, Dockery WD. Long-term absorption of poly-L-lactic Acid interference screws. Arthroscopy 2006;22:820-6.
- Song GL, Atrens A. Corrosion mechanisms of magnesium alloys. Adv Eng Mater 1999;1:11-33.
- Staiger MP, Pietak AM, Huadmai J, Dias G. Magnesium and its alloys as orthopedic biomaterials: A review. Biomaterials 2006;27:1728-34.
- Zheng Y, Gu X, Witte F. Biodegradable metals. Mater Sci Eng R Rep 2014;77:1-34.
- Willbold E, Gu X, Albert D, Kalla K, Bobe K, Brauneis M, et al. Effect of the addition of low rare earth elements (lanthanum, neodymium, cerium) on the biodegradation and biocompatibility of magnesium. Acta Biomater 2015;11:554-62.