

ABSTRACT Bone grafts are used to regenerate the lost architecture and structure of the periodontium. A plethora of materials have been tried and tested in search of the ideal material. Various researches have led to the development of a new graft material InductigraftTM. It is a novel graft material which has osteogenic and osteoinductive properties similar to that of autogenous bone grafts. There have been many researches and studies carried out using InductigraftTM in Orthopaedic- spinal fusion surgeries, wherein its bone forming capacity has been demonstrated. The excellent bioactivity of this graft and its ability to accelerate bone formation in as little as four weeks as compared to that of eight to 12 weeks is of advantage and hence further research in the field of Periodontology is required for the use of InductigraftTM, to avail its benefits.

KEYWORDS : bone grafts; Silica substituted Calcium Phosphate; guided tissue regeneration; osteoinductive, osteoconductive

INTRODUCTION:

Periodontitis is an inflammatory disease of the periodontium and tooth supporting tissues which leads to loss of alveolar bone. This loss of bone leads to tooth loss which is detrimental to stability of the dentition. The ultimate goal of therapy using regenerative techniques is to form new structure, thereby restoring the function of the periodontium.¹

Various treatment modalities help restore the periodontal status, which include non-surgical therapy, surgical therapy, regenerative and resective therapy. Bone grafting is a dynamic process which utilizes the concepts of osteogenesis, osteoinduction, osteoconduction and osteointegration.² Current literature suggests that Guided Tissue Regeneration and bone augmentation procedures show evidence of periodontal regeneration.³ A wide range of graft materials have been utilised and evaluated for the regeneration which include autografts, allografts, xenografts, alloplasts, bone substitutes for the treatment of osseous defects;^{4,5} all of which have shown to have certain limitations. Bone substitutes are synthetic, organic or inorganic substances which can used as a replacement to either autogenous or allogenous bone grafts.⁴ Modern day periodontics aims at regenerating maximum amount of the lost tissue with maximum benefits. The goal of this article is to evaluate the benefits of a synthetic, newer bone graft material, with excellent bone forming capacity: InductigraftTM, which could help overcome the barriers of regeneration and be a revolutionary graft material.

CLASSIFICATION:

There are various systems of classifying bone grafts, this classification states the properties and disadvantages of bone grafts.⁶

Table 1

Autologous Autologous cancellous +++ Autologous ++++ Autologous + cortical + Allogenic +	+++	+++	Limited availability, donor site morbidity
cortical Allogenic Allogenic			
	+	+	Same as above
Bone grafts cancellous	+	-	Risk of disease transmission ,immune reaction

0	0	,			
	Allogenic cortical	+	-	-	Same as above
	De - mineralised bone matrix	+	++	-	Variable osteo inductivity associated with donors, processing methods
Synthetic Bone substitutes	Calcium sulfate	+	-	-	Rapid resorption, osteo conductive only
	Hydroxy apaptite	+	-	-	Slow resorption, osteoconduc tive only
	Calcium phosphate ceramic	+	-	-	Osteo conductive only
	Calcium phosphate cement	+	-	-	Osteo conductive only
	Bioactive glass	+	-	-	Bioactive osteo conductive only
	Polymethyl meth-acrylate	-	-	-	Inert, exothermic, monomer- mediate toxic

NEED FOR A NEWER GRAFTING MATERIAL:

According to Schallhorn (1977), certain factors need to be considered in the selection of the graft material, they are: biologic acceptability, predictability, clinical feasibility, minimal operative hazards, minimal postoperative sequelae and patient acceptance.⁷

Despite the plethora of materials available for grafting, autogenous bone grafts are considered to be the gold standard graft materials.⁸ Autografts have a greater osteogenic capacity than any of the other graft materials available.⁹ However, a number of disadvantages are associated with their use which include donor site morbidity associated with 20% of cases, the requirement of a second surgical site, difficulty in harvesting the bone graft, quantity of material obtained and complications like chronic pain with a range of 2.5% to 8%, dysesthesia (6%) and infection (2%).^{10,11}

There are many alternatives to autogenous grafts, which include allografts and xenografts all associated with various disadvantages. Allografts comparatively have a lower osteogenic potential and can cause immunologic reactions. Xenografts have the risk of immunogenicity and disease transmission. Xenograft disease transmission is associated with prions causing Creutzfeldt-Jakob disease and bovine spongiform encephalopathy (BSE).¹²

Various synthetic substitutes have also been researched, but none possess the qualities of an ideal graft material. In an effort to find an able substitute for the autografts clinicians and investigators have sought alternative synthetic graft materials, which could substitute or enhance the use autografts. Continuous research to incorporate all the ideal properties and osteogenic capabilities, has led to the development of a new synthetic graft material, InductigraftTM.

INDUCTIGRAFTTM:

Inductigraft[™] [Silica substituted Calcium Phosphate, enhanced porosity bone graft (SiCaP EP)] is a novel bone graft which has demonstrated efficacy in various clinical trials. It is osteogenic and osteoinductive and is comparable to autografts with respect to its properties. It contains microgranules, sized 1–2 mm with 80-85% macro porosity, 31-47% micro porosity and 0.8% silica.¹³

The properties of InductigraftTM that make it special are its increased strut porosity, increased neovascularization, 0.8% silica, physiologic bone formation, osteoinductive, osteoconductive and bioresorbable nature. InductigraftTM has an added Silica 0.8%, which is similar to the natural levels in bone,¹⁴ in the basic hydroxyapatite matrix, causing a negative charge on the surface leading to increased protein adsorption, increased neovascularisation and subsequent osteoblastic cell attachment and proliferation compared with that seen on stoichiometric hydroxyapatite.¹⁵¹⁷

Inductigraft[™] has enhanced strut porosity. Strut porosity is micro porosity wherein the pore size is less than 50 micrometers. Strut pores or microporosity are basically formed by interconnected spaces between particles.¹⁸ Studies comparing porosity of 23% to that of 46% SiCaP reported formation of larger hydroxyapatite crystals with that of higher porosity.⁹ This interconnected and porous structure resembles that of human cancellous bone facilitating osteogenic bone formation.

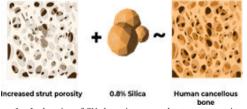


Figure 1: InductigraftTM has increased strut porosity with interconnected open porous structures and 0.8% added silica which makes it similar to human cancellous bone

This enhanced porosity, increases bone formation, by mimicking a network of microporous osteocyte lacunae similar to that of normal bone as well as increases the surface area which affects the protein binding and promotes osteogenic protein adsorption and cell anchorage, leading to faster bone apposition.²⁰ Studies done invitro, comparing Inductigraft™ (SiCaP EP), SiCaP and Bioglass bone graft, shows greater cell proliferation and earlier osteoblastic differentiation using SiCaP Ep²¹.



Figure 2a: The added silica increases protein adsorption which

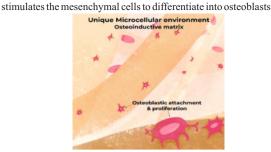


Figure 2b: Osteoblasts then attach and proliferate forming an osteoinductive matrix

It has a 3-D microcellular structure, creating a micro-environment similar to that of bone, causing mesenchymal bone cells to be stimulated, which then differentiate to osteoblasts. It also increases the permeability, thereby increasing the accessibility of nutrients into the graft.²⁰



Figure 3: Shows the process of faster apposition of bone graft in InductigraftTM

Studies have also proven that the high microporosity of InductigraftTM, allows for bone implant contact, thereby increasing the growth of natural bone.²⁰ An in vitro study carried out on rat model by Fredericks et al²² compared InductigraftTM with an iliac crest autograft and showed greater posterolateral bone fusion rates clinically and radiographically using InductigraftTM compared to that of an autograft. Studies by Campion et al²³ concluded that increased strut porosity, using InductigraftTM, causes increased neovascularisation, leading to faster bone growth at 8 weeks.

Hence, demonstrating the benefits of using InductigraftTM, which shows faster neovascularisation and faster bone apposition at 8 weeks compared to other grafts. Another invitro study by Smucker JD et al²⁴ in a rat model, demonstrated SiCaEP having a higher fusion rate compared with that of autograft, SiCaP and β TCP-bioglass.

Various surgeries have been carried out using Inductigraft[™] in the orthopaedic field, showing promising results. Studies by Mokawem et al²⁵ showed excellent bone fusion results using Inductigraft[™] in spinal fusion surgeries. A study by Bolger et al²⁰, showed fusion rate of 86.3% at 12 months with SiCaP EP, compared to 52–80% observed with traditional autologous iliac crest and allograft material.

LIMITATIONS:

InductigraftTM cannot withstand forces of torsion, compression, shear or bending forces and hence should be avoided in areas where such forces are exerted. $^{\rm 13}$

PROSPECTS IN PERIODONTOLOGY:

Inductigraft[™] can be used as bone graft substitute instead of autografts, corticocancellous and cancellous allografts in periodontology. Due to its faster bone apposition, osteoinductivity, bioresorbable characteristics along with other essential properties like neovascularisation, which help it simulate natural bone, it can be used as a graft material in various regenerative procedures, intrabony defects and hard tissue augmentation in implant cases.

CONCLUSION:

Various studies have focused on the formation of materials that will closely mimic the structure and chemical composition of natural bone. InductigraftTM is one such material, which possess characteristics which could possibly cater to bone regeneration procedures in the field of Periodontology. Despite certain limitations that the graft holds, InductigraftTM, is a novel bone graft, and hence its applications in Periodontology should be tested.

REFERENCES:

- Rosen PS, Reynolds MA, Bowers GM. The treatment of intrabony defects with bone 1. grafts. Periodontol 2000. 2000 Feb;22:88-103. Mahajan A, Kedige S. Periodontal bone regeneration in intrabony defects using
- 2. osteoconductive bone graft versus combination of osteoconductive and osteostimulative bone graft: A comparative study. Dent Res J (Isfahan). 2015 Jan-Feb;12(1):25-30.
- Bowers GM, Chadroff B, Carnevale R, Mellonig J, Corio R, Emerson J, Stevens M, 3 Romberg E. Histologic evaluation of new attachment apparatus formation in humans. Part III. J Periodontol. 1989 Dec;60(12):683-93. Schlickewei, W. and Schlickewei, C. (2007), The Use of Bone Substitutes in the
- 4. Treatment of Bone Defects - the Clinical View and History. Macromol. Symp., 253: 10-23
- Reynolds MA, Aichelmann-Reidy ME, Branch-Mays GL, Gunsolley JC. The efficacy 5. of bone replacement grafts in the treatment of periodontal osseous defects. A systematic review. Ann Periodontol. 2003 Dec;8(1):227-65.
- Wang W, Yeung KWK. Bone grafts and biomaterials substitutes for bone defect repair: A review. Bioact Mater. 2017 Jun 7;2(4):224-247. 6.
- 7. Schallhorn RG. Present status of osseous grafting procedures. J Periodontol. 1977 Sep:48(9):570-6.
- Campana V, Milano G, Pagano E, Barba M, Cicione C, Salonna G, Lattanzi W, 8. Logroscino G. Bone substitutes in orthopaedic surgery: from basic science to clinical practice. J Mater Sci Mater Med. 2014 Oct;25(10):2445-61.
- Damien CJ, Parsons JR. Bone graft and bone graft substitutes: a review of current technology and applications. J Appl Biomater. 1991 Fall;2(3):187-208. 9
- Younger EM, Chapman MW. Morbidity at bone graft donor sites. J Orthop Trauma. 1989;3(3):192-5. 10
- Fernandez de Grado G, Keller L, Idoux-Gillet Y, Wagner Q, Musset AM, Benkirane-11. Jessel N, Bornert F, Offner D, Bone substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management. J Tissue Eng. 2018 Jun 4:9:2041731418776819.
- Weihl CC, Roos RP. Creutzfeldt-Jakob disease, new variant creutzfeldt-jakob disease, 12 and bovine spongiform encephalopathy. Neurol Clin. 1999 Nov;17(4):835-59. Inductigraft advanced surgery baxter.https://globaladvancedsurgery.baxter.com/sites
- 13. Alimi M, Navarro-Ramirez R, Parikh K, Njoku I, Hofstetter CP, Tsiouris AJ, Härtl R. 14. Radiographic and Clinical Outcome of Silicate-substituted Calcium Phosphate (Si-CaP) Ceramic Bone Graft in Spinal Fusion Procedures. Clin Spine Surg. 2017 Jul;30(6):E845-E852.
- Guth, K., Campion, C., Buckland, T. and Hing, K.A. (2010), Effect of Silicate 15 Substitution on Attachment and Early Development of Human Osteoblast-Like Cells Seeded on Microporous Hydroxyapatite Discs. Adv. Eng. Mater., 12: B26-B36.
- 16 Hing KA, Revell PA, Smith N, Buckland T. Effect of silicon level on rate, quality and progression of bone healing within silicate-substituted porous hydroxyapatite scaffolds. Biomaterials. 2006 Oct;27(29):5014-26.
- Patel, N., Brooks, R.A., Clarke, M.T. et al. In vivo assessment of hydroxyapatite and silicate-substituted hydroxyapatite granules using an ovine defect model. J Mater Sci: 17. Mater Med 16, 429-440 (2005).
- hutchens, S.A., Campion, C., Assad, M. et al. Efficacy of silicate-substituted calcium phosphate with enhanced strut porosity as a standalone bone graft substitute and 18 autograft extender in an ovine distal femoral critical defect model. J Mater Sci: Mater Med 27.20 (2016).
- Chan O, Coathup MJ, Nesbitt A, Ho CY, Hing KA, Buckland T, Campion C, Blunn GW. The effects of microporosity on osteoinduction of calcium phosphate bone graft 19 substitute biomaterials. Acta Biomater. 2012 Jul;8(7):2788-94. Bolger C, Jones D, Czop S. Evaluation of an increased strut porosity silicate-substituted
- 20
- Boiger C, Jones D, Czop S. Evaluation of an increased strut porosity sticate-substituted calcium phosphate, SiCaP EP, as a synthetic bone graft substitute in spinal fusion surgery: a prospective, open-label study. Eur Spine J. 2019 Jul;28(7):1733-1742. De Godoy RF, Hutchens S, Campion C, Blunn G. Silicate-substituted calcium phosphate with enhanced strut porosity stimulates osteogenic differentiation of human mesenchymal stem cells. J Mater Sci Mater Med. 2015 Jan;26(1):5387. 21.
- mesenchymal stem cells. J Mater Sci Mater Med. 2015 Jan;26(1):587. Fredericks DC, Petersen EB, Sahai N, Corley KG, DeVries N, Grosland NM, et al. Evaluation of a novel silicate substituted hydroxyapatite bone graft substitute in a rabbit posterolateral fusion model. Iowa Orthop J 2013;33:25–32. Campion CR, Chander C, Buckland T, Hing K. Increasing strut porosity in silicate-substituted calcium-phosphate bone graft substitutes enhances osteogenesis. J Biomed Marca Rear B. and B. Dartherm 2011 Marcif 2012(2):045-65. 22
- 23 Mater Res B Appl Biomater. 2011 May;97(2):245-54. Smucker JD, Petersen EB, Al-Hili A, Nepola JV, Fredericks DC (2015) Assessment of
- 24 SiCaP-30 in a rabbit postrolateral fusion model with concurrent chemotherapy. Iowa Orthop J 35:140–146
- Mokawem M, Katzouraki G, Harman CL, Lee R. Lumbar interbody fusion rates with 25 3D-printed lamellar titanium cages using a silicate-substituted calcium phosphate bone graft. J Clin Neurosci. 2019 Oct;68:134-139.