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Mini Review

Biological action of calcium phosphate grafts on the spine

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Abstract

Despite the evolution in the field of grafting alternatives for spinal surgery, autologous iliac crest bone graft remains the gold standard for spinal fusion. However, donor site morbidity and limited availability stress the need for reliable substitutes. Calcium phosphate grafts, such as hydroxyapatite (HA) and tricalcium phosphate β (TCP-β), are a promising group of bone grafts in spinal surgery. The advantages of these grafts in spinal surgery are large availability, relatively rigid structure, low immunogenicity and high biocompatibility. However, they contain no living cells, no growth factors, no organic matrix and they are characterized by limited cortical stability and lack of osteogenic properties. Most studies have noticed that calcium phosphate grafts are efficient alternatives of autografts with similar fusion rates and functional outcome, in spinal fusion surgery. However, most of these studies are of low quality, lacking proper control groups. More prospective, randomized trials are needed in order to fully elucidate the optimal use of calcium phosphate grafts in spinal surgery.

Keywords: Calcium phosphate, Grafts, Hydroxyapatite, Spinal fusion, Spine

Introduction

Calcium phosphate ceramic grafts are the most popular and widespread synthetic bone graft substitutes that are characterized by mineral structure similar to the inorganic phase of calcified tissues such as the biological apatite of human bone[1]. They are used alternatively instead of autografts and allografts. They come in the form of powder, pellets or mortar and possess only osteoconductive properties. As they are not osteoinductive on their own, calcium phosphate grafts can be augmented with bone marrow aspirate, bone morphogenetic proteins, or traditional bone autografts and allografts. The main representatives of calcium phosphate grafts are: 1) Hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$; HA] 2)Tricalcium phosphate α or β [$Ca_3(PO_4)_2$] (TCP-α, TCP-β) 3) Biphasic ceramic materials consisting of HA and TCP-β in specific proportions (biphasic calcium phosphates, BCP) and 4) Graft combinations consisting of HA, TCP-β and dicalcium phosphate dihydrated (DCPD)[2]. Synthetic calcium phosphate ceramic materials are fully biocompatible grafts that do not elicit an immune or other toxic reaction of the host to the foreign body.

The porous structure of calcium phosphate grafts includes the micropores between the micro-crystals with dimensions less than 10 μm and the macropores with dimensions of 100-600 μm. The porous structure corresponds to an average of 30-45% of the ceramic material and determines its solidity. The whole process of manufacturing of synthetic ceramic materials determines both the mechanical and biological properties of these grafts. The osteoconductive characteristics of synthetic calcium phosphate grafts depend on the network of macropores and their size, the host osteogenetic potential, and the bone – graft interface. Osteoconductive implants allow osteogenesis both on the surface and inside of the graft thanks to the network of macropores and without the intervention of connective tissue.

Synthetic calcium phosphate grafts are not all characterized by the same solubility that determines the rate of biodegradation and bio-absorption over time. HA, whose

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chemical composition is very close to the crystalline form of bone and with a calcium/phosphorus ratio of 1.67 has the lowest solubility. Its biodegradation and bio-absorption can last up to several years. TCP-β with a calcium/phosphorus ratio of 1.5 has a higher solubility and therefore its biodegradation and bio-absorption extends from a few months to 2-3 years. Biphasic grafts are characterized by a specific solubility and biodegradation and bio-absorption time depending on the ratio of HA and TCP-β with the most common ratio being 60-65% to 35-40% respectively.

Osteoconduction is a fundamental property of synthetic calcium phosphate grafts and is associated with their biodegradation and bio-absorption. As soon as they are implanted, they are in constant interaction with the host biological environment. As the micropores of the graft are flooded by the host biological fluids, the graft crystals are progressively disoluted, releasing calcium and that forms apatite crystals similar to the apatite of host bone. These crystals then react with the protein environment and collagen of the host bone. This is a process of calcification that will eventually lead to ossification. Simultaneously, host macrophages and osteoclasts partially degrade the graft, which is colonized by mesenchymal stem cells and osteogenetic cells using the macropores network and creating a medium rich in substrates for osteogenesis with the ultimate goal of new bone formation. If this degradation process is too fast, remaining debris may cause inflammatory reaction[3].

Synthetic calcium phosphate grafts are fragile due to their porous structure. For this reason, synthetic ceramic materials should be applied with complementary internal fixation once the bone deficit imposes it. The mechanical strength of these grafts is gradually improved as the process of osteogenesis and osteointegration progresses. As solid fusion is the ultimate goal, interference with bone formation due to inadequate dissolution must be taken into account when considering the optimal graft for a patient.

Grafts in spinal surgery

In spinal surgery, autologous cancellous bone grafting, especially from iliac crest has been considered as the "gold standard" for spinal fusion[4]. Autologous bone grafts have the advantages of excellent fusion rates and time; however they are associated with increased operating time and donor-site morbidity[5-7]. The laminectomy-derived bone grafts solve the problem of donor-site morbidity, but as they are mostly cortical, they include fewer live cells and channels for vascularization[8]. On the other hand, allografts are abundant, they have no donor-site morbidity, but they have high immunogenicity and risk of disease transmission[9]. As a result, in order to avoid these drawbacks, alternative methods and techniques have been searched and calcium phosphate grafts have recently gained popularity.

Hydroxyapatite

Synthetic HA can be produced from sea coral, with different porosities and pore diameters, in order to be used in bone grafting. Because of its rigidity, HA can function well as a structural graft. HA grafts are typically resorbed at a rate of 2% to 5% per year providing structural support for many years[1]. In spinal surgery, HA, like TCP-β, can be used as a graft extender, but it should be used in graft combinations because it does not possess any osteoinductive properties. Although HA has shown successful outcome in animal models[10], HA has shown mixed results in clinical spinal fusion studies.

Cervical spine

A prospective, randomized study by McConnell et al, showed that HA was structurally inferior to iliac crest bone for cervical interbody fusion, as it is associated with higher graft fragmentation rate[11]. A retrospective analysis of 45 patients, who underwent anterior cervical discectomy and fusion, investigated the use of cancellous bone marrow and HA grafts. At a mean follow-up of 12 months, the fusion rates were similar between groups, while functional scores were higher in the HA group, suggesting that HA grafts are safe and efficient when used as a cage filler[12]. A case-series study by Yoshii et al examined the combination of HA with percutaneously harvested trephine chips, inserted into the intervertebral spaces of 51 patients who underwent anterior cervical discectomy and fusion. Outcomes were compared with the use of iliac crest bone grafts. Fusion rates were similar between the two groups, without any major collapse or fragmentation of the HA composite[13]. Good results, with anterior cervical fusion rates greater than 90%, were reported by level IV studies, suggesting that HA had similar radiological outcome with iliac crest bone grafts[14-16].

Lumbar spine

A prospective and randomised clinical and radiological study investigated the outcome of posterior lumbar fusion with the use of HA, autologous bone graft or their combination. Authors found that the patients who had undergone posterior lumbar fusion with a graft consisting of HA, local bone, and bone marrow aspirate had significantly less operating time, blood loss, and pain in comparison to other graft combinations. Adequate fusion was achieved in all patients. HA was less successful when used with small amounts of local bone. Successful fusion required proper bone preparation[4]. At 1 year follow-up, the use of HA with local bone produced not statistically different results in comparison to autologous bone grafting in patients undergoing posterolateral lumbar interbody fusion, in terms of fusion rates and functional outcome scores[17]. A retrospective study by Kim et al, in 130 patients who had undergone posterior lumbar fusion, found that porous

HA bone chips when used in combination with local bone graft produced similar clinical and radiological results with iliac crest bone grafts[18]. A recent prospective, randomised, single-blinded study that included 48 patients undergoing transforaminal lumbar interbody fusion (TLIF), investigated the use of autologous bone grafts with the combination of HA and decompression-derived bone grafts. Fusion rates, complication rates and outcome were similar between the 2 groups, suggesting that the investigated graft mixture can replace iliac crest grafts in lumbar spondylodesis[19]. HA with local bone grafts and bone marrow aspirate have led to a successful fusion in all patients treated with posterolateral fusion, in a retrospective study, with a 6-month follow-up[20]. When combined with demineralized bone matrix (DBM), HA produced similar fusion rates, in patients undergoing lumbar interbody fusion surgery, in comparison with the use of post-laminectomy acquired autologous bone graft[21]. Three other level IV studies also supported the use of HA as a successful option in posterior lumbar fusions when combined with other bone graft substitutes such as allograft and autograft[22-24].

On the contrary, another case-control study, including 58 patients who underwent PLIF, concluded that HA was only effective at augmenting autologous iliac cancellous bone graft but not laminectomy-derived bone, at 1-year follow-up[25]. In order to find the optimal mixture ratio of HA plus iliac crest bone grafts, Yoo et al analyzed the fusion rate among 88 patients undergoing minimally invasive transforaminal lumbar interbody fusion. Fusion rates increased according to the ratio of autologous bone graft, without any statistical significance[26].

Scoliosis

A case series including 27 patients treated with posterior fusion for idiopathic adolescent scoliosis, concluded that HA was associated with solid fusion at an average follow-up of 27 months[27]. How do these results compare to those previously published?

TCP-β

A histologic analysis was performed on a cohort of patients undergoing revision spinal fusion. Researchers observed that 40% of the removed tissue samples had capillary proliferation and collagen formation within the micropores along with bone formation on the graft surface and osseointegration into the native trabecular bone at 1 and 18 months after implantation. Two weeks after implantation, removed grafts were infiltrated by osteoclast precursors, along with collagen and microvascular proliferation without any superficial bone deposition. Grafts removed between 12 days and 3 years after implantation showed minimal bone deposition and cellular proliferation. Authors concluded that TCP-β has osteoconductive properties[28].

Cervical spine

A retrospective study by Yamagata et al included 55 consecutive patients who underwent anterior cervical discectomy and fusion with titanium cages with the use of autologous iliac crest bone grafting and 45 consecutive patients with TCP-β grafting. With a minimum 2-year follow-up, there were no differences in fusion rates, neurological outcome and cage subsidence between the 2 groups[29]. Anterior cervical fusion with interbody cages containing TCP-β is associated with successful fusion seen in all patients at 6 months follow-up[30]. For anterior cervical fusions, TCP-β compared to HA packed in cylindrical titanium cages, has proven to provide superior fusion rates, in 1-year follow-up[31]. In comparison to autologous bone grafts, TCP-β has good efficacy and satisfactory outcomes, for posterior cervical fusions[32-33].

Lumbar spine

In 2006, Epstein et al, reported that 91% of 53 posterior lumbar fusion levels were successfully fused with a 1:1 mixture of TCP-β and lamina autograft, in 12-months follow-up. Only one case required secondary fusion[3]. A subsequent report by the same author found that TCP-β combined with autologous bone graft and bone marrow aspirate for non-instrumented posterior lumbar fusion resulted in a 15% non-union rate in 60 patients at 2 years follow-up. Factors associated with non-union were older age, female sex and a past history of smoking[34]. More recently, the same research team reported that among 100 patients with lumbar spinal stenosis subjected to posterior lumbar fusion with the use of TCP-β combined with lamina autograft, fusion rate was 96%. Non-union occurred only in smokers[35]. However, final conclusions are debatable, as there were no control groups.

In a prospective, randomized clinical study, Dai and Jiang found equivalent self-reported outcome scores and fusion rates in 62 patients undergoing single-level PLIF with TCP-β and local autograft or iliac crest bone graft, after a 3-year follow-up. Authors concluded that the use of TCP-β may eliminate the need of iliac crest bone harvesting[36]. A prospective study comparing the use of local bone with a mixture of local bone and TCP-β in posterior lumbar fusion found that local bone underwent earlier resorption and stabilization compared with the combination of TCP-β and local bone, after a 1-year follow-up[37]. Another prospective comparative study, by Yamada et al, included 61 patients undergoing instrumented posterolateral spinal fusion with combinations of TCP-β, iliac crest bone grafts and bone marrow aspirates that were placed on one side in all patients. Post-laminotomy autologous bone grafts were placed on the contralateral side as control. Fusion rates were significantly higher for the combination bone graft side than that for the local bone graft side, with a minimum follow-up of 1 year[38]. On the contrary, a case series including 34 patients using the combination of TCP-β and autologous bone marrow aspirate for instrumented posterior lumbar interbody fusion, concluded that the use of β-TCP should be avoided due to high non-union rates[39].

Scoliosis

TCP-β, has also been used in scoliosis correction. In 1998, Ransford et al conducted a multi-center, prospective, randomised study comparing iliac crest bone graft and/or rib autograft with TCP-β in 341 patients undergoing posterior spinal fusion for idiopathic scoliosis. At a 18-months follow-up, the autologous graft group had an 8% loss of correction compared with 3% in the TCP-β group, suggesting that TCP-β is a safe alternative for bone grafting in these patients[40]. Later, a prospective study compared iliac crest bone graft and local bone grafts with a combination of TCP-β and HA, in 58 patients with idiopathic scoliosis that received posterior correction and fusion. Cases in the experimental group had lower blood loss and similar incorporation rates at a minimum of 2 years' follow-up. Authors recommended the use of calcium phosphate ceramics in adolescents and young adults as young age favoured better healing[41]. Muschik et al found similar clinical and radiological results between patients who received combination of allograft and autograft and patients who received combination of TCP-β and autograft[42]. Another prospective, randomised, comparative study found that, after a 2-year follow-up, loss of curve correction was 2.6° in 20 patients who received ultraporous TCP-β in comparison with 4.2° in 20 patients who received iliac crest bone graft. Authors stated that TCP-β is an effective bone substitute in scoliosis surgery[43].

Conclusion

The advantages of calcium phosphate grafts in spinal surgery are large availability, relatively rigid structure, low immunogenicity and high biocompatibility. However, they contain no alive cells, no growth factors, no organic matrix and they are characterised by limited cortical stability and lack of osteogenic properties. Most studies have noticed that calcium phosphate grafts are efficient alternatives of autografts with similar fusion rates and functional outcome, in spinal fusion surgery. However, most of these studies are of low quality, lacking proper control groups. More prospective, randomised trials are needed in order to fully elucidate the optimal use of calcium phosphate grafts in spinal surgery.

References

1. Brandoff JF, Silber JS, Vaccaro AR. Contemporary alternatives to synthetic bone grafts for spine surgery. Am J Orthop (Belle Mead NJ) 2008; 37:410-414.
2. Bohner M, Santoni BLG, Döbelin N. β-tricalcium phosphate for bone substitution: Synthesis and properties. Acta Biomaterialia 2020; 113:23-41.
3. Epstein NE. A preliminary study of the efficacy of Beta Tricalcium Phosphate as a bone expander for instrumented posterolateral lumbar fusions. J Spinal Disord Tech 2006; 19:424-429.
4. Korovessis P, Koureas G, Zacharatos S, Papazisis Z, Lambiris E. Correlative radiological, self-assessment and clinical analysis of evolution in instrumented dorsal and lateral fusion for degenerative lumbar spine disease. Autograft versus coralline hydroxyapatite. Eur Spine J 2005; 14:630-638.
5. Kim DH, Rhim R, Li L, Martha J, Swaim BH, Banco RJ, et al. Prospective study of iliac crest bone graft harvest site pain and morbidity. Spine J 2009; 9:886-892.
6. Sasso RC, LeHuec JC, Shaffrey C. Iliac crest bone graft donor site pain after anterior lumbar interbody fusion: a prospective patient satisfaction outcome assessment. J Spinal Disord Tech 2005; 18Suppl:S77-81.
7. Schwartz CE, Martha JF, Kowalski P, Wang DA, Bode R, Li L, et al. Prospective evaluation of chronic pain associated with posterior autologous iliac crest bone graft harvest and its effect on postoperative outcome. Health Qual Life Outcomes 2009; 7:49.
8. Dempster DW, Ferguson-Pell MW, Mellish RW, Cochran GV, Xie F, Fey C, et al. Relationships between bone structure in the iliac crest and bone structure and strength in the lumbar spine. Osteoporos Int 1993; 3:90-96.
9. Ehrler DM, Vaccaro AR. The use of allograft bone in lumbar spine surgery. Clin Orthop Relat Res 2000: 38-45.
10. Boden SD, Martin GJ, Jr, Morone M, Ugbo JL, Titus L, Hutton WC. The use of coralline hydroxyapatite with bone marrow, autogenous bone graft, or osteoinductive bone protein extract for posterolateral lumbar spine fusion. Spine (Phila Pa 1976) 1999; 24:320-327.
11. McConnell JR, Freeman BJ, Debnath UK, Grevitt MP, Prince HG, Webb JK. A prospective randomized comparison of coralline hydroxyapatite with autograft in cervical interbody fusion. Spine (Phila Pa 1976) 2003; 28:317-323.
12. Chang WC, Tsou HK, Chen WS, Chen CC, Shen CC. Preliminary comparison of radiolucent cages containing either autogenous cancellous bone or hydroxyapatite graft in multilevel cervical fusion. J Clin Neurosci 2009; 16:793-796.
13. Yoshii T, Yuasa M, Sotome S, Yamada T, Sakaki K, Hirai T, et al. Porous/dense composite hydroxyapatite for anterior cervical discectomy and fusion. Spine (Phila Pa 1976) 2013; 38:833-840.
14. Thalgott JS, Fritts K, Giuffre JM, Timlin M. Anterior interbody fusion of the cervical spine with coralline hydroxyapatite. Spine (Phila Pa 1976) 1999; 24:1295-1299.
15. Suetsuna F, Yokoyama T, Kenuka E, Harata S. Anterior cervical fusion using porous hydroxyapatite ceramics for cervical disc herniation. a two-year follow-up. Spine J 2001; 1:348-357.
16. Yang X, Liu L, Song Y, Kong Q, Zeng J, Tu C. Outcome of single level anterior cervical discectomy and fusion using nano-hydroxyapatite/polyamide-66 cage. Indian J Orthop 2014; 48:152-157.
17. Lee JH, Hwang CJ, Song BW, Koo KH, Chang BS, Lee CK. A prospective consecutive study of instrumented posterolateral lumbar fusion using synthetic hydroxyapatite (Bongros-HA) as a bone graft extender. J Biomed Mater Res A 2009; 90:804-810.
18. Kim H, Lee CK, Yeom JS, Lee JH, Lee KH, Chang BS. The efficacy of porous hydroxyapatite bone chip as an extender of local bone graft in posterior lumbar interbody fusion. Eur Spine J 2012; 21:1324-1330.
19. vonderHoeh NH, Voelker A, Heyde CE. Results of lumbar spondylodeses using different bone grafting materials after transforaminal lumbar interbody fusion (TLIF). Eur Spine J. 2017; 26:2835-2842.
20. Garin C, Boutrand S. Natural hydroxyapatite as a bone graft extender for posterolateral spine arthrodesis. Int Orthop 2016; 40:1875-1882.
21. Kim DH, Lee N, Shin DA, Yi S, Kim KN, Ha Y. Matched Comparison

of Fusion Rates between Hydroxyapatite Demineralized Bone Matrix and Autograft in Lumbar Interbody Fusion. J Korean Neurosurg Soc 2016; 59:363-367.
22. Robbins S, Lauryssen C, Songer MN. Use of Nanocrystalline Hydroxyapatite With Autologous BMA and Local Bone in the Lumbar Spine: A Retrospective CT Analysis of Posterolateral Fusion Results. Clin Spine Surg 2017; 30:E192-E197.
23. Thalgott JS, Giuffre JM, Fritts K, Timlin M, Klezl Z. Instrumented posterolateral lumbar fusion using coralline hydroxyapatite with or without demineralized bone matrix, as an adjunct to autologous bone. Spine J 2001; 1:131-137.
24. Thalgott JS, Klezl Z, Timlin M, Giuffre JM. Anterior lumbar interbody fusion with processed sea coral (coralline hydroxyapatite) as part of a circumferential fusion. Spine (Phila Pa 1976) 2002; 27:E518-525; discussion E526-517.
25. Hsu CJ, Chou WY, Teng HP, Chang WN, Chou YJ. Coralline hydroxyapatite and laminectomy-derived bone as adjuvant graft material for lumbar posterolateral fusion. J Neurosurg Spine 2005; 3:271-275.
26. Yoo JS, Min SH, Yoon SH. Fusion rate according to mixture ratio and volumes of bone graft in minimally invasive transforaminal lumbar interbody fusion: minimum 2-year follow-up. Eur J Orthop Surg Traumatol 2015; 25 Suppl 1:S183-189.
27. Mashoof AA, Siddiqui SA, Otero M, Tucci JJ. Supplementation of autogenous bone graft with coralline hydroxyapatite in posterior spine fusion for idiopathic adolescent scoliosis. Orthopedics 2002; 25:1073-1076.
28. Ogose A, Kondo N, Umezu H, Hotta T, Kawashima H, Tokunaga K, et al. Histological assessment in grafts of highly purified beta-tricalcium phosphate (OSferion) in human bones. Biomaterials 2006; 27:1542-1549.
29. Yamagata T, Naito K, Arima H, Yoshimura M, Ohata K, Takami T. A minimum 2-year comparative study of autologous cancellous bone grafting versus beta-tricalcium phosphate in anterior cervical discectomy and fusion using a rectangular titanium stand-alone cage. Neurosurg Rev 2016; 39:475-482.
30. Dai LY, Jiang LS. Anterior cervical fusion with interbody cage containing beta-tricalcium phosphate augmented with plate fixation: a prospective randomized study with 2-year follow-up. Eur Spine J 2008; 17:698-705.
31. Sugawara T, Itoh Y, Hirano Y, Higashiyama N, Mizoi K. β-Tricalcium phosphate promotes bony fusion after anterior cervical discectomy and fusion using titanium cages. Spine (Phila Pa 1976) 2011; 36:E1509-1514.
32. Epstein NE. Efficacy of posterior cervical fusions utilizing an artificial bone graft expander, beta tricalcium phosphate. Surg Neurol Int 2011; 2:15.
33. Ahn JS, Lee JK, Kim JH. Comparative study of clinical outcomes of anterior cervical discectomy and fusion using autobone graft or cage with bone substitute. Asian Spine J 2011; 5:169-175.
34. Epstein NE. An analysis of noninstrumented posterolateral lumbar fusions performed in predominantly geriatric patients using lamina autograft and beta tricalcium phosphate. Spine J 2008; 8:882-887.
35. Epstein NE. Beta tricalcium phosphate: observation of use in 100 posterolateral lumbar instrumented fusions. Spine J 2009; 9:630-638.
36. Dai LY, Jiang LS. Single-level instrumented posterolateral fusion of lumbar spine with beta-tricalcium phosphate versus autograft: a prospective, randomized study with 3-year follow-up. Spine (Phila Pa 1976) 2008; 33:1299-1304.
37. Kong S, Park JH, Roh SW. A prospective comparative study of radiological outcomes after instrumented posterolateral fusion mass using autologous local bone or a mixture of beta-tcp and autologous local bone in the same patient. Acta Neurochir (Wien) 2013; 155:765-770.
38. Yamada T, Yoshii T, Sotome S, Yuasa M, Kato T, Arai Y, et al. Hybrid grafting using bone marrow aspirate combined with porous β-tricalcium phosphate and trephine bone for lumbar posterolateral spinal fusion: a prospective, comparative study versus local bone grafting. Spine (Phila Pa 1976) 2012; 37:E174-179.
39. Thaler M, Lechner R, Gstöttner M, Kobel C, Bach C. The use of beta-tricalcium phosphate and bone marrow aspirate as a bone graft substitute in posterior lumbar interbody fusion. Eur Spine J 2013; 22:1173-1182.
40. Ransford AO, Morley T, Edgar MA, Webb P, Passuti N, Chopin D, et al. Synthetic porous ceramic compared with autograft in scoliosis surgery. A prospective, randomized study of 341 patients. J Bone Joint Surg Br. 1998; 80: 13-18.
41. Delécrin J, Takahashi S, Gouin F, Passuti N. A synthetic porous ceramic as a bone graft substitute in the surgical management of scoliosis: a prospective, randomized study. Spine (Phila Pa 1976). 2000; 25: 563-569.
42. Muschik M, Ludwig R, Halbhübner S, Bursche K, Stoll T. Beta-tricalcium phosphate as a bone substitute for dorsal spinal fusion in adolescent idiopathic scoliosis: preliminary results of a prospective clinical study. Eur Spine J 2001; 10 Suppl 2:S178-184.
43. Lerner T, Bullmann V, Schulte TL, Schneider M, Liljenqvist U. A level-1 pilot study to evaluate of ultraporous beta-tricalcium phosphate as a graft extender in the posterior correction of adolescent idiopathic scoliosis. Eur Spine J 2009; 18:170-179.