



Case Report

Neurologic impairment from ectopic bone in the lumbar canal: a potential complication of off-label PLIF/TLIF use of bone morphogenetic protein-2 (BMP-2)

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Abstract

BACKGROUND CONTEXT: Bone morphogenetic protein-2 (BMP-2) (Infuse) has been approved for use in anterior lumbar fusion in conjunction with an LT cage. However, off-label use is seen with anterior cervical fusion, posterior lumbar interbody fusion (PLIF), and transforaminal lumbar interbody fusion (TLIF). The Federal Food and Drug Administration trial of BMP-2 in a PLIF application was halted because of a high incidence of ectopic bone forming in the neural canal (75%). The authors did not find a correlation between ectopic bone and increased leg pain. They concluded that the ectopic bone was a radiographic phenomenon and not associated with clinical findings. Complications using BMP in the cervical spine have been reported. Heretofore, there has not been a similar warning voiced for use of BMP in a lumbar PLIF or TLIF.

PURPOSE: The purpose was to report five cases of ectopic bone in the canal associated with PLIF/TLIF off-label use of BMP-2 potentially contributing to abnormal neurologic findings.

STUDY DESIGN/SETTING: This is an observational cohort study of patients referred to a tertiary care private medical center.

METHODS: This was a retrospective chart review of patients referred to a tertiary spine institute with complications after surgery where BMP-2 had been used in an off-label PLIF or TLIF application. Patient demographics, operating room (OR) notes from the index BMP surgery, imaging studies, and current clinical status were reviewed.

RESULTS: Five cases of ectopic bone in the spinal canal with potential neurologic compromise were identified.

CONCLUSIONS: It does appear that ectopic bone in the spinal canal associated with BMP-2 use in PLIF or TLIF may contribute to symptomatic neurologic findings in rare cases. Revision surgeries are difficult. This article challenges a previous publication, which concluded that the high incidence of ectopic bone was of no clinical significance. Isolating BMP anteriorly in the disc space using layered barriers of bone graft between the BMP and the annular defect may reduce the incidence of ectopic bone in the spinal canal. Surgeons need to weigh the benefits versus risks of any technology used off label when making treatment decisions with their patients. © 2007 Elsevier Inc. All rights reserved.

Keywords:

BMP-2; Ectopic bone; Complications; Nerve compression

FDA device/drug status: not approved for this indication (Infuse-BMP-2); investigational/not approved (OP-1, BMP7, MP-52).

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Background

Spinal fusion rates of less than 100% and fracture non-unions have led physicians to explore recombinant human bone morphogenetic proteins as an adjunct biotechnology to help solve these vexing clinical problems. Numerous studies in both the basic science and clinical realms have demonstrated that bone morphogenetic proteins (BMPs) are powerful agents in the stimulation of bone formation [1–11].

The US Federal Food and Drug Administration (FDA) has reviewed Investigational Device Exemption (IDE) randomized controlled clinical studies involving the lumbar spine from two BMPs (bone morphogenetic protein-2 [BMP-2] and bone morphogenetic protein-2 [BMP-7]) [12,13].

At this time, only BMP-2 (Infuse; Medtronic Sofamor Danek, Memphis, TN) has received unrestricted approval by the US FDA [12] and is marketed commercially. BMP-2 is only FDA approved for use in an anterior lumbar interbody fusion (ALIF) application in conjunction with an LT cage (Medtronic Sofamor Danek, Memphis, TN). A collagen sponge is the carrier used with Infuse (BMP-2) in this approved FDA application. BMP in liquid form is dripped onto the sponge during surgery. The FDA decided not to require sales and marketing of BMP-2 in a package with the LT cage. Off-label use of BMP-2 is seen in clinical practice in both the cervical and lumbar spine. Published reports have raised concerns about clinically significant complications of off-label use of BMP-2 in the cervical spine [14–16] (local swelling, sterile fluid formation, airway compromise, dysphagia). However, there has not been a similar warning for off-label use in the lumbar region.

In recent months, five patients (Tables 1 and 2) were referred to the senior author for consultation concerning poor outcomes with a primary lumbar surgery done at other centers using BMP-2 (Infuse) with a collagen sponge carrier in an off-label application. These five patients had either posterior lumbar interbody fusion (PLIF) or transforaminal lumbar interbody fusions (TLIFs) with BMP. All presented with the complication of ectopic bone in the lumbar spinal canal and possible associated clinical neural complaints.

This experience led us to review the literature on the complication of ectopic bone presentation in the lumbar canal in association with BMPs used with PLIF or TLIF. Only one peer-reviewed, published article was found with significant discussion on this issue (Haid et al. [17]). The Haid et al.'s study of BMP-2 versus autologous bone in a PLIF application was originally tested in an FDA IDE. One BMP sponge was reconstituted and placed within two INTER FIX cages before PLIF insertion. In their publication, Haid et al. reported ectopic bone in the canal on post-op computed tomography (CT) scans in 24 out of 32 (75%) of the BMP group and 4 of 31 (13%) of the control group. This difference was highly statistically significant ($p < .0001$) and led to the early cessation of the trial by the FDA. However, the authors ultimately concluded that development of ectopic bone was not clinically significant [17]. They found that the presence of ectopic

Table 1
Patient demographics and clinical course/time/frames

Patient	Age at index BMP fusion surgery	Sex	Occupation	1° Dx	Work status at visit	Hematoma or sterile fluid pocket	Time from index BMP surgery to post-op MRI/CT for pain	Time from index BMP surgery to post-op CT with ectopic bone	Time from index BMP fuse to DAW office appointment
1	29	M	Framer	Lysis L5 No Spond	off	Yes Evac at 3 mo	2.5 mo	9 mo	10 mo
2	26	F	Home maker	Discogenic	off	No	12 mo	12 mo	13 mo
3	38	M	Auto body shop	Discogenic	off	No	7.75 mo	7.75 mo	9 mo
4	35	F	Packer	Discogenic	off	Yes, but no Evac	7 mo	7 mo	5 mo
5	39	F	Housekeeper	Lysis L5 Grade I Spond L5-S1	off	Yes, Evac at 3 mo	1.5 mo	6 mo	17 mo
							Average 6.15 mo	Average 8.35 mo	

BMP = bone morphogenetic protein; MRI = magnetic resonance imaging; CT = computed tomography; 1° Dx = primary diagnosis at index BMP surgery; Evac = surgical evacuation of hematoma or sterile fluid collection; DAW = senior author; Lysis = spondylolysis; Spond = spondylolisthesis.

Table 2

Surgical details of index surgery with BMP—level(s) fused, end plate preparation, dosage, approach, sponge placement

Patient	Original surgery levels fused with BMP	Original surgery end plate preparation to bleeding bone	# BMP sponges	TLIF PLIF	BMP in disc space	BMP in cage	Irrigation post-BMP placement	Drain	Revision Surgery by DAW
1	L5–S1	Yes	5	TLIF	Contralateral	?	Yes	Yes	No
2	L5–S1	Yes	?	PLIF	Ant	?	Yes	No	Yes
3	L5–S1	Yes	?	TLIF	Contralateral	?	Yes	Yes	Yes
4	L3–L4 L4–L5 L5–S1	Yes	?	TLIF	Ant	Y	Yes	Yes	Yes
5	L5–S1	Yes	2	TLIF	Contralateral	Y	Yes	No	No

BMP = bone morphogenetic protein; PLIF = posterior lumbar interbody fusion; TLIF = transforaminal lumbar interbody fusion; Ant = sponge placed anterior in the disc space; ? = data not specified in the operative report from the index BMP surgery.

bone after surgery was “not correlated to a recurrence or increase in leg pain from the preoperative state.” Thus, the authors did not signal a warning about ectopic bone formation in the canal to physicians contemplating off-label PLIF/TLIF use of BMP.

The present report outlines five cases of ectopic bone in the lumbar spinal canal that were likely associated with neural complaints after use of BMP-2 and a collagen sponge carrier for PLIF/TLIF. These cases question the conclusion of Haid et al. [17] that “bone formation in the spinal canal after the PLIF procedure with stand-alone cylindrical interbody fusion cages appears to be primarily just a radiographic finding that is not associated with any clinical outcome.” Potential causal issues are discussed and relevant literature is reviewed. Although neural compromise by ectopic bone is not a common occurrence, this report is a cautionary note to surgeons using BMPs in a lumbar, off-label PLIF/TLIF application.

Case illustration (Tables 1 and 2, Patient 1)

A 29-year-old male construction worker/framer was injured in a fall at work. Postinjury, the patient reported primarily aching and sometimes sharp pain in the low back area. Less bothersome minor intermittent pain radiated to the right lower extremity. He continued to have discomfort for 6 months despite conservative treatment with analgesics, anti-inflammatories, muscle relaxants, physiotherapy, activity modification, and time off work.

Investigations showed a magnetic resonance imaging (MRI) with a desiccated disc at L5–S1, undisplaced L5 spondylolysis, and a mild associated bulge of the disc. No significant canal compromise. Discography demonstrated concordant reproduction of back pain and discogenic mechanical back pain was felt to be the patient’s primary diagnosis.

Six months after his injury, the patient underwent a posterior L5–S1 laminectomy, TLIF from the right with metal cage, and BMP-2/collagen sponge carrier plus pedicle screw instrumentation. End plates were prepared down to bleeding bone. A total of five BMP sponges were used. Sponges were placed contralaterally and anteriorly in the disc space before insertion of the cage obliquely. A

posterior pedicle screw instrumentation and intertransverse fusion were also performed. The patient continued to have back and right lower extremity pain postoperatively. The right leg pain worsened over a period of weeks and became his dominant complaint. The patient was also noted to have persistent swelling and inflammation in the incision area. An MRI was performed 2.5 months post-op (Fig. 1). A fluid collection was noted in the canal adjacent to the PLIF insertion site. No ectopic bone or bone fragments were noted in the canal at that point. Thus, the subsequent development of ectopic bone in the canal is not likely to be related to any bone fragments in the canal from the decompression or disc space preparation at the time of the index BMP surgery.

The MRI results led to surgical wound drainage. No bacterial growth and no ectopic bone were identified at that procedure. The patient’s right radiating lower extremity pain continued to increase. Clinically, the patient had primarily a right L5 radiculopathy.

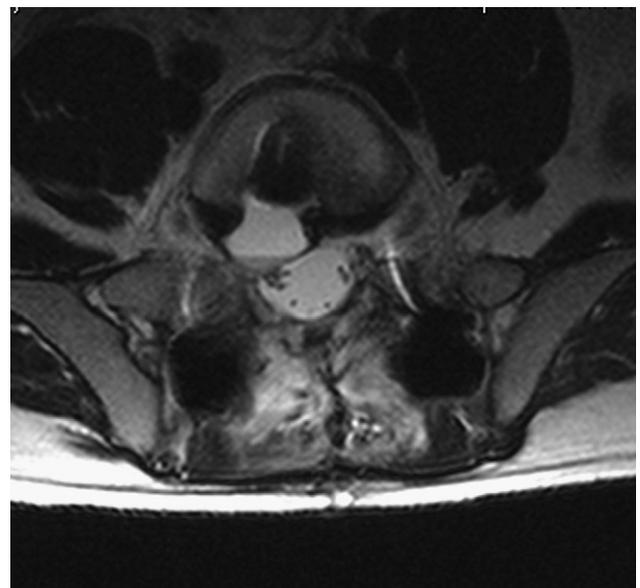


Fig. 1. Patient 1: Post-op magnetic resonance imaging scan 2.5 months post-op showing a fluid collection in the surgical area but no bone in the spinal canal at that point. Thus, bone fragments from the decompression or the disc space preparation are unlikely to be an explanation for presence of ectopic bone. No bacteria were cultured at surgical drainage of the fluid collection.

Investigations including a myelogram and computerized axial tomogram at 9 months post-op the index surgery and 6 months post-op from the wound drainage, showed a corticated bone mass extending from the annular defect for the PLIF back into the spinal canal (Fig. 2). The lateral recess of L5 on the right and the right L5–S1 foramen was compromised by this mass (Figs. 3 and 4). The ectopic bone appeared to extend posteriorly directly associated with the annular defect from the right-sided TLIF procedure (Fig. 2). The side and level of the stenosis from ectopic bone corresponded clinically with the patients worsened radicular pain post-op. A selective right L5 root block temporarily relieved a significant portion of the patient's right lower extremity pain. The block served as confirmatory evidence that the nerve root compromised by the ectopic bone was potentially clinically significant, but is not absolutely specific. Radiculopathy can be multifaceted. The patient is being treated for chronic pain in the workers compensation system before consideration of revision surgery.

Case illustration (Tables 1 and 2, Case 5)

A 39-year-old housekeeper sustained a back injury in a fall at work. Clinically, she had low back pain and right lower extremity radicular pain and was diagnosed with a Grade I spondylolytic spondylolisthesis with associated L5 and S1 radiculopathy. She ultimately underwent an L5–S1 decompression, pedicle screw tension band instrumentation, and TLIF from the right using minimally invasive tube-based technology. Two BMP sponges were used (placed contralateral and in a polyetheretherketone cage). Over a period of several weeks post-op, the patient developed increased pain in the back and leg. MRI at 2 months post-op disclosed a fluid mass in the canal and adjacent to the TLIF annular defect (Figs. 5 and 6). Surgical drainage

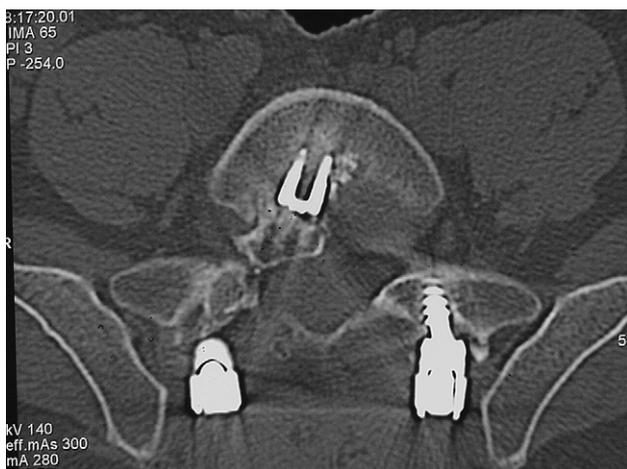


Fig. 2. Patient 1: Post-op axial computed tomography scan at L5–S1 9 months postindex surgery and 6 months post-op surgical wound drainage. Note the ectopic bone adjacent to the transforaminal lumbar interbody fusion entry site and extending posterior into the spinal canal. The bone mass has a well corticated exterior shell.



Fig. 3. Patient 1: Post-op sagittal reconstructed computed tomography through the right side of the spinal canal. Ectopic bone in the canal is located opposite the transforaminal lumbar interbody fusion entry site and extending up posterior to the lower L5 vertebral body.

was performed. No evidence of bone in the canal from the decompression or disc space preparation was found at that point. A CT scan at 6 months post-op the index surgery showed ectopic bone forming in the canal compromising the entry zone of the L5–S1 foramen (Fig. 7). The patient had corresponding L5 radicular changes clinically.

Additional patient issues with index BMP surgery (Table 2)

The OR notes for all five patients indicated that the end plates had been prepared down to bleeding bone. BMP sponges were placed anteriorly or contralaterally in the disc space in all cases before insertion of a cage or allograft strut. Two OR notes made specific mention of BMP placed in the cage. Only one of the five cases (Patient 2) had additional barriers placed between the BMP and the annular defect (structural allograft then cancellous allograft chips posteriorly). Three of the five cases reported irrigation of the operative area before BMP placement. All five OR



Fig. 4. Patient 1: Post-op sagittal reconstructed computed tomography more to the right than Fig. 3, through the entry zone of the L5–S1 foramen. Still, a large mass of ectopic bone in the entry zone of the foramen. Note at higher levels with more medial pedicles, the cut is through the main portion of the foramen with the pedicles (roof and floor of the foramen) clearly visible.

notes specified irrigation after BMP insertion. In addition, three patients had a suction drain left in the deep wound. None of the notes specifically mentioned using gelfoam for hemostasis. Four of the five patients had single level L5–S1 fusions with BMP and had ectopic bone formation at those segments. One of the patients (Patient 4) had the lowest three lumbar levels fused with ectopic bone developing at L5–S1.

Postindex BMP surgery symptom time frames

The patients described here did not have acute perioperative exacerbation of radicular pain. Radicular symptoms generally increased postoperatively in a gradual fashion over a time frame of weeks to months. Four of the five patients presented for another opinion after their index BMP surgery primarily with increasing radicular pain. The fifth patient (Patient 3) had numbness in a radicular pattern that was more bothersome than pain. The evolution of symptoms is reflected in the time interval from index surgery to the first post-op MRI or CT done to investigate pain/

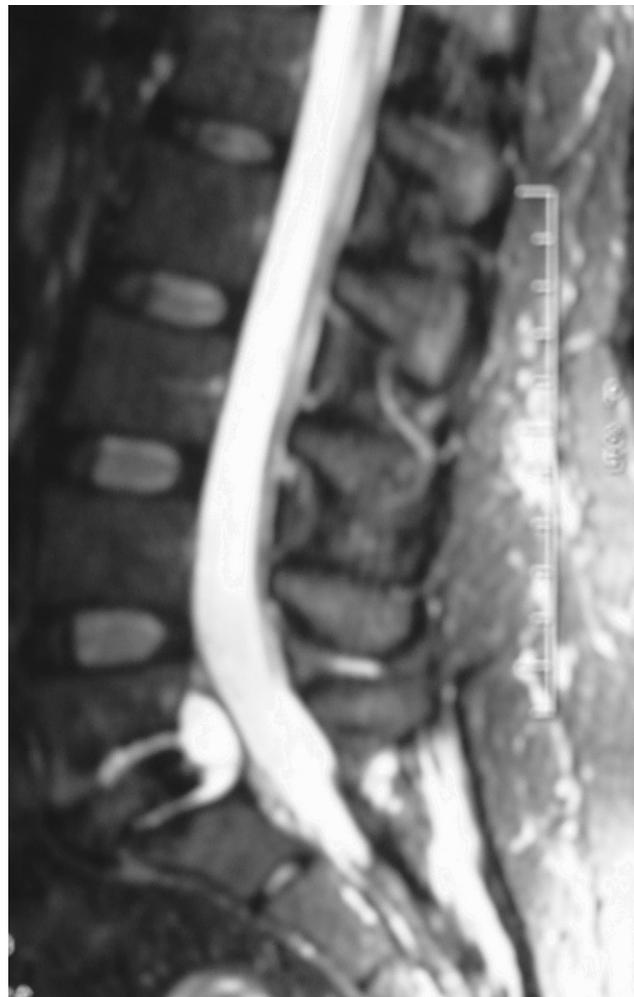


Fig. 5. Patient 5: Post-op sagittal magnetic resonance imaging scan 1.5 months postindex BMP surgery showing fluid formation in the area of BMP application in the L5–S1 interspace and extending into the canal. No bone fragments in the canal from the surgery at that point.

numbness (range 1.5–12 mo, average 6.15 mo) (Table 1). The average time to the scan that showed definitive ectopic bone was 8.35 months (range 6–12) and the time to presentation for consultation by the senior author averaged 10.8 months postindex BMP surgery (Table 1).

Revision surgical findings

Three of the five patients have had revision surgery by the senior author including resection of the ectopic bone in the canal and decompression of nerve roots. In all three cases, the neural structures were adherent to the surface of the ectopic bone and required careful microscopic dissection to free the dura and nerve root sheath. No dural tears were encountered, but areas of somewhat thin dura were seen after teasing the root sheath off the surface of the ectopic bone. The exterior façade of the ectopic bone was hard and well corticated in all three instances. Bone resection with a high-speed burr and Kerrison rongeurs was

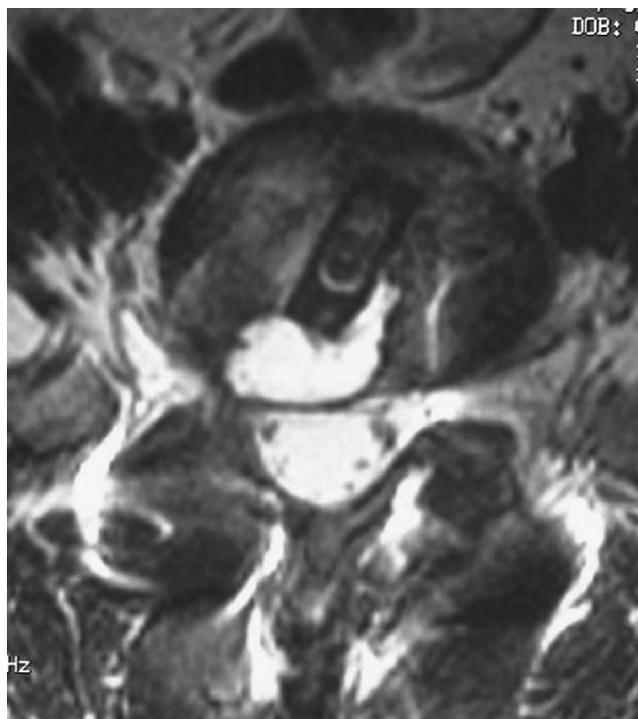


Fig. 6. Patient 5: Post-op axial magnetic resonance imaging scan illustrating the fluid collection in the spinal canal. No bone fragments in the canal. No growth on cultures on surgical drainage.

required. Because of the fragmentation, microscopic analysis yielded no good bone specimens. The bony prominences all had a shell of hard cortical bone with softer, more cancellous, or cartilaginous tissue lying a millimeter or two below. Removal of the outer cortical rim exposed a surface, which tended to ooze a small amount of blood.

All three patients had partial improvement in their corresponding radicular pain postoperatively, suggesting that at

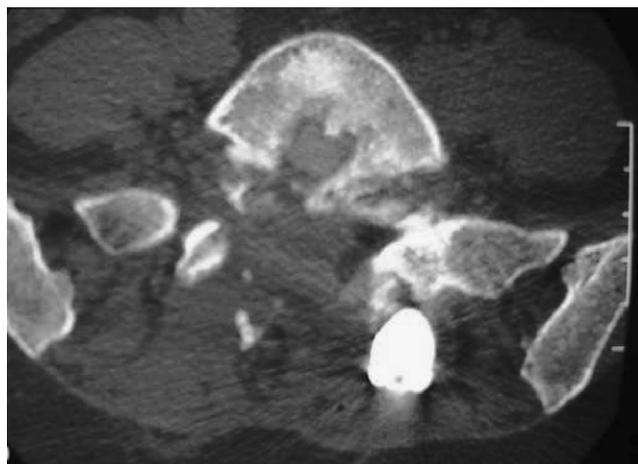


Fig. 7. Patient 5: Six months post-op axial computed tomography (CT) scan showing ectopic bone in the canal on the right in the entry zone of the foramen. Ectopic bone is not as mature on this CT taken 6 months post-op compared with Patient 1's 9-month post-op CT (Fig. 2).

least a portion of their root pain was associated with the extrinsic pressure or tethering of the root. Both the patients who have not had revision surgery are undergoing chronic pain management in the workers compensation system.

Discussion

Case reports inherently have limited utility and are considered Level IV evidence. As we were not the original primary surgeons, OR notes and imaging studies were the main data source for the index BMP surgery. This situation limited our ability to accurately ascertain details such as the number of BMP sponges used (specifically reported in two patients). Nevertheless, such case series have some relevance, particularly as an alerting mechanism in the situation of off-label, postmarketing product surveillance. Previous reports concerning BMP-2 off-label use in the cervical spine have signaled surgeons to be aware of several clinical problems such as neck swelling, sterile fluid collection, airway compromise, and dysphagia [14–16].

In respect to off-label use of BMP-2 in the lumbar spine, three of our cases illustrate that sterile fluid collections can occur on occasion during the first few weeks post-op (similar to the cervical spine) (Figs. 1, 5, and 6).

The early post-op imaging studies (2.5 and 1.5 mo post-index BMP surgery) in our two case illustrations showed no bone fragments in the canal from the decompression or end plate preparation. This considerably reduces the chance that ectopic bone formation was preexisting.

Haid et al. [17] have already pointed out a high incidence of ectopic bone in the spinal canal after the use of BMP-2 in a PLIF application (75% of the BMP-treated patients). However, in Haid et al.'s study there was no statistical correlation between increased leg pain and corresponding ectopic bone formation. It should be noted that the authors did not suggest that neural compromise from ectopic bone could never happen. Our report suggests that neural compression from ectopic bone can indeed occur on occasion (Figs. 2–4, and 7).

Three factors seem to have practical influence on the risk of ectopic bone formation in the lumbar spinal canal. These considerations are the dosage of BMP, the properties of the carrier, and any barrier (such as an intact posterior annulus in an interbody application) that would resist migration of BMP into the spinal canal.

In the cervical spine, the dosage of BMP was felt to be a significant factor in the off-label BMP complications [14–16]. It is interesting to note that of our five patients, the largest mass of ectopic bone occurred in the case where the OR note documented that five BMP sponges were used (Patient 1—Figs. 3–5). The Haid et al.'s study [17] (the original PLIF FDA IDE) used one BMP sponge (dose 4–8 mg) and attained 92% interbody fusion at 1 year. One sponge was also used in the TLIF paper by Villavicencio et al. [18] They reported 100% fusion at 12 months and

noted no ectopic bone in their 71 patients. In the literature review concerning the safety profile of BMPs by Poynton and Lane [19], the authors pointed out animal studies of the dose-response curve had demonstrated an increased quantity of new bone formation related to the dose of BMP up to a threshold. However, the exact dose giving a reliable fusion as opposed to increasing the likelihood of ectopic bone formation is less clear.

In terms of the carrier, it appears that the susceptibility of the carrier to compression and leaching of BMP along with the relative fixation of BMP to the carrier are the relevant issues [9,20–23]. Several carriers have been trialed with BMP-2 [9,20–23]. Preliminary studies in animals clearly indicate that BMP-2 used with a compression resistant and more tightly bound carrier (not a sponge) has superior clinical characteristics for use in the posterolateral and PLIF/TLIF applications [9,20–23]. These carriers are presently not approved by the FDA and thus are not available for general use.

The barrier of the intact posterior annulus appears to restrict the potential for leaching of BMP into the spinal canal in the FDA-approved ALIF application. No reports of ectopic bone in the canal were included in the FDA IDE of ALIF with BMP-2 and an LT cage or an additional similar study [24,25]. The primary off-label use of BMP-2 comprising the case reports in this article is the TLIF or PLIF application where the posterior annulus adjacent to the spinal canal is breached in the process of insertion of BMP and an interbody spacer. A TLIF or PLIF spacer should provide the same compression protections to the BMP and carrier that the LT cage provides in the approved anterior interbody technique. Thus, theoretically at least, when a mechanical spacer is used, the difference between the anterior versus posterior situations appears to be the lack of a barrier (primarily an intact annulus) to protect the spinal canal.

It is also noteworthy to compare and contrast the surgical technique relating to a potential barrier between Haid et al. [17] (75% ectopic bone in the canal) and Villavicencio et al. [18] (0% ectopic bone). Both authors performed end plate preparation and used a single BMP sponge. In the Haid et al.'s study, the BMP was placed within threaded Bagby and Kuslich cages before insertion and then the cages positioned in the interspace through bilateral PLIF annular defects. There was no specific effort made to recess the cages and no artificial barrier of any kind was placed posterior to the cages to try to isolate the BMP from the neural elements. Thus, there was a direct, open pathway from the location of the BMP within the cages (through the annular defects) into the spinal canal. In contrast, the surgical technique used in the Villavicencio et al.'s study made a deliberate attempt to isolate the BMP anteriorly and incorporate three barriers between the BMP and the annular defect. The BMP sponge was positioned "anteriorly against the anterior annulus fibrosis" in their technique. Next came a layer of "locally harvested autograft bone obtained during the TLIF approach (partial removal of the

facet joint)" (first barrier). One or two structural bone allografts were then placed (second barrier), followed by an additional layer of cancellous bone (autograft or allograft) as the third barrier.

The Villavicencio et al.'s technique used layers of different bone products. However, there have also been animal studies performed to try to substitute an artificial interposition barrier (fibrin glue) adjacent to the annular defect in an effort to prevent ectopic bone formation in the spinal canal [26]. We have been unable to find human clinical applications of this technique.

The Haid et al.'s [17] study also noted that almost all instances of ectopic bone formation occurred when the PLIF cage was recessed less than 3 mm below the posterior border of the vertebral body. This association did not hold in our series as in all five-case constructs were recessed more than 3 mm. However, this does bring up the question of other potential factors, which might predispose to leaching of the BMP into the canal as a facilitator of ectopic bone formation. Three of our cases were noted to have hematoma or sterile fluid collections in the area of the decompression (Figs. 4 and 5). Two were drained because of clinical symptoms and concern about infection but no bacteria were cultured. Additionally, all five cases in our series had wound irrigation performed after BMP insertion and three of the five had a drain placed. Both of these interventions were forbidden in the FDA IDE surgical technique of posterolateral fusion using BMP [13].

We speculate that the adherence of the neural structures to the ectopic bone surface at revision surgery may be a reaction to the inflammatory process involved in bone formation. This adherence has been a significant technical challenge in our three revision surgeries. Meticulous microscopic dissection of the nerve root sheath has been required. Post-op scarring and the effects of the original neurological abnormality are other potential factors to adherence/tethering of a nerve root sheath.

Conclusions

Physicians contemplating use of a technology or medication in an off-label application need to evaluate the benefit/risk ratio in relation to their patient's clinical situation.

Complications seen in off-label use need to be reported in the literature as off-label use is not as strictly regulated by the FDA compared with the oversight seen in an official FDA IDE trial for a specific clinical indication. There are mechanisms to report complications to the FDA as part of their postmarketing surveillance program Medwatch (www.fda.gov/medwatch). Physicians can query the database as part of the decision-making process when considering an off-label use of a drug or device. The FDA also periodically issues Medical and Safety Alerts to keep physicians, the public, and the media apprised of concerns, recalls, or withdrawals.

In terms of issues specific to the off-label use of BMP-2 in a PLIF or TLIF applications, there appear to be several considerations.

Some patients may develop a sterile fluid collection in the area of BMP application in the lumbar spine that is similar to the phenomenon seen in the cervical area [14–16].

Reports using a single BMP sponge in a PLIF/TLIF application suggest a high rate of fusion (92% [17] and 100% [18]). The use of multiple sponges (five in one of our patients) may not yield any higher fusion rate. Animal studies of the BMP dose/effect curve suggest a threshold effect [19]. Thus, “more is better” does not necessarily apply with BMP.

The present, commercially available form of BMP-2 (Infuse) has a collagen sponge carrier. Off-label use, in the TLIF and PLIF application, has a potential risk of ectopic bone formation in the spinal canal (75% incidence in the Haid et al.’s [17] study). The bone formation can sometimes be of sufficient size to worsen or be a possible cause of neural dysfunction (our five cases). Isolating the BMP anteriorly/contralaterally by the use of additional barriers (similar to the Villavicencio et al.’s study—no cases of ectopic bone reported) may be a technique to consider.

Irrigation of the spinal canal after BMP insertion and the use of subfascial suction drains were prohibited in the FDA IDE surgical technique used in the posterolateral BMP study [13]. These steps were taken as a precautionary measure to try to prevent ectopic bone formation. All five of our patients had wound irrigation post-BMP placement and two of the five had suction drains placed. The risk of using irrigation after BMP placement and a suction drain need to be better understood.

Surgeons contemplating the use of BMP-2 in a PLIF or TLIF need to be aware of the frequency of ectopic bone formation in the spinal canal, the potential for bringing about or adding to neurologic dysfunction and the surgical technique options, which may reduce the risk of these complications.

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