

# Minimally Effective Dose of Bone Morphogenetic Protein (BMP) in Minimally Invasive (MIS) Lumbar

## Interbody Fusions: 714 Patients in a Dose-Finding Statistical Modeling Cohort Study

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### Introduction

With increasing doses of BMP, the risk of adverse events increases. We seek to demonstrate the minimally effective BMP dose to achieve a fusion in MIS TLIF.

### Methods

Consecutive patients from 2009-2014, who underwent MIS lumbar interbody fusion, were reviewed. We excluded patients without radiographic (XR) follow up =3m postop. Dose of BMP/interspace was determined. Fusion was determined by XR evaluated by independent radiologists. A pilot study was performed to determine the baseline fusion rate in our population and sample size. We used multiple logistic regression with fusion at =3m and =6m as the dependent variable and BMP dose/interspace, single vs. multi-level, postop XR interval, smoking, gender, and age as covariates. The Exp $\beta$  coefficient represented change in odds of fusion for one-unit change in an independent variable. Minimally effective dose of BMP was determined by running separate logistic regressions for discrete BMP dose ranges for all fusion levels and a subgroup of multi-level fusions. We considered p-value = 0.0083 as significant to compensate for multiple comparisons.

**Table 1: Patient/Interspace Demographics**

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Total Patients	714	
Total Levels	1,168	
Dose (mg/level) Mean $\pm$ SD	1.25 $\pm$ 0.047	
Age at surgery (yrs) (Mean $\pm$ SD)	60.7 $\pm$ 8.9	
Interval of XR (months) (Mean $\pm$ SD)	12.4 ( $\pm$ 0.59)	
		Patients
		Interspaces
Single vs. Multi-level Fusions (n%)		
Single level	366 (51%)	367 (31%)
Multi-level	348 (49%)	801 (69%)
Gender (n%)		
Male	296 (42%)	498 (43%)
Female	418 (58%)	670 (57%)
Tobacco use (n%)		
Smoker	156 (22%)	256 (22%)
Non-smoker	558 (78%)	912 (78%)

### Results

We identified 1,168 interspaces among 714 unique patients. Average BMP dose was 1.25mg/level (Table 1). Dose/level, and multi-level fusion were significant predictors for fusion at =6m postop with an overall fusion rates of 95% (Table 2). Odds of fusion increased by 4.7 when BMP dose was increased from range 1 (0.16-1mg/lvl) to range 2 (1.01-2mg/lvl), but did not increase when BMP dose increased from range 2 to range 3 (>2mg/lvl) (Table 3). The odds of fusion in multi-level fusions increased by 4.0 when BMP dose increased from range 1-2, but fusion odds did not increase when increased from range 2-3 (Table 4).

**Table 2: Overall Fusion Rates/level**

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	N	Fusion Rate (n%)	95% CI	
Overall at $\geq$ 3 months postop	1,168	95.0%	93.63%	96.00%
Overall at $\geq$ 6 months postop	874	95.00%	93.71%	96.14%
Predictors for Fusion/level $\geq$ 3 months Postop				
	P value	Odds Ratio	95% CI OR	
Dose of BMP/lvl	0.004	2.042	1.248	3.341
Single vs. Multilevel Fusion	0.002	2.449	1.381	4.345
Predictors for Fusion/level $\geq$ 6 months Postop				
	P value	Odds Ratio	95% CI OR	
Dose of BMP/lvl	0.000	4.925	2.077	11.676
Single vs. Multilevel Fusion	0.001	4.141	2.004	8.556

\* P <0.008, 95% CI OR >1

**Table 3: Fusion Rates/level per BMP dose range/level**

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	N	Fusion Rate (n%)	95% CI	
Dose (mg/level): range at $\geq$ 6 months postop	874			
0.16-1.0	207	91	86.00%	94.40%
1.01-2.0	487	95	92.50%	96.70%
>2.0	180	98	94.40%	99.40%
Predictors for Fusion/level Between Dose Ranges at $\geq$ 6 months Postop				
	P value	Odds Ratio	95% CI OR	
BMP Dose Range 1 vs. Range 2	0.001	4.761	1.827	12.406
BMP dose Range 2 vs. Range 3	0.021	4.258	1.241	14.611

\* P <0.008, 95% CI OR >1

**Table 4: Multi-level Fusions: Fusion Rates/level**

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	N	Fusion Rate (n%)	95% CI	
Overall	801	96.0%	94.40%	97.17%
Dose (mg/level): Range at $\geq$ 3 months postop for multi-level fusions				
0.16-1.0	272	92	88.43%	94.95%
1.01-2.0	416	98	96.50%	99.26%
>2.0	113	96	94.40%	98.91%
Multi-level Fusion: Predictors for Fusion/level Between Dose Ranges at $\geq$ 3 months Postop				
	P value	Odds Ratio	95% CI OR	
BMP Dose Range 1 vs. Range 2	0.001	3.966	1.777	8.851
BMP dose Range 2 vs. Range 3	0.332	0.544	0.159	1.86

\* P <0.01, 95% CI OR >1

### Conclusions

We found using a BMP dose of 1.01-2mg/level had a fusion rate of 95%. Increasing the dose above 2mg/level does not correlate with an increase in odds of fusion.

### Learning Objectives

By the conclusion of this session, participants should be able to:

- 1) Describe current recommendation with regards to BMP use in transforaminal interbody fusions.
- 2) Identify a minimally effective BMP dose/level and associated fusion rate.