

Failure Rates based on Alveolar Cleft Size: An Analysis of the Critical Size Defect for rhBMP-2/DBM and ICBG in Alveolar Bone Grafting

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Background

- Cleft lip $\pm$ palate (CLP) is one of the most common congenital anomalies worldwide
- Iliac crest bone graft (**ICBG**) is the standard of care for **alveolar bone grafting**
- Recombinant human bone morphogenetic protein with demineralized bone matrix (**rhBMP-2/DBM**) has been proposed as an alternative
 - Avoids donor site morbidity** associated with harvesting bone
- A “**critical-sized**” defect is one that is *more likely to fail treatment* beyond an identified point
 - Has **yet to be determined** for ABG

Objective

- This study aims to **determine the critical-sized defects** by analyzing graft failure rates for ICBG and rhBMP-2/DBM to **guide graft selection** in ABG management

Methods

- Retrospective review of patients with **unilateral CLP** who underwent ABG from 2009-2022
 - Inclusion Criteria:* Pre- and postoperative cone beam CT
- Graft success** defined as bony bridge formation based on *postoperative imaging*
- Cleft volume** was calculated using a *trapezoidal pyramid model*
- Statistical analyses:** Fisher-exact test, Receiver operating characteristic (ROC) analysis, and logistic regressions using conditional margins

Figure 1. ROC curves for predicting graft failure based on preoperative alveolar cleft volume for each bone graft type

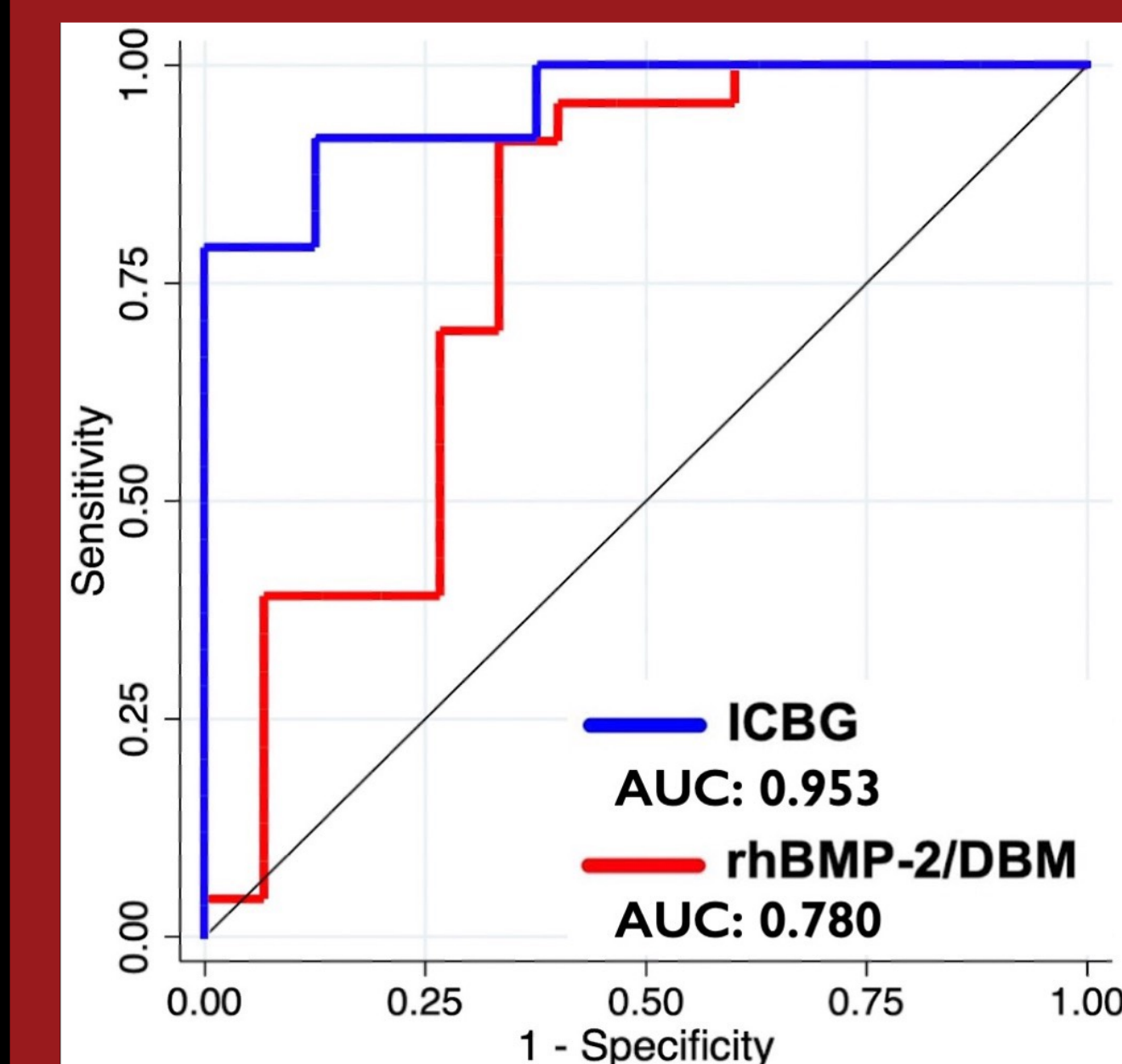


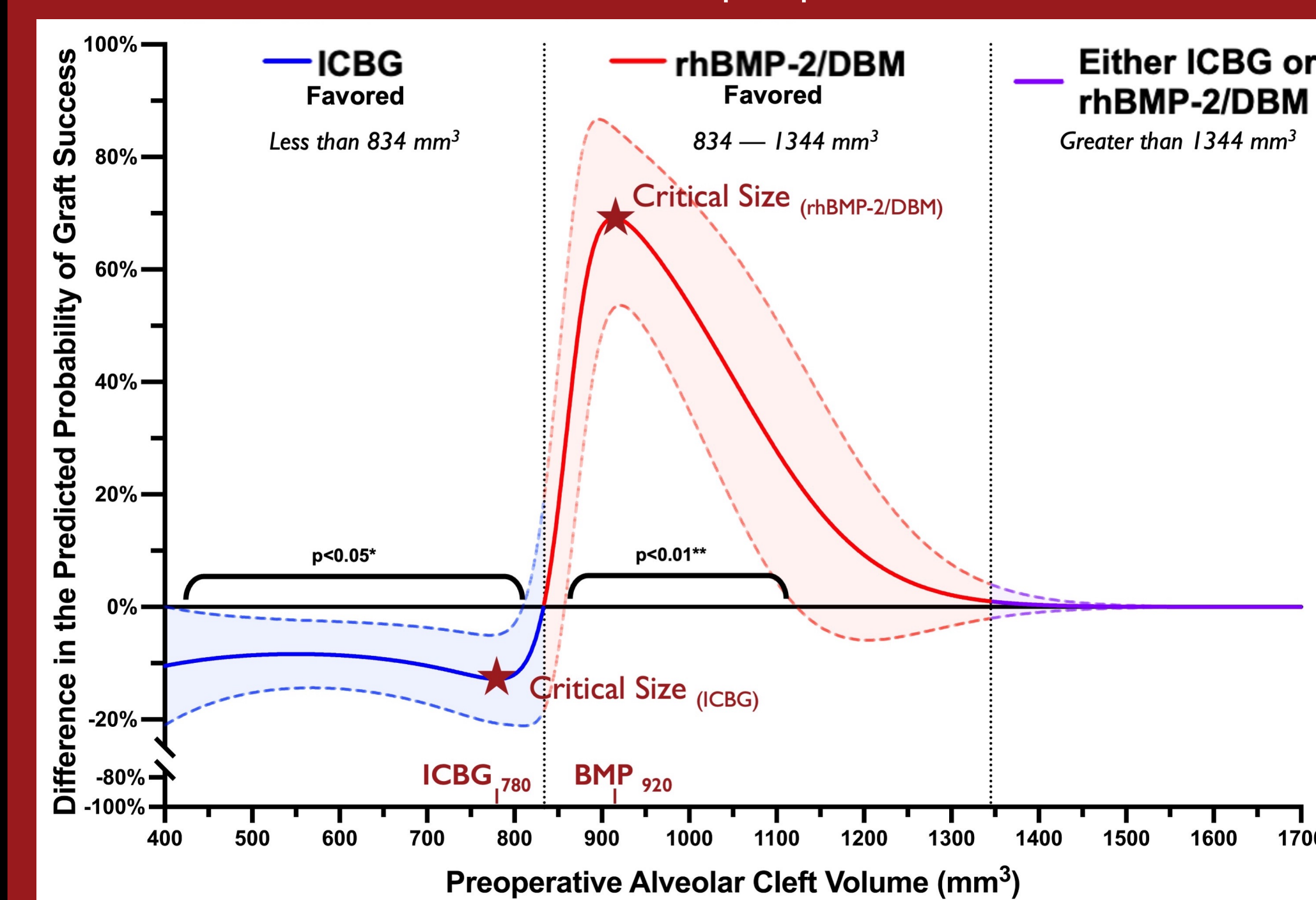
Table 1. Optimal cutoff values (i.e. critical-sized defect) for each graft type

	Sensitivity	Specificity	Optimal Cutoff
ICBG	88%	92%	780 mm ³
rhBMP-2/DBM	67%	91%	920 mm ³

Table 2. Comparison of CBCT-based graft failure rates below versus above each bone graft's critical size

ICBG (n=30)	Below 780 mm ³	Above 780 mm ³	p-value
Graft Failure	0/19 (0.0%)	7/11 (63.6%)	<0.001*
rhBMP-2/DBM (n=38)	Below 920 mm ³	Above 920 mm ³	p-value
Graft Failure	5/26 (19.2%)	10/12 (83.3%)	<0.001*

Figure 2. Adjusted difference in the predicted probability of graft success for rhBMP-2/DBM minus that of ICBG based preoperative alveolar cleft volume



*Regression analysis was used to determine the predicted probability of graft success based on cleft volume at 1-cubic millimeter increments, while controlling for age and surgeon by holding the covariates at their mean value.

Legend

- Solid Line:** Mean predicted probability
- Dotted Lines:** Standard error margins
- x-axis:** Alveolar cleft volume
- y-axis:** Difference in the predicted probability of graft success of rhBMP-2/DBM minus that of ICBG
- Positive values:** Favor rhBMP-2/DBM (Red Line)
- Negative values:** Favor ICBG (Blue Line)
- Approx. Zero:** Equivalent (Purple Line)

Results

- 68 patients included: **30 ICBG** and **38 rhBMP-2/DBM**
- Overall **clinical graft success rate: 94.3%**
 - Only 4 (5.7%) cases of revision surgeries
- Bony bridge formation based on CBCT: 67.7%
 - ICBG: 76.7% vs. rhBMP-2/DBM: 60.5%; p=0.199
- No significant difference in age, cleft volume, or graft success between cohorts
- Cleft volume **accurately predicted graft success:** AUC 0.953 (ICBG) and AUC 0.780 (rhBMP-2/DBM)
- Optimal cutoff values (i.e. critical-sized defect) were determined for each graft type
 - ICBG: **780 mm³**; rhBMP-2/DBM: **920 mm³**
- Significantly **higher graft failure rates beyond the critical size** compared to below for both ICBG (**p<0.001**) and rhBMP-2/DBM (**p<0.001**)
- Adjusted difference in the **predicted probability graft success of rhBMP-2/DBM minus ICBG** based on cleft volume were calculated:
 - < 834 mm³ $\rightarrow$ negative values $\rightarrow$ **Favor ICBG**
 - 834 - 1344 mm³ $\rightarrow$ positive values $\rightarrow$ **Favor rhBMP-2/DBM**
 - > 1344 mm³ $\rightarrow$ approximately zero $\rightarrow$ **Equivalent**

Conclusion

- Direct correlation** between cleft volume and graft failure $\rightarrow$ *regardless of graft type*
- Higher probability of graft failure **beyond the predicted critical size** for each graft
- Distinct regions** in cleft volume were identified which may guide alveolar bone graft selection
- Future Directions:** Assess whether a **hybrid of materials**, a **higher dose of rhBMP-2**, or the use of **placental stem cells** improves treatment efficacy