

INFUSE[®] Bone Graft

Oral Maxillofacial Bone Grafting Procedures

Dental Products Advisory
Panel Committee

Ed Chin, DPh
Group Director, Regulatory Affairs
Medtronic Spinal and Biologics

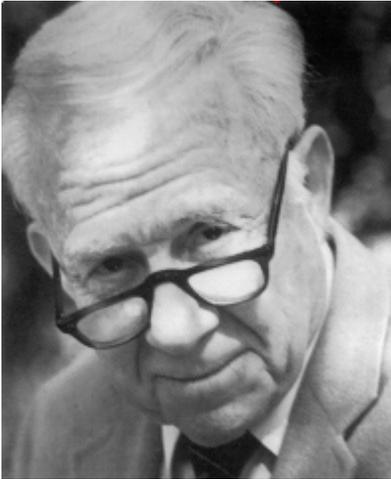
INFUSE[®] Bone Graft FDA Panel Presentations

Agenda	Speaker
Welcome & Introduction	Ed Chin, DPh
Clinical Need	Robert Marx, DDS
Clinical Evidence – Sinus Augmentation	Robert Marx, DDS
Clinical Evidence – Extraction Socket and Overall Safety	David Cochran, DDS, PhD
Conclusions	Ed Chin, DPh

Additional Resources

- Leon Assael, DMD
- Philip Boyne, DMD, MS, DSc
- James T. Mellonig, DDS, MS
- Myron Nevins, DDS
- Daniel B. Spagnoli, DDS, MS, PhD
- R. Gilbert Triplett, DDS, PhD
- Pirkka Nummikoski, DDS
- Steve Cook, PhD
- Hal Mathews, MD
- Mildred Christian, PhD
- Scott Kern, MD
- Douglas Hawkins, PhD
- Barbara Boyan, PhD
- Jeffrey Toth, PhD
- Medtronic Staff
- Wyeth Staff
- Alquest Staff

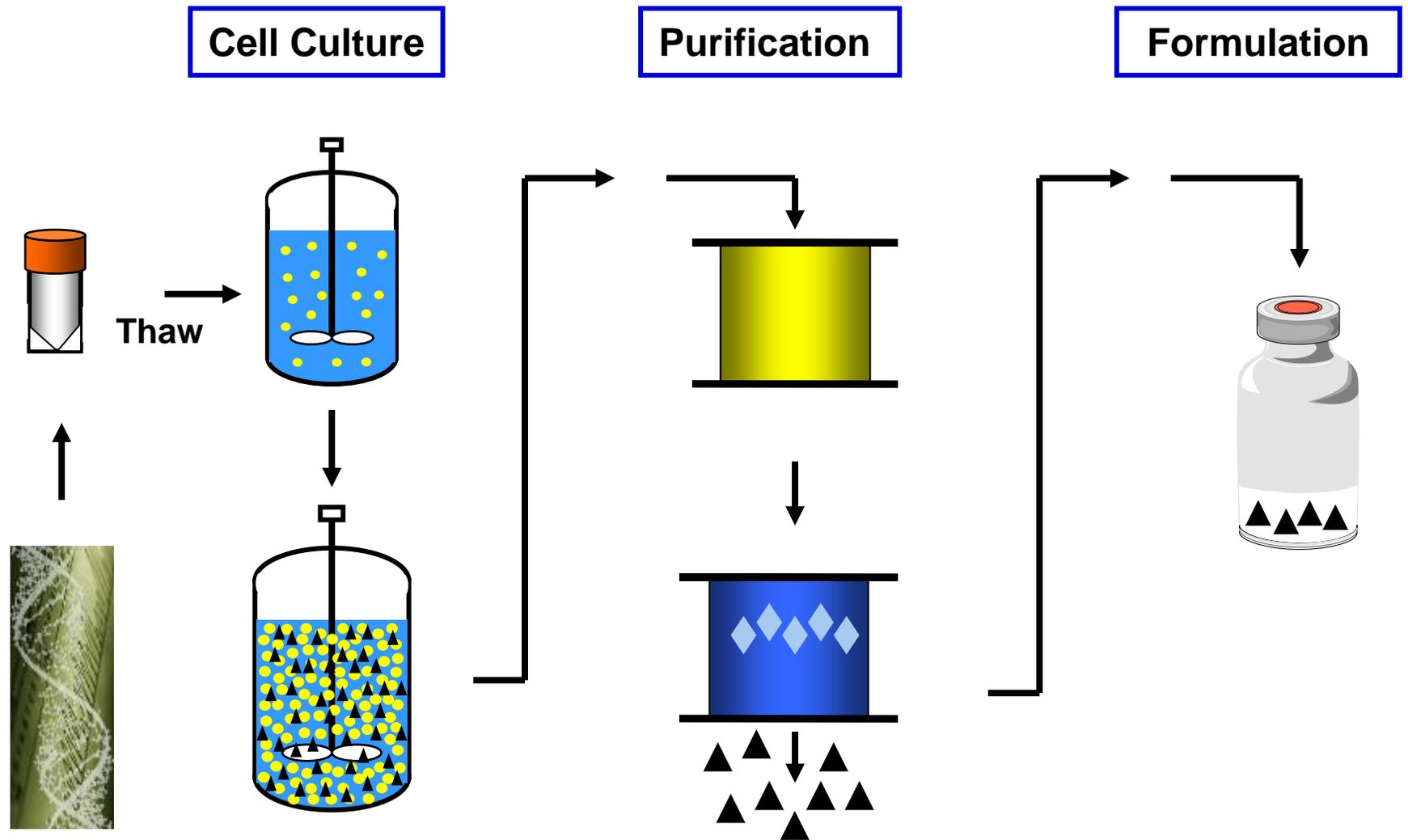
BMP History



- **1965 Urist discovers demineralized bone induces new bone**
- **1971 Urist coins the term BMP**
- **1977 BMP extracted from bone is inductive**
- **1988 First recombinant human BMP produced (Wozney)**

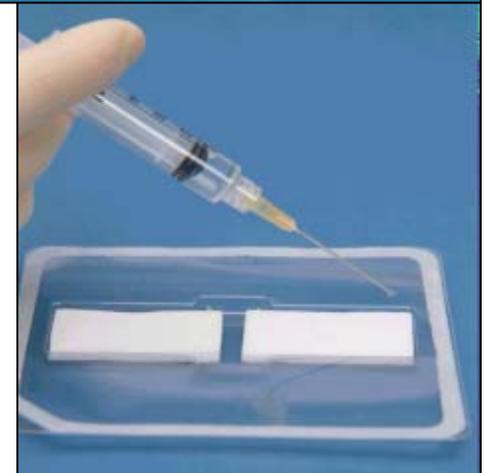
"BMP is destined to bring osteogenesis under the control of surgeons..."
Urist MR, J NIH Res, 1997

Recombinant rhBMP-2 Manufacture



INFUSE[®] Bone Graft (rhBMP-2/ACS)

- recombinant human Bone Morphogenetic Protein–2 (rhBMP-2)
 - 4.2 or 12 mg vials
 - 1.5 mg/ml concentration
- Absorbable Collagen Sponge (ACS)
 - Carrier for rhBMP-2
 - Type I bovine collagen sponge
 - 1"X 2" or 3"X 4" size
 - Over 20 years of clinical use as Helistat[®]
- Same product used in OMF pivotal study

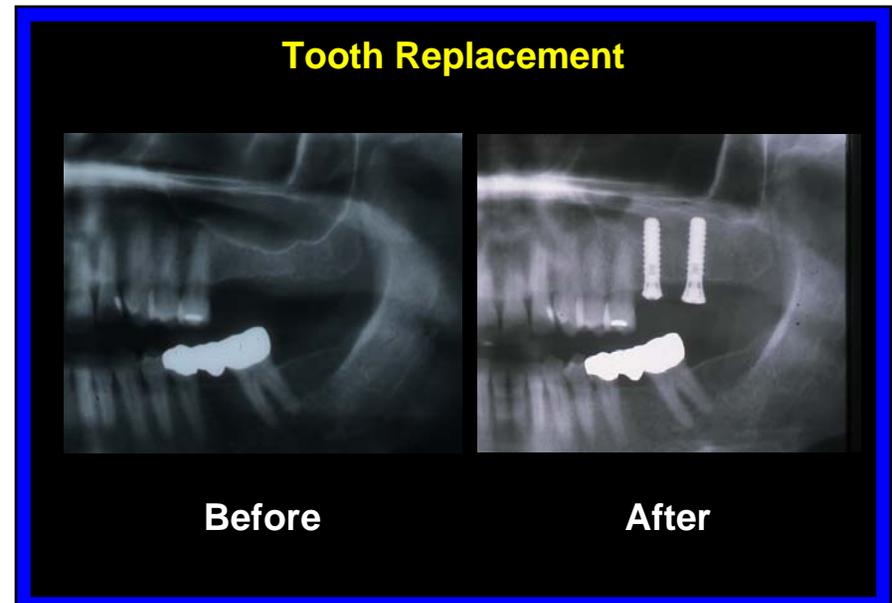
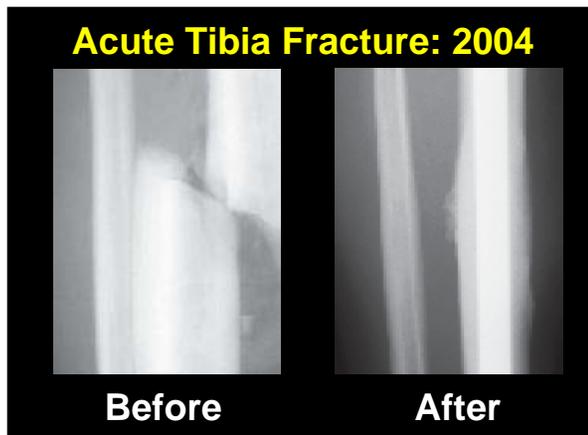
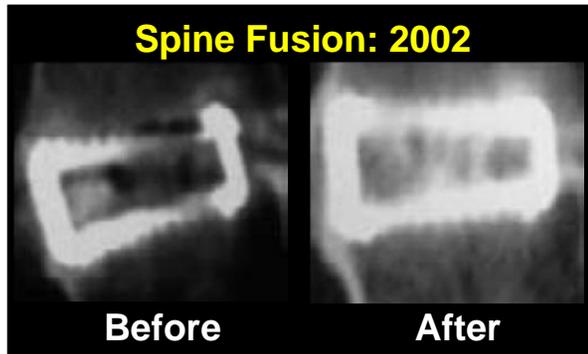
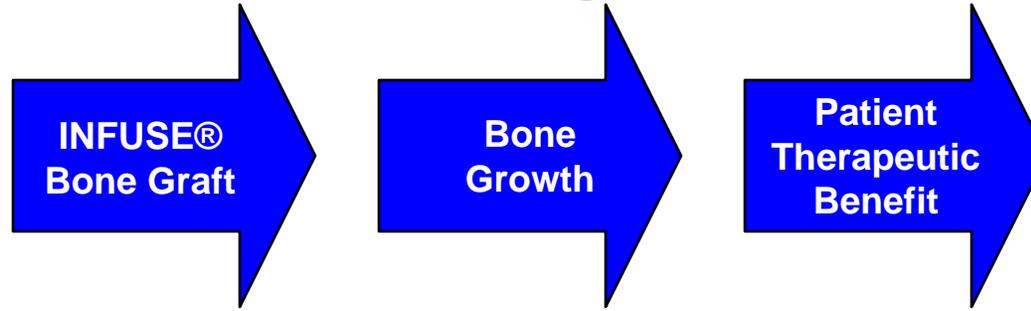


INFUSE[®] Bone Graft (rhBMP-2/ACS)

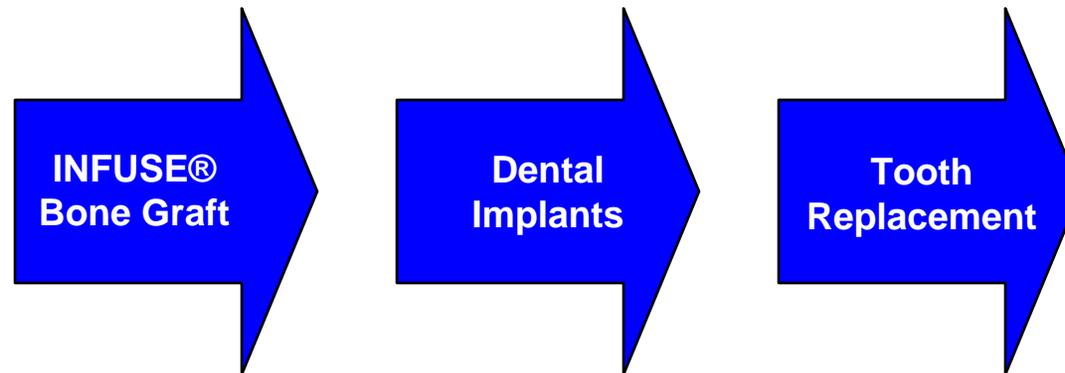
- **Two PMAs proved safety and efficacy:**
 - **2002: Single level spinal fusion procedures**
 - **2004: Open tibia fractures**
 - **437 patients received rhBMP-2/ACS in IDE clinical trials which supported these PMAs**
- **In addition, over 1,200 patients received INFUSE[®] Bone Graft or rhBMP-2 with other carriers in clinical studies**



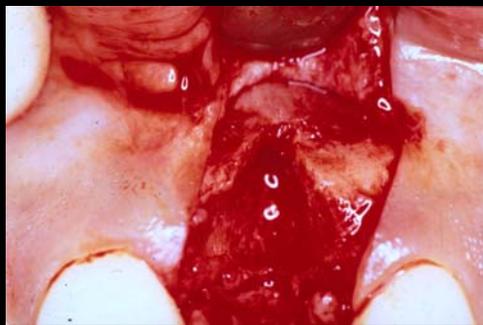
Overall Program Aim



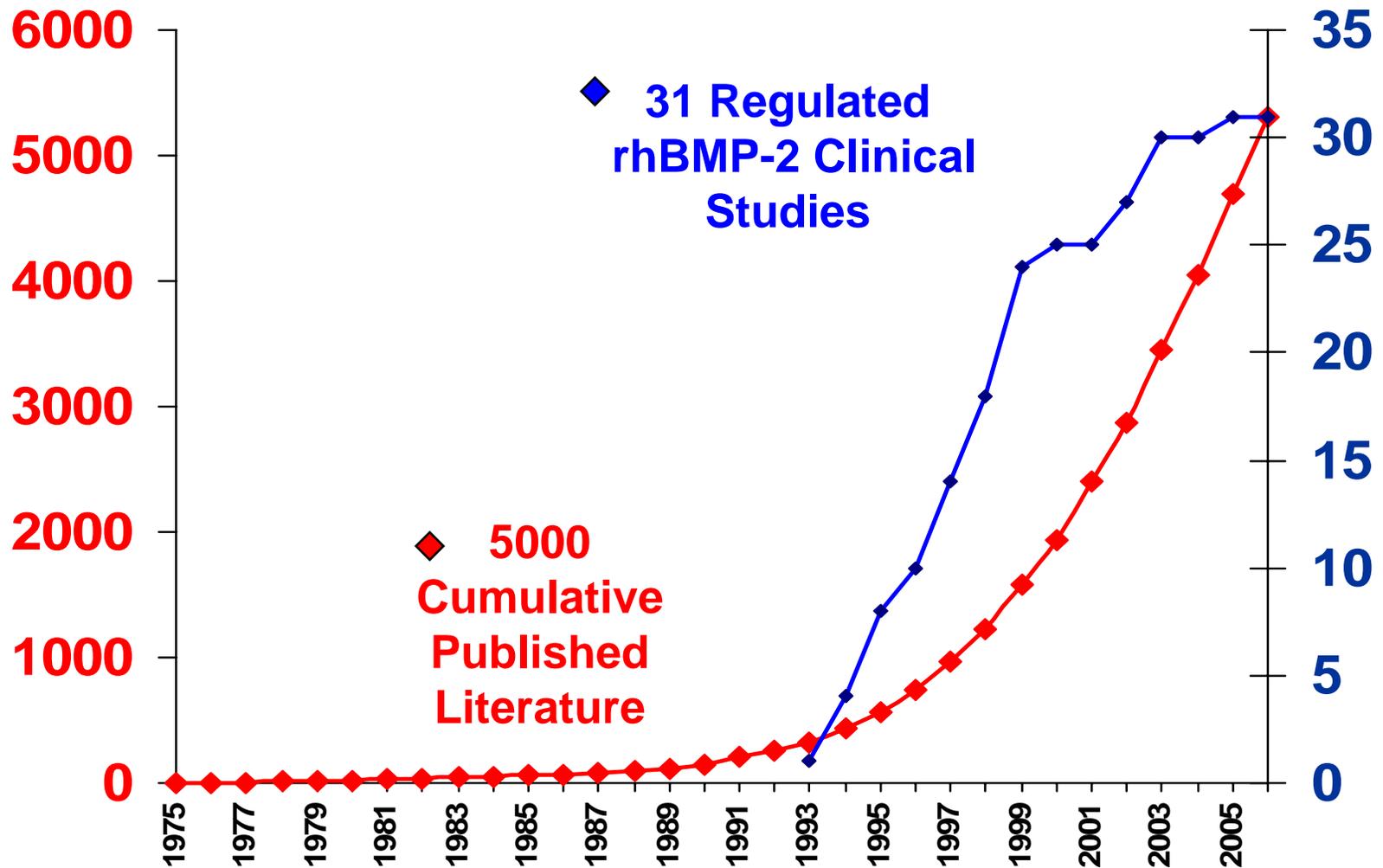
Clinical Oral Indications



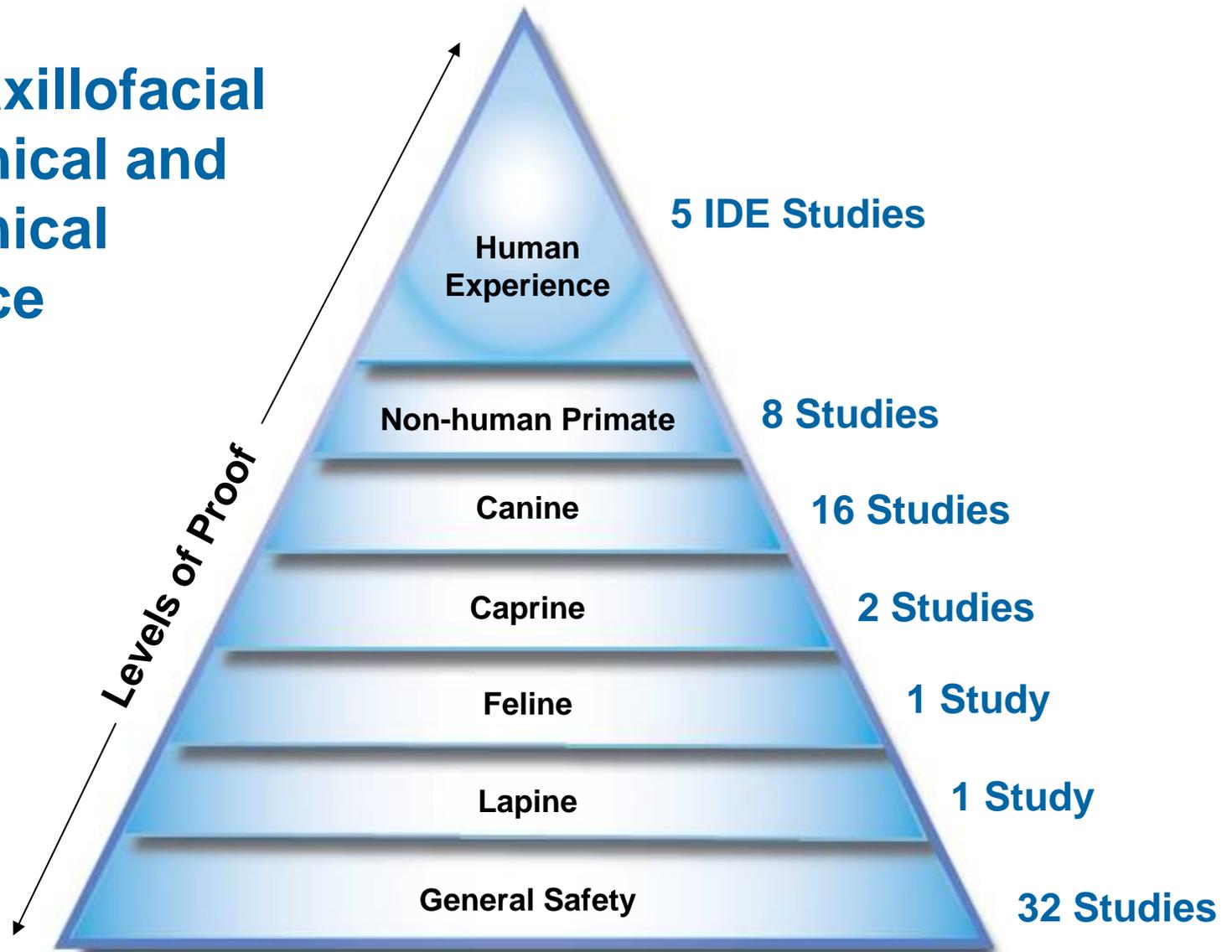
Models Examined

Sinus Augmentation IDE	Extraction Socket IDE
 <p data-bbox="877 1094 1035 1211">3 Studies</p>	 <p data-bbox="1619 1094 1776 1211">2 Studies</p>

BMP Scientific Research



Oral Maxillofacial IDE Clinical and Pre-Clinical Evidence



Proposed Indication For Use Statement

"INFUSE[®] Bone Graft is indicated as an alternative to autogenous bone graft for sinus augmentations and localized alveolar ridge augmentations for defects associated with extraction sockets."

INFUSE[®] Bone Graft Program Objectives

- **Regenerates bone in these oral indications**
- **Supports dental implant placement**
- **Supports long term functional loading**

De Novo Bone Induction by Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) in Maxillary Sinus Floor Augmentation

Philip J. Boyne, DMD, MS, DSc, Leslie C. Lilly, BSN, RN,†
Robert E. Marx, DDS,‡ Peter K. Moy, DMD,§
Myron Nevins, DDS,|| Daniel B. Spagnoli, PhD, DDS,¶
and R. Gilbert Triplett, DDS, PhD#*

Purpose: This phase II study was designed to evaluate 2 concentrations of recombinant human bone morphogenetic protein-2 (rhBMP-2) for safety and efficacy in inducing adequate bone for endosseous dental implant in patients requiring staged maxillary sinus floor augmentation.

The AAOMS Journal Editorial Board 2005 Daniel M. Laskin Award

11.3 mm, 9.5 mm, and 10.2 mm, respectively, in the bone graft, 0.75 mg/mL, and 1.50 mg/mL rhBMP-2/ACS treatment groups. Mean increases in alveolar ridge width (buccal to lingual) at the crest of the ridge were statistically different among the treatment groups; 4.7 mm, 2.0 mm, and 2.0 mm, respectively, in the bone graft, 0.75 mg/mL, and 1.50 mg/mL treatment groups ($P \leq .01$ vs 0.75 mg/mL; $P < .01$ vs 1.50 mg/mL). At 4 months postoperative new bone density was statistically different among the treatment groups; 350 mg/cc, 84 mg/cc, and 134 mg/cc for the bone graft, 0.75 mg/mL, and 1.50 mg/mL rhBMP-2/ACS treatment groups, respectively ($P = .003$ vs 0.75 mg/mL, $P = .0137$ vs 1.50 mg/mL, $P = .0188$; 1.50 mg/mL vs 0.75 mg/mL). Core bone biopsies obtained at the time of dental implant placement confirmed normal bone formation. The proportion of patients who received dental implants that were functionally loaded and remained functional

Randomized Study Evaluating Recombinant Human Bone Morphogenetic Protein-2 for Extraction Socket Augmentation

Joseph P. Fiorellini,* T. Howard Howell,* David Cochran,[†] Jay Malmquist,[‡] Leslie C. Lilly,[§] Daniel Spagnoli,^{||} Joseph Toljanic,^{||} Archie Jones,[†] and Myron Nevins*[#]

Background: Conventional dentoalveolar osseous reconstruction often involves the use of grafting materials with or without barrier membranes. The purpose of this study was to evaluate the efficacy of bone induction for the placement of dental implants by two concentrations of recombinant human bone morphogenetic protein-2 (rhBMP-2) delivered on a bioabsorbable collagen sponge

**The American Academy of Periodontology
Foundation 2005 Tarrson Research Award in Oral
Plastic Surgery**

quacy of the alveolar bone volume to support an endosseous dental implant, and the need for a secondary augmentation.

Results: Assessment of the alveolar bone indicated that patients treated with 1.50 mg/ml rhBMP-2/ACS had significantly greater bone augmentation compared to controls ($P \leq 0.05$). The adequacy of bone for the placement of a dental implant was approximately

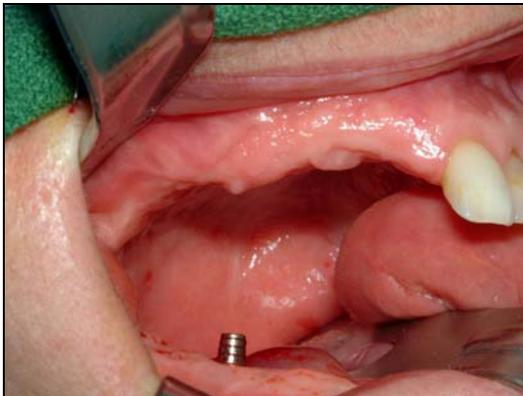
lizing various materials has been considered standard to obtain adequate bone volume.¹ During the past several years, the application of recombinant technologies has included biomimetic devices that stimulate the replacement of anatomic structures.²⁻⁶ These promote the in vitro

Robert E. Marx, DDS

**Professor of Surgery
Chief, Oral and Maxillofacial Surgery
University of Miami
Miller School of Medicine**

Clinical Need for Maxillofacial Bone Grafting

- **Regenerate bone lost due to disease, trauma or developmental defects:**
 - Provide bone support to replace missing teeth
 - Restore structure and function
 - Improve patient's appearance (esthetics and self image)





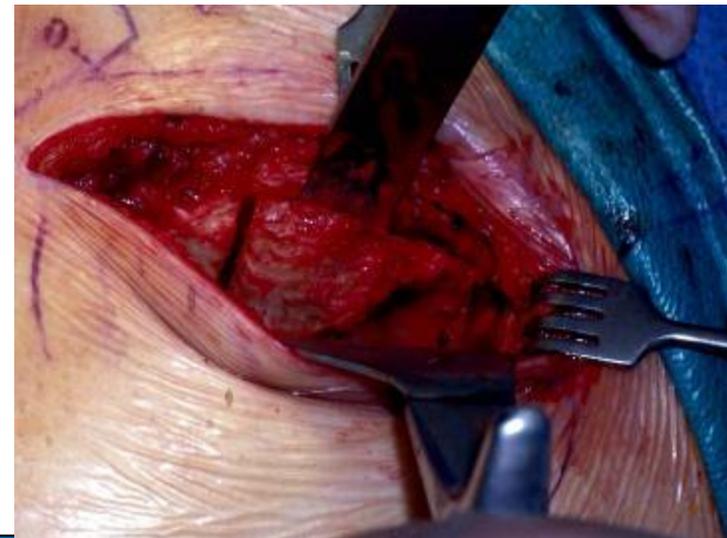
Maxilla

Mandible



Current Standard - Autogenous Bone Graft

- **Advantages**
 - Patient's own bone
 - Proven effectiveness
- **Disadvantages**
 - Donor site morbidity
 - Extended surgical and anesthesia time
 - Limited availability



Bone Graft Harvest Morbidity

- Hematoma
- Edema
- Erythema
- Exudate
- Infection
- Wound Dehiscence
- Blood loss
- Sensitive and painful scar

COMPARISON OF ANTERIOR AND POSTERIOR ILIAC CREST BONE GRAFTS IN TERMS OF HARVEST-SITE MORBIDITY AND FUNCTIONAL OUTCOMES

BY ELKE AHLMANN, MD, MICHAEL PATZAKIS, MD,
NIKOLAOS ROIDIS, MD, MSc, LANE SHEPHERD, MD, AND PAUL HOLTOM, MD
*Investigation performed at the Department of Orthopaedics, Keck School of Medicine,
University of Southern California, USC University Hospital, Los Angeles, California*

Background: Previous studies have demonstrated high complication rates after harvest of iliac crest bone grafts. This study was undertaken to compare the morbidity related to the harvest of anterior iliac crest bone graft with that related to the harvest of posterior iliac crest bone graft and to determine the functional outcomes of both procedures.

Methods: The medical records of eighty-eight consecutive patients who underwent bone-grafting procedures for the treatment of chronic osteomyelitis were reviewed. Demographic characteristics, the location of the harvest, the estimated blood loss, and postoperative complications were recorded. A questionnaire pertaining to postoperative and residual pain, sensory deficit, cosmetic appearance, and overall satisfaction with the bone-graft harvest was administered to the patients.

Results: Sixty-six anterior and forty-two posterior bone-graft harvest sites were reviewed. A major complication was associated with 2% (one) of the forty-two posterior sites. The rates of minor complications in the series as a whole, there were ten minor complications (9%) and all complications ($p = 0.006$) and all complications ($p = 0.006$) were significantly higher after anterior harvest procedures than they were after the posterior procedures. The postoperative pain at the donor

Blood Loss = 232 cc

Hematoma = 3%

Sensory loss = 8% (5% permanent)

Chronic pain = 2%



Oral Maxillofacial Human Clinical Trial Objectives

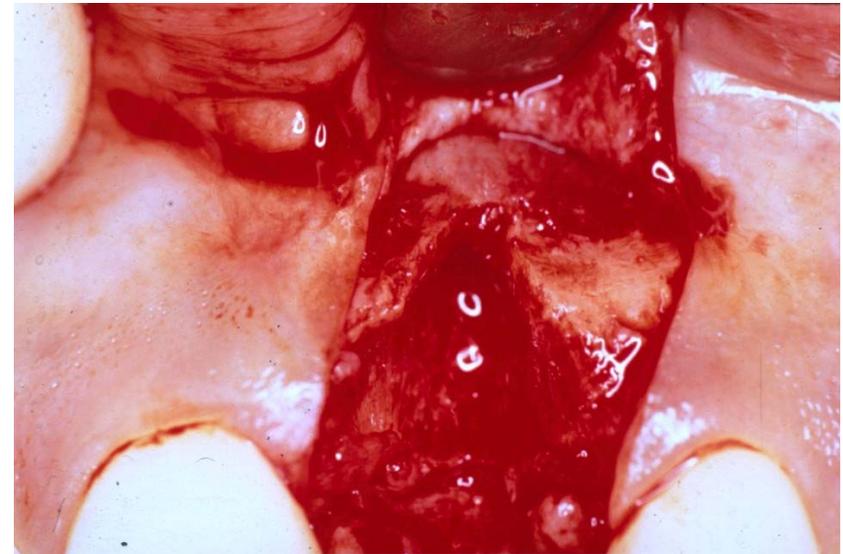
- **Demonstrate that rhBMP-2/ACS**
 - regenerates or grows normal physiologic bone
 - provides bone for dental restorations or placement of dental implants
 - produces stable bone under functional loading
- **To demonstrate safety in oral maxillofacial indications**

Clinical Models

Sinus Augmentation



Extraction Socket



Sinus Augmentation Studies Methods and Definition

- **Prospective, multi-center (21), controlled human clinical trials with high level of evidence**
 - **Pilot:** 0.43 mg/ml
 - **Dosing (randomized):** 0.75 and 1.50 mg/ml
 - **Pivotal (randomized):** 1.5 mg/ml
- **Pooled Data - Dosing and Pivotal Studies (1.5 mg/ml)**
- **Efficacy Endpoint**
 - **Implant-borne restoration after 6 months of functional loading**
 - **Target Success Rate - Greater than 73%**
- **Safety Endpoints**

Sinus Augmentation Studies Primary Objectives

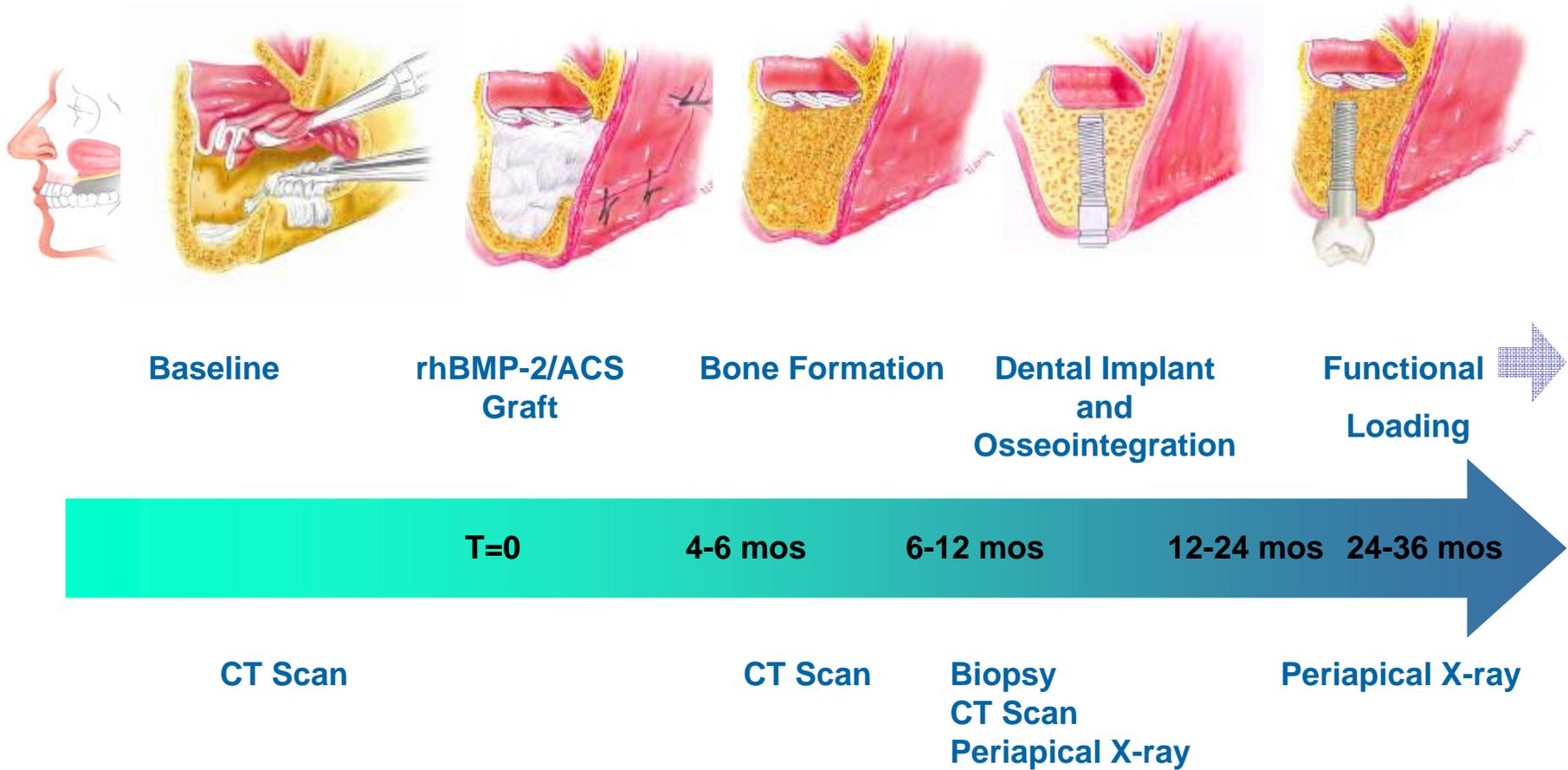
- **Effectiveness**
 - **Induce bone to successfully support implant-borne restoration after 6 months of functional loading**

- **Safety**
 - **Evaluate the safety of rhBMP-2/ACS and autogenous bone graft in two-stage maxillary sinus floor augmentation procedures**

Sinus Augmentation Studies Secondary Objectives

- **Evaluate new bone radiographically**
- **Evaluate histology of the new bone**
- **Functional loading: INFUSE® Bone Graft compared to autogenous bone graft**

Sinus Augmentation Studies

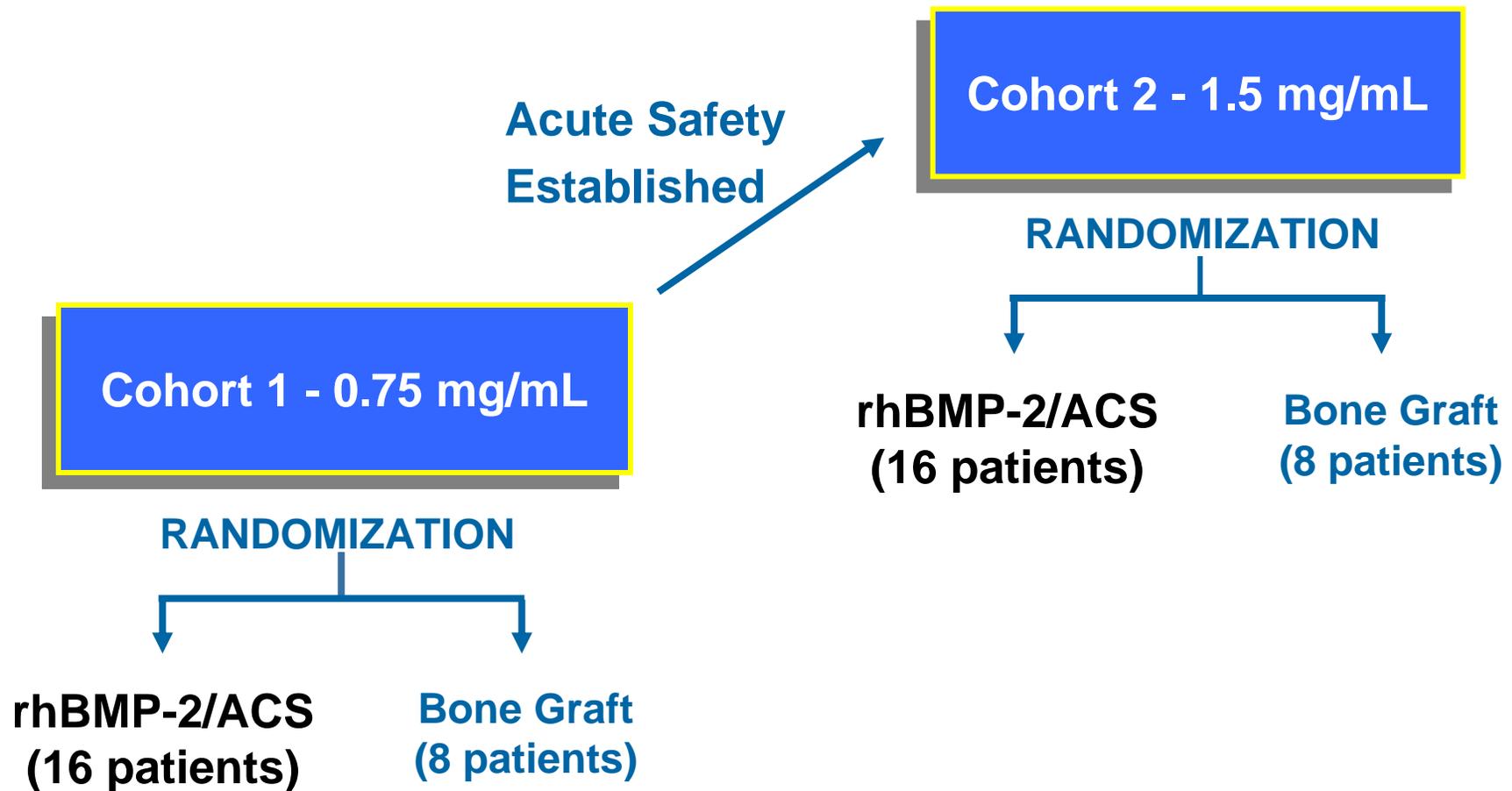


Safety Evaluation Throughout the Study

Study Design Schematic

Sinus Augmentation Dosing Study

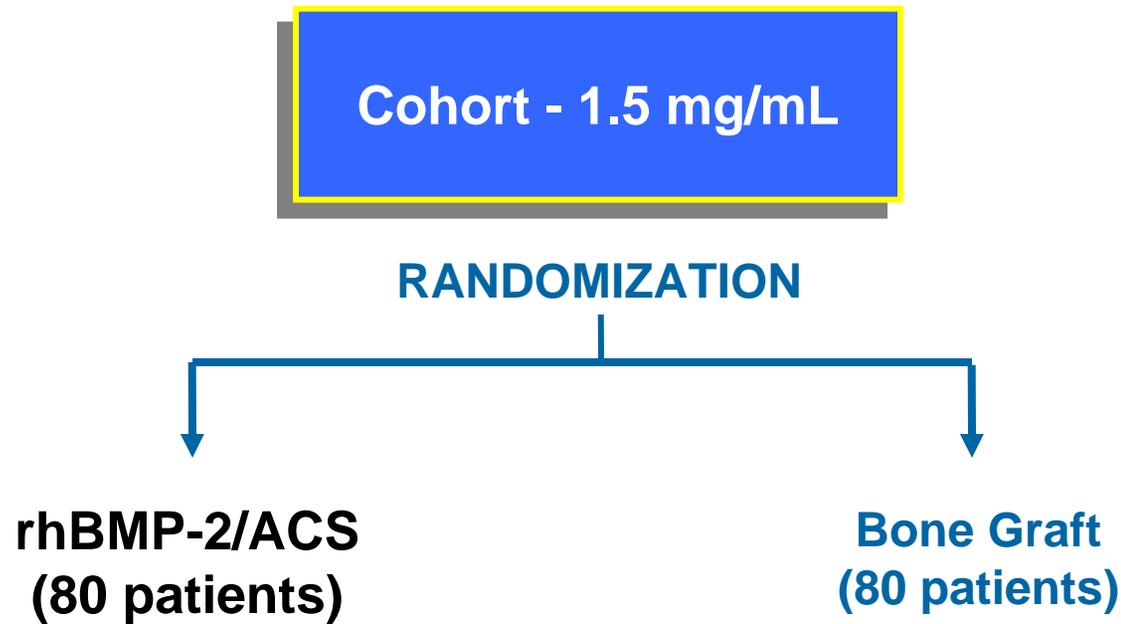
N=48



Study Design Schematic

Sinus Augmentation Pivotal Study

N=160

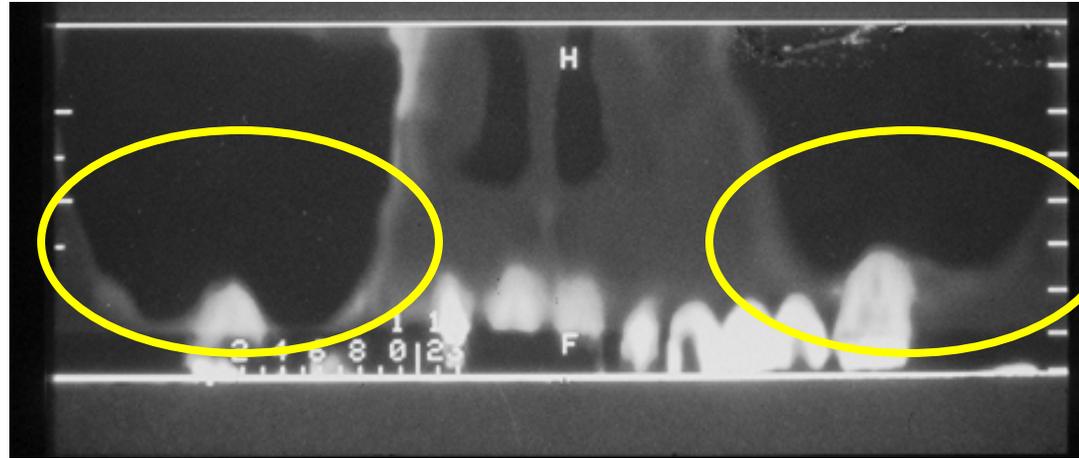


Prospective, Controlled Sinus Augmentation IDE Studies (N=220)

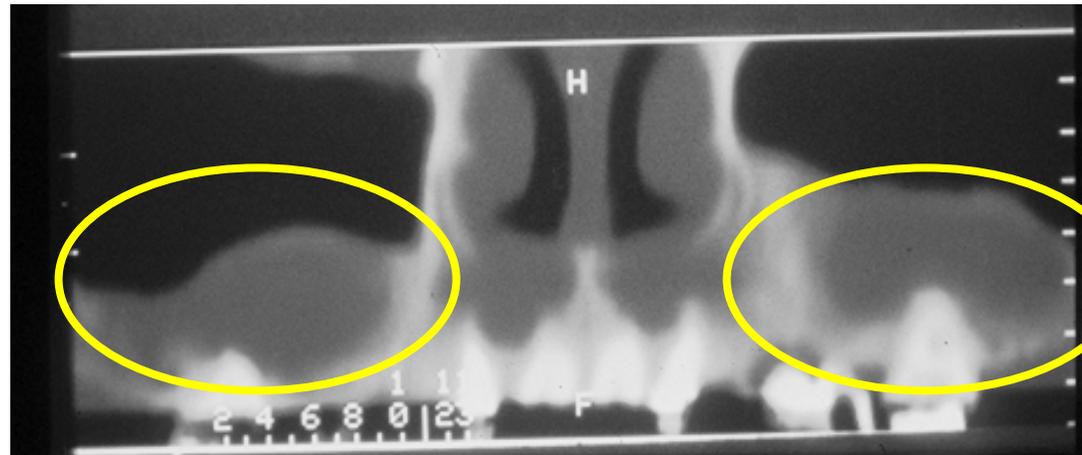
Sinus Augmentation	<u>N</u>	
– Pivotal Study		
• rhBMP-2/ACS (1.5 mg/ml)	82	} rhBMP-2/ACS Effectiveness N= 99
• Bone Graft	78	
– Dosing Study		
• rhBMP-2/ACS (1.5 mg/ml)	17	
• Bone Graft	13	
• rhBMP-2/ACS (0.75 mg/ml)	18	
– Pilot Study		
• rhBMP-2/ACS (0.43 mg/ml)	12	

CT Scan of *de novo* Bone Induced by rhBMP-2/ACS

Pre-op



16-weeks
Post rhBMP-2/ACS
Placement

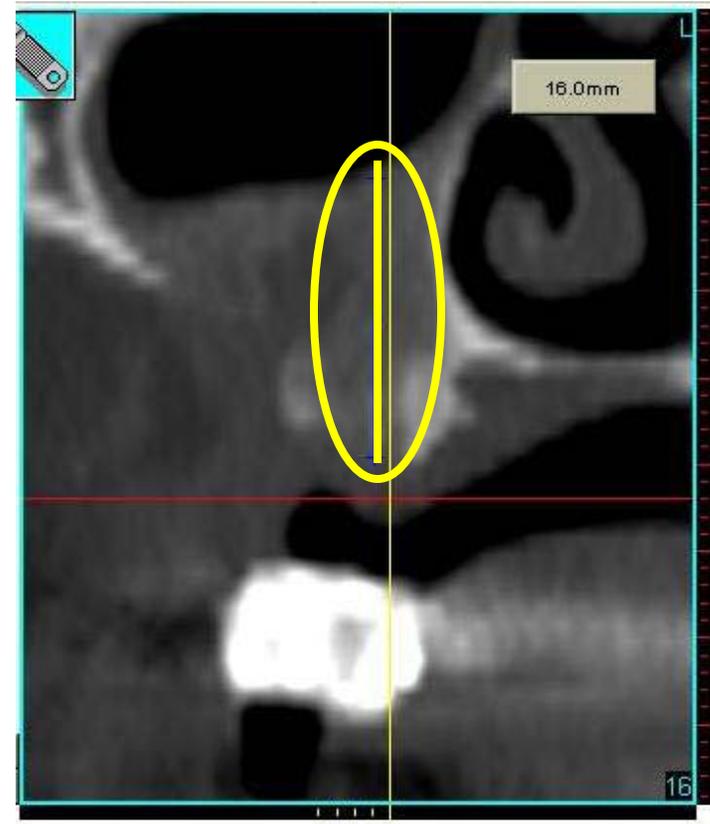


CT Scan of *de novo* Bone

Pre-Op
(3.9 mm Baseline)

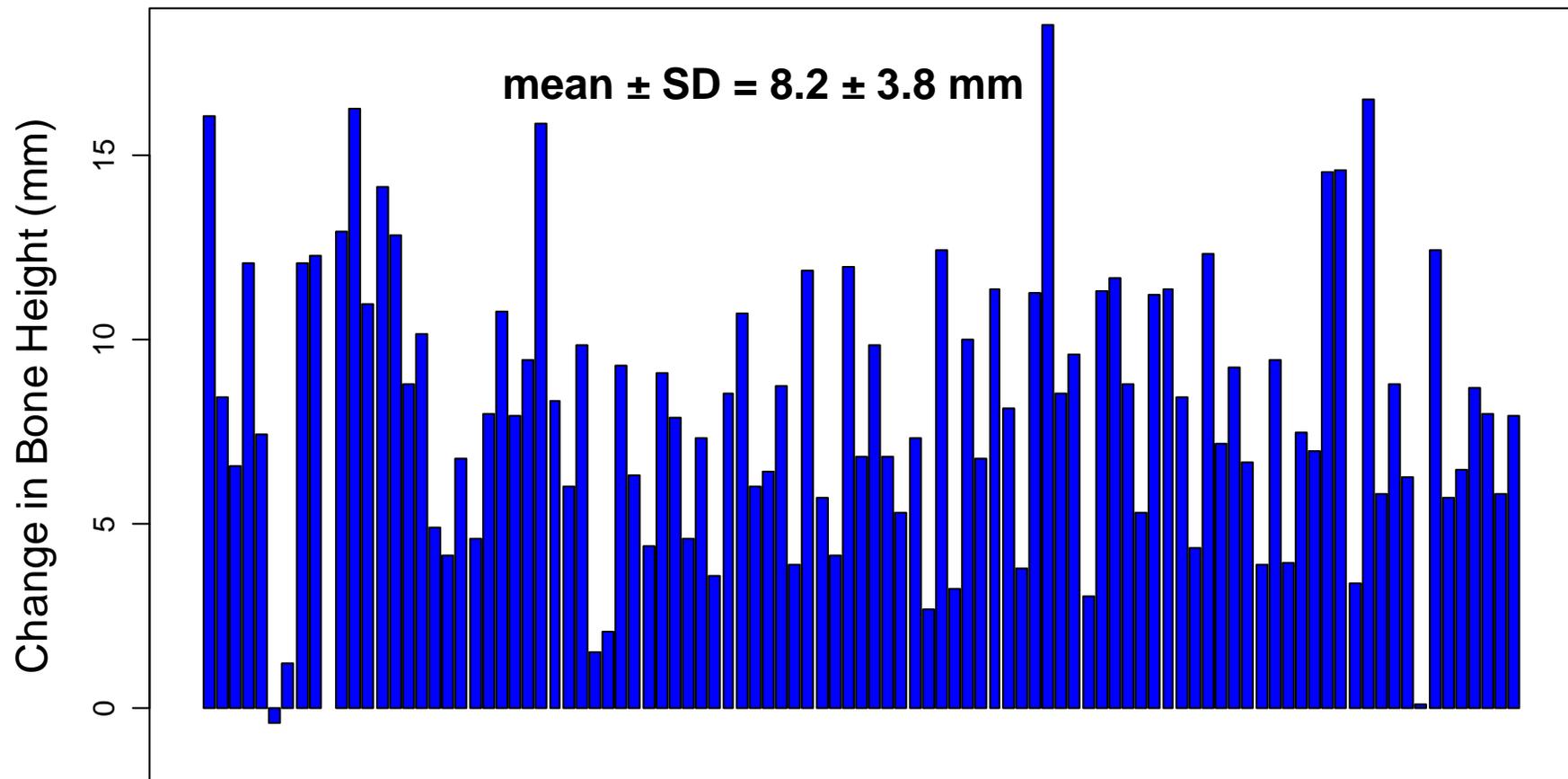


6 months Post-Op
(16.0 mm)



Sinus Augmentation Bone Growth Treated with rhBMP-2/ACS 1.5mg/ml (N=98)

Bone Height Change by Subject

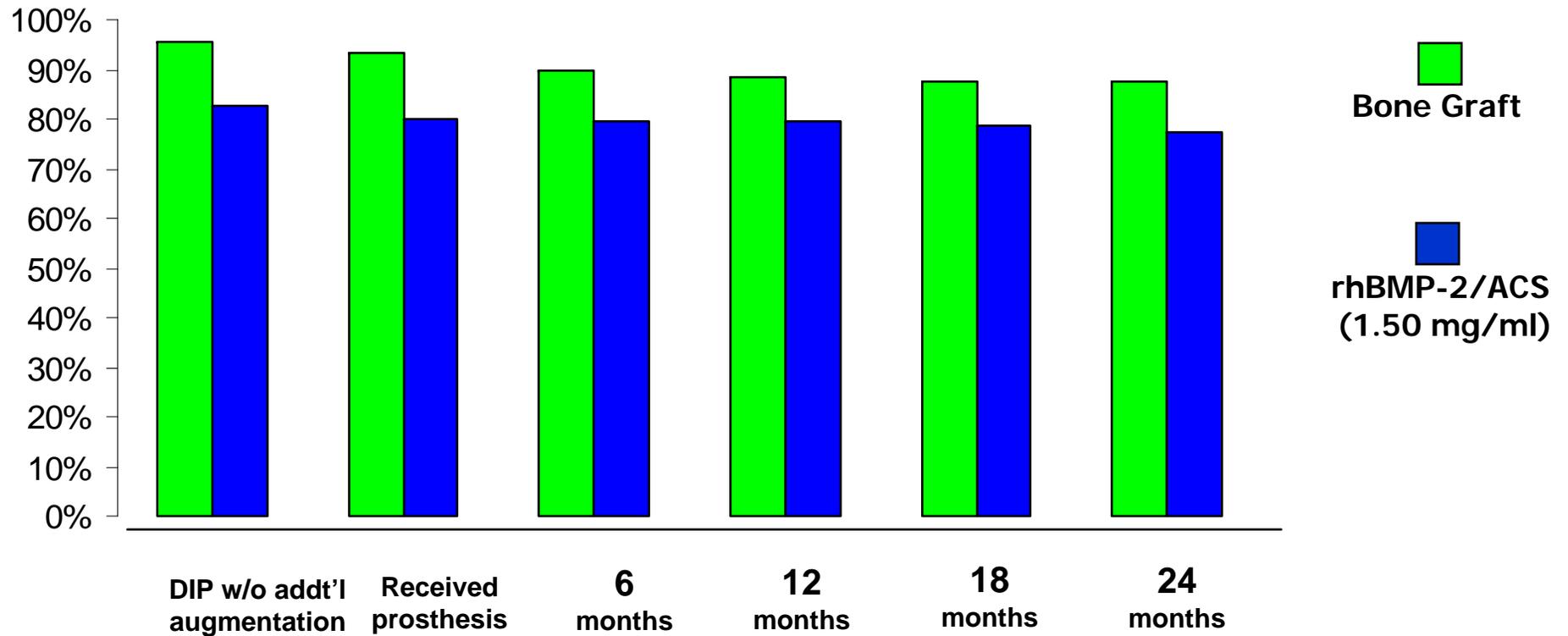


**Primary Objective
INFUSE[®] Bone Graft
Functional Loading Success**

Time Period	Sinus Augmentation Studies
Dental implants without augmentation	82.8% (82/99)
Received prosthesis (functionally loaded)	79.8% (79/99)
6 months	79.6%* (78/98)

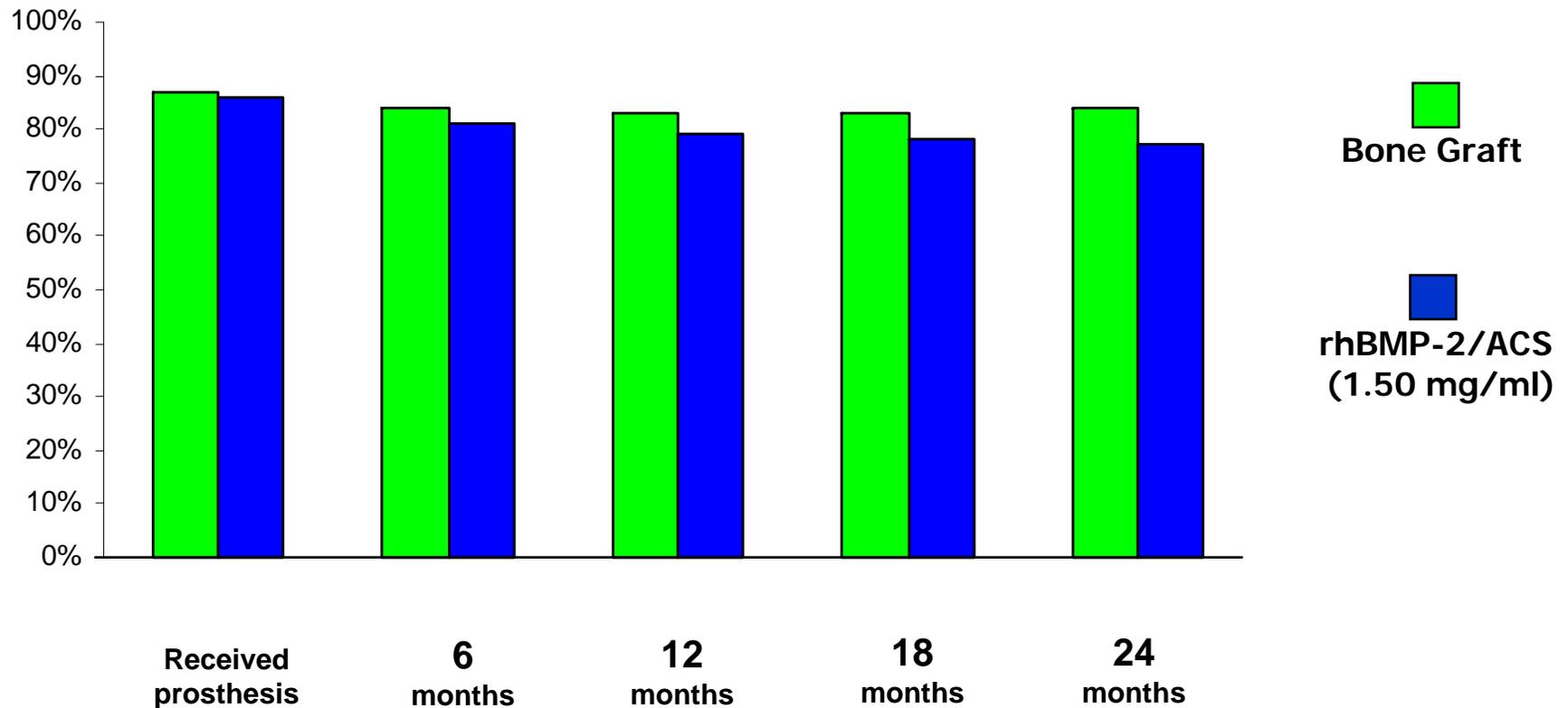
***Target Success Rate 73%**

Secondary Objective Functional Loading by Patient



P Value	0.0683	0.1117	0.0667	0.0286
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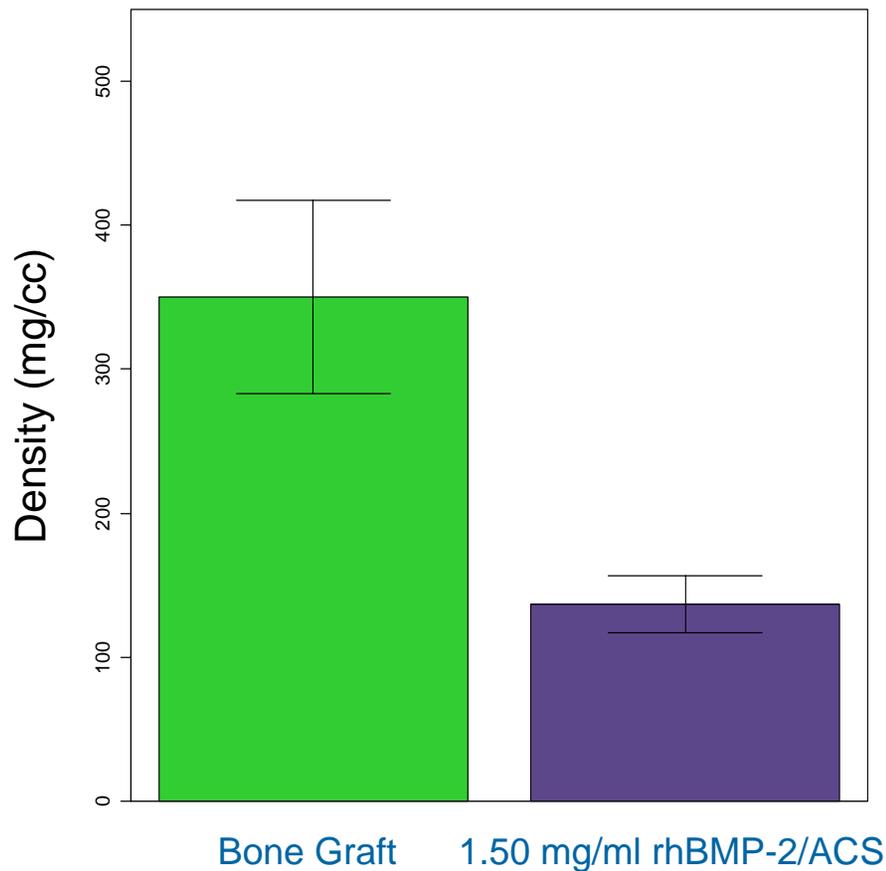
Secondary Objective Functional Loading by Implant



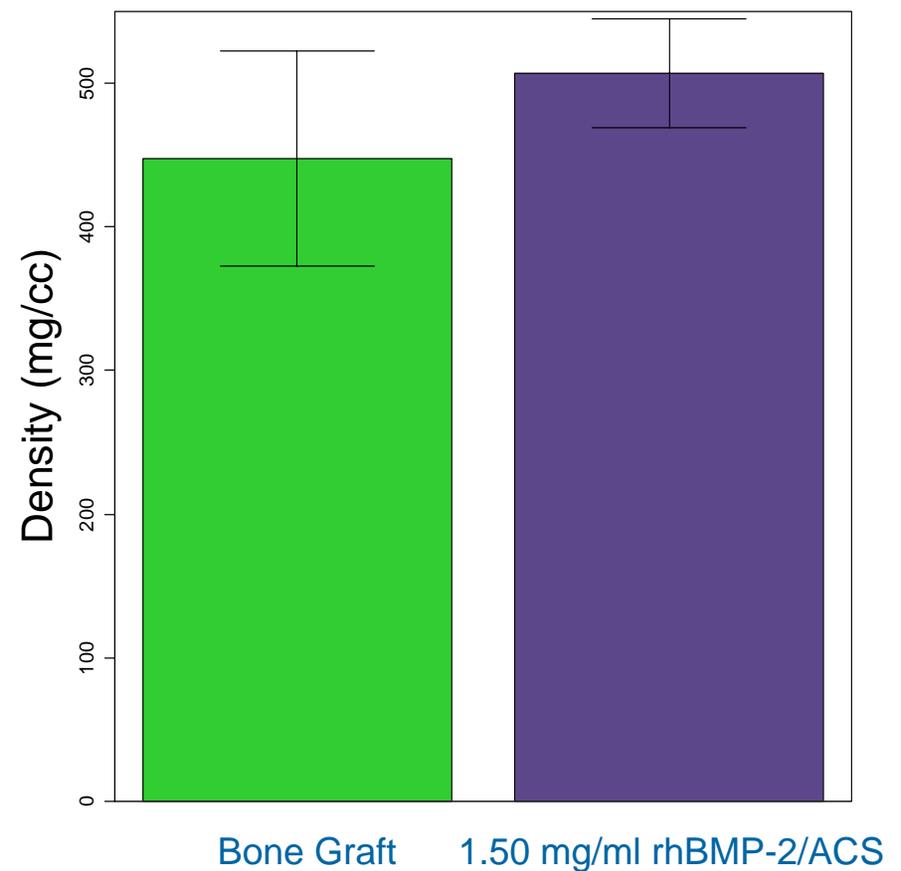
P Value	0.8218	0.6645	0.4579	0.3643	0.2112
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Bone Density from CT Scan Sinus Augmentation Dosing Study

Density at 4 months Post Grafting



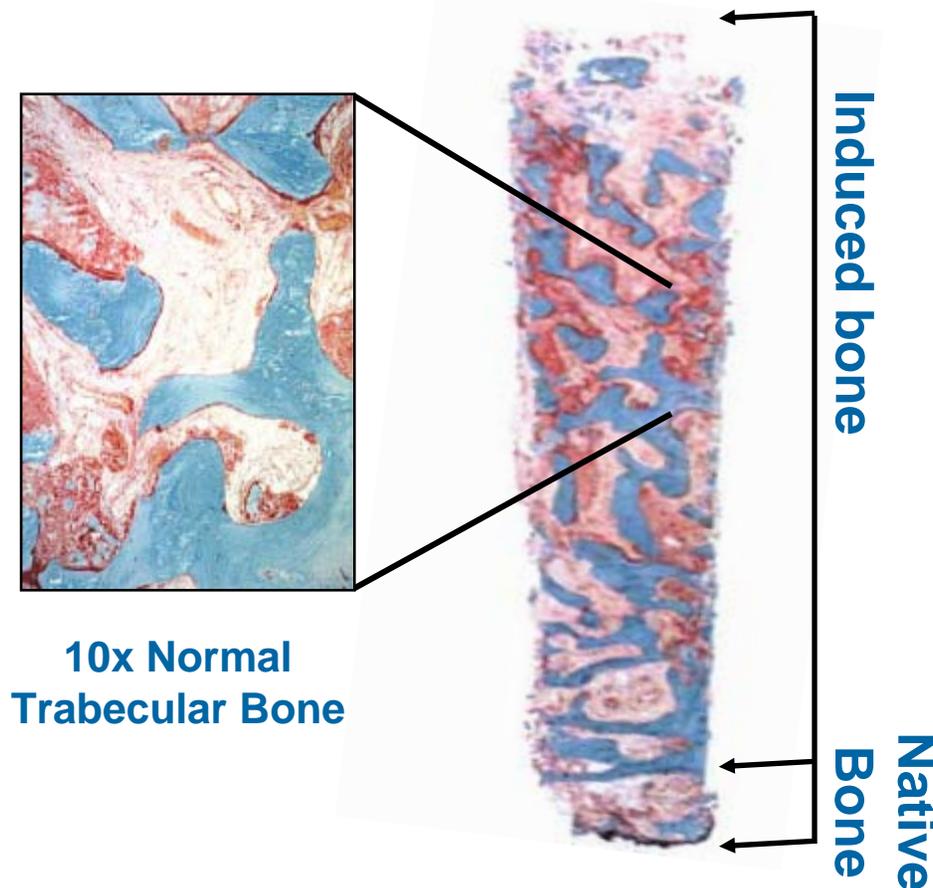
Density at 6 months Post Prosthesis



Sinus Augmentation

Histology Demonstrates Normal Physiologic Bone

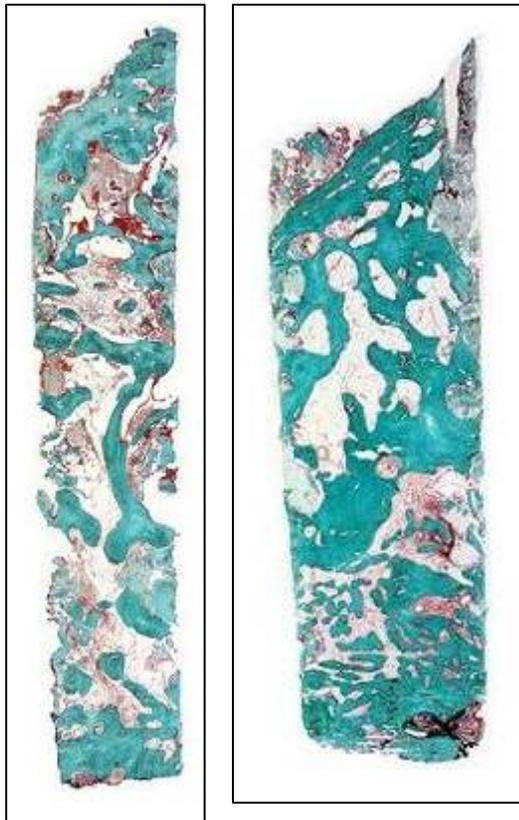
rhBMP-2/ACS



- Longitudinal section core biopsy
- Samples taken at time of dental implant placement (6-12 months)
- Residual Bone Graft fragments were included in the quantitative histomorphometric measurements

Sinus Augmentation Studies Bone Quality Supports Dental Implant

Bone Graft



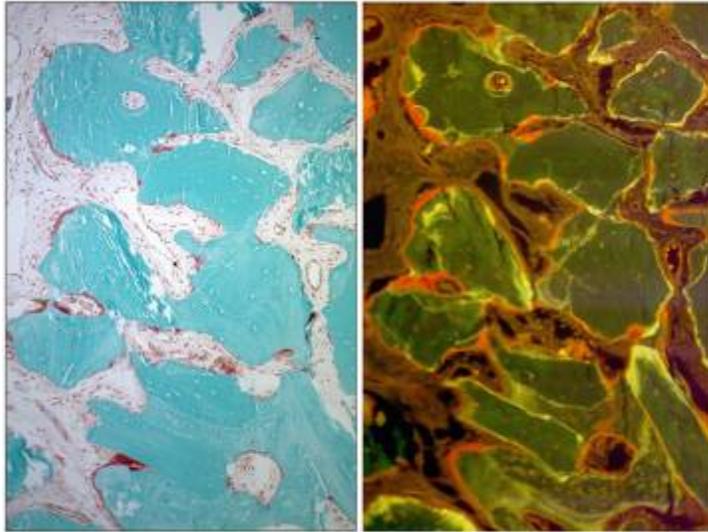
- **Similar Trabecular Volume and Thickness**
- **Both with 90-95% lamellar bone with small amounts of immature bone**
- **Residual lamellar bone fragments in Bone Graft group may have accounted for statistical differences**
- **Differences did not affect clinical outcomes**

INFUSE[®] Bone Graft

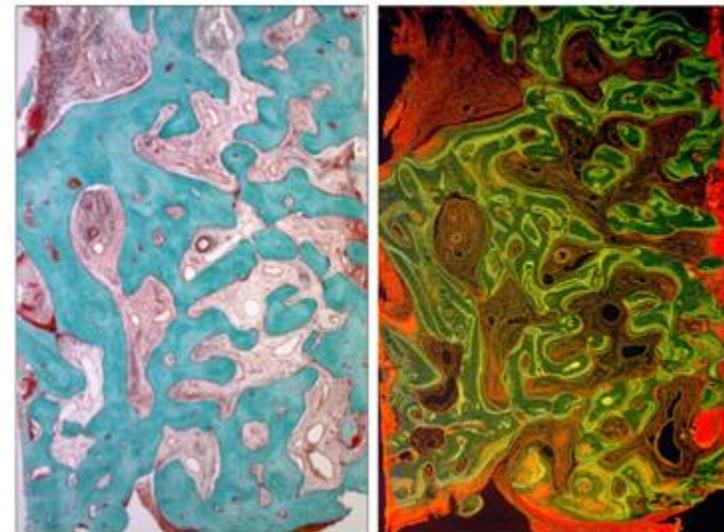


Sinus Augmentation *De Novo* Bone Formation

Bone Graft



rhBMP-2/ACS



- **Labeling**
 - **Yellow** - 10 days post-op (tetracycline hydrochloride)
 - **Orange** - 3 months post-op (democlocycline)
- rhBMP-2/ACS demonstrated substantial, rapid *de novo* bone formation
- Bone Graft group demonstrated variable *de novo* bone

Histology Summary

“...autogenous bone and rhBMP-2/ACS grafted sites resulted in significant formation of new trabecular bone comparable in density and structure to the host site. The bone that formed was biologically and structurally normal...”

***– Dr. Stephen Cook, Independent Histology Reviewer,
Tulane University***

Sinus Augmentation Clinical Effectiveness Summary

INFUSE[®] Bone Graft:

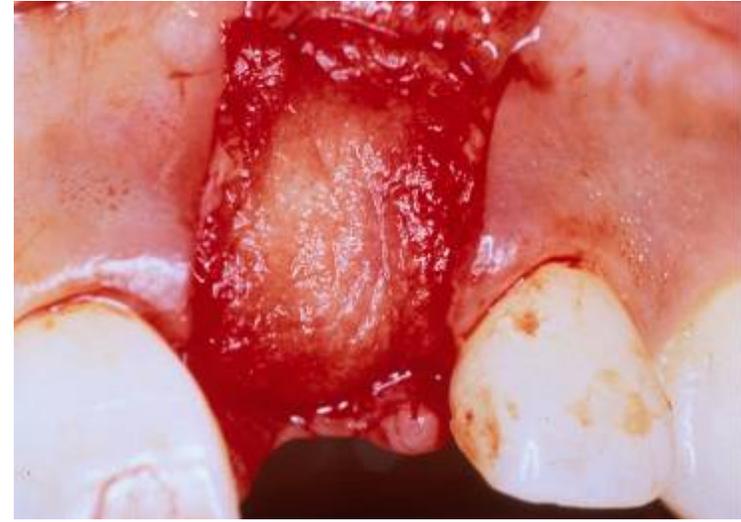
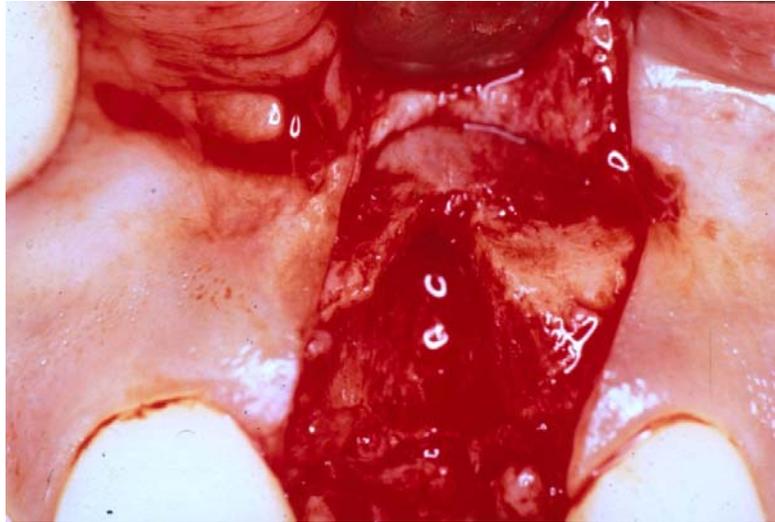
- **Combined Study Result: 79.6% Success Rate (exceeded target success rate)**
- **Induced *de novo* bone formation**
- **Exceeded primary outcome objective**
- **Clinically effective for:**
 - **Generating bone in the maxillary sinus allowing for**
 - **Dental restoration**



David L. Cochran, DDS, PhD, MMSc

**Chairman
Department of Periodontics
UT Health Sciences Center
at San Antonio**

Extraction Socket Augmentation Clinical Need

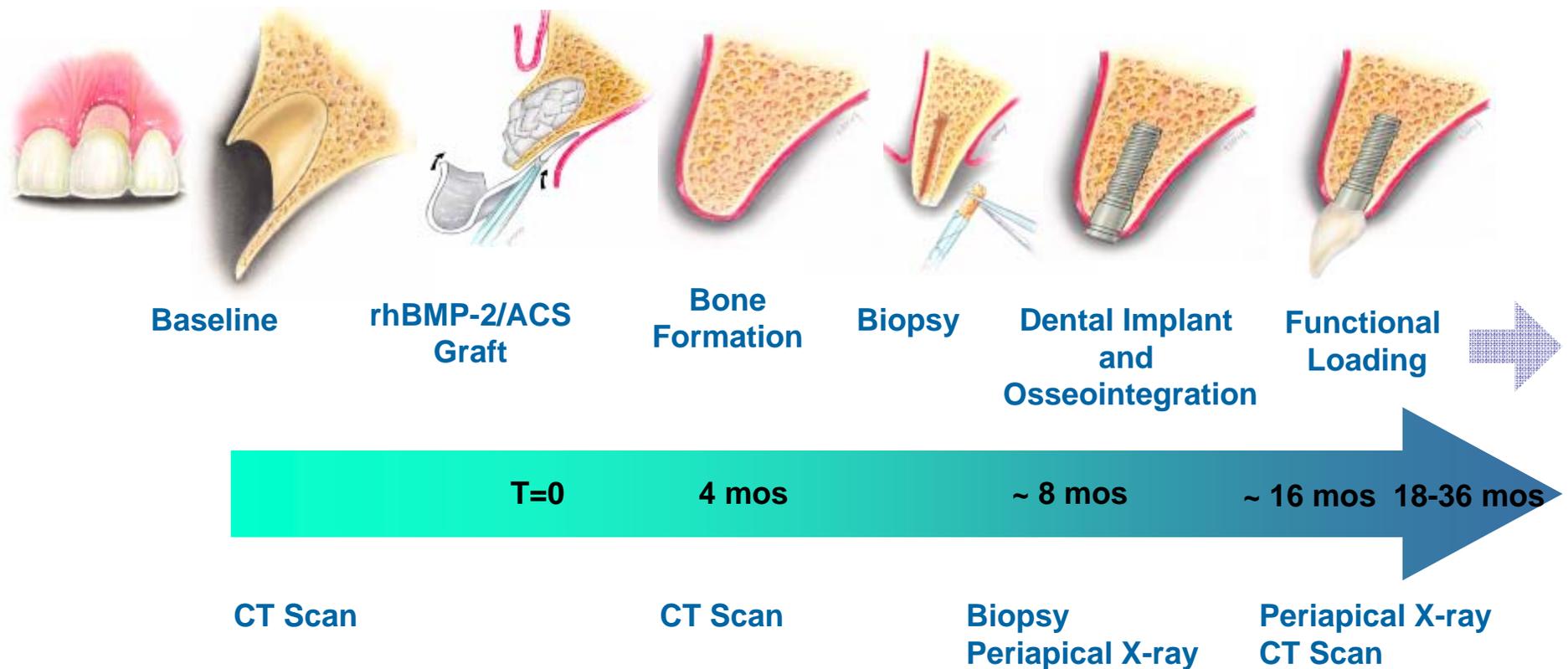


Goal: Restore ridge width and preserve height to replace missing teeth

Extraction Socket Augmentation Methods and Definition

- **Prospective, randomized, multi-center (8), double-blinded controlled 80-patient human clinical trial providing high level of evidence**
- **Buccal wall defect (~ 50% of the extraction socket depth)**
- **Effectiveness endpoint: adequate alveolar bone formation for implant placement**
- **Safety Endpoints**

Extraction Socket Augmentation Studies

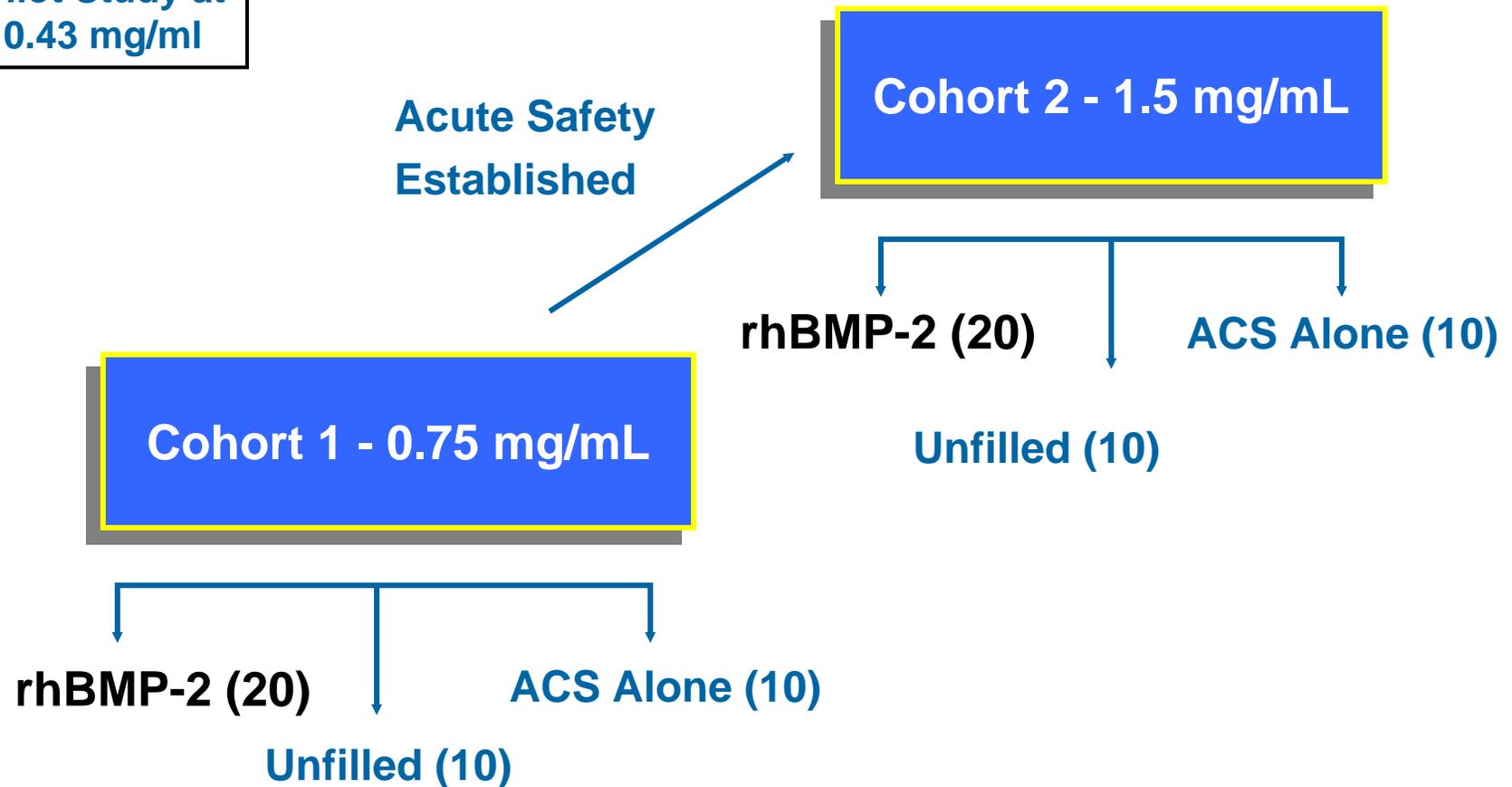


Safety Evaluation Throughout the Study

Study Design Schematic Extraction Socket Study

N=80

Preceded by
Pilot Study at
0.43 mg/ml

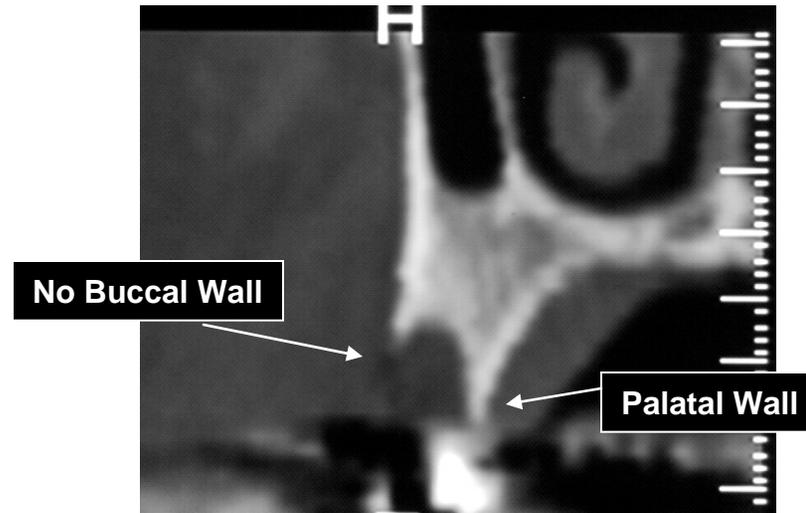


Prospective, Controlled Extraction Socket IDE Studies

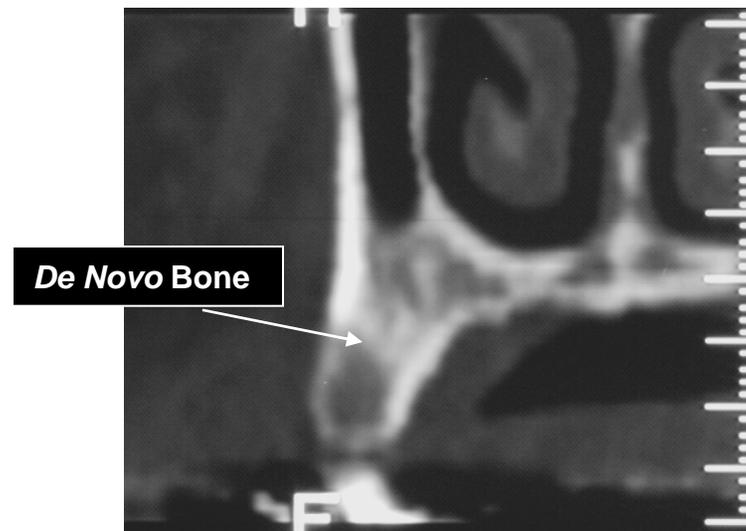
▪ Extraction Socket (N=92)	<u>N</u>	
– Dosing Study (80)		
• rhBMP-2/ACS (1.5 mg/ml)	21	rhBMP-2/ACS Effectiveness N= 21
• Unfilled Control Treatment	20	
• ACS Alone (0.0 mg/ml)	17	
• rhBMP-2/ACS (0.75 mg/ml)	22	
– Pilot Study (12)		
• rhBMP-2/ACS (0.43 mg/ml)	12	

Extraction Socket Augmentation

Baseline

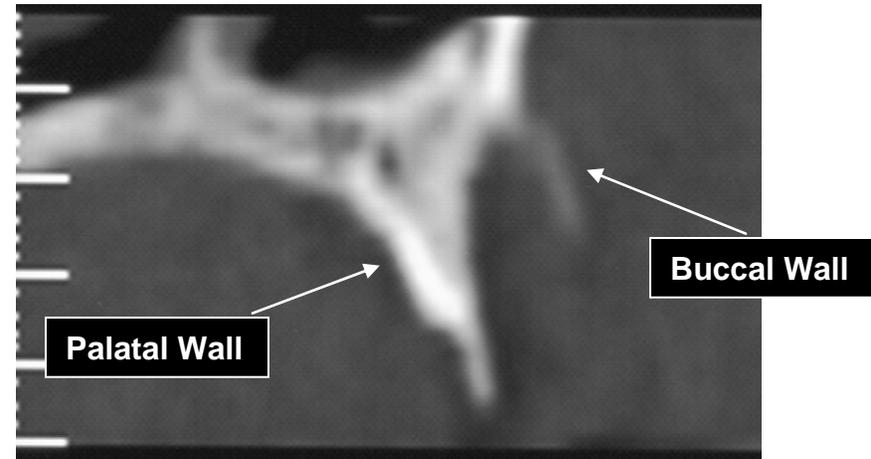


**16-weeks
Post rhBMP-2/ACS
Placement
(1.5 mg/ml)**

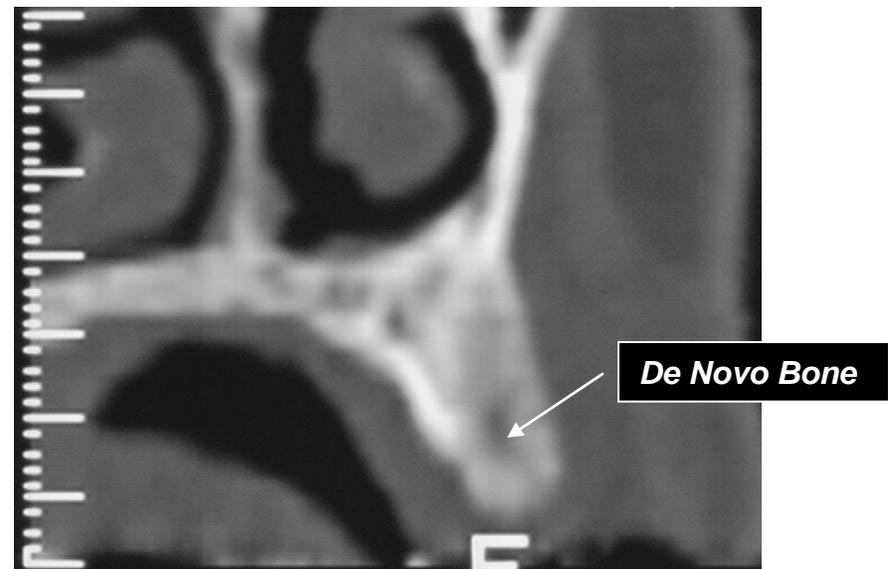


INFUSE[®] Bone Graft Patient

Baseline

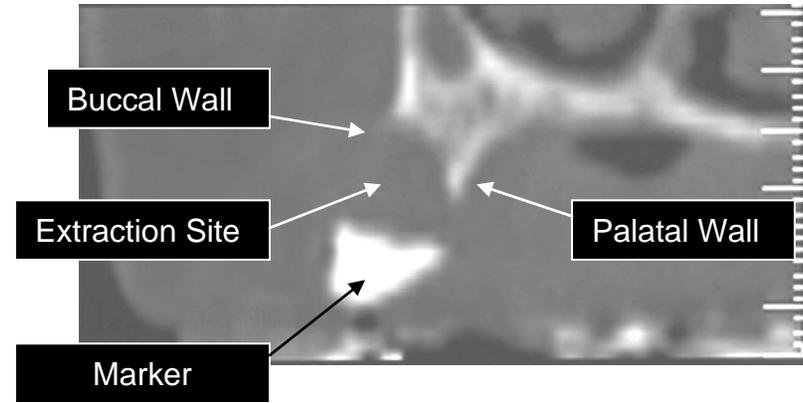


**16-weeks
Post rhBMP-2/ACS
Placement
(1.5 mg/ml)**

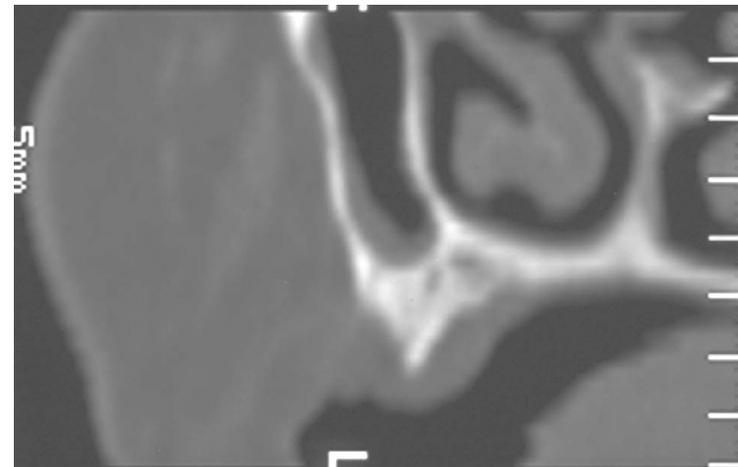


Patient with Unfilled Defect

Baseline



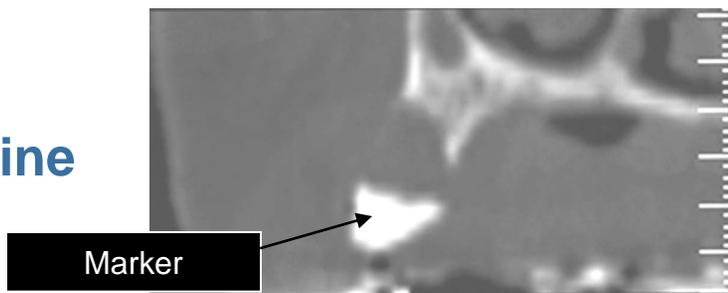
**16-weeks
Post Extraction**



Clinically Significant Results vs. Unfilled

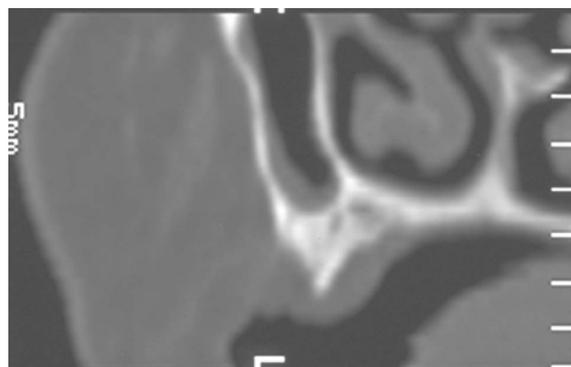
Unfilled Defect/
Standard of Care

Baseline



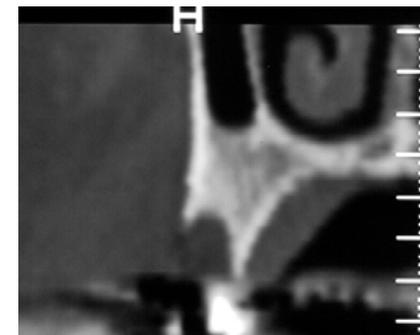
Unfilled defect at time of extraction

16-weeks
Post



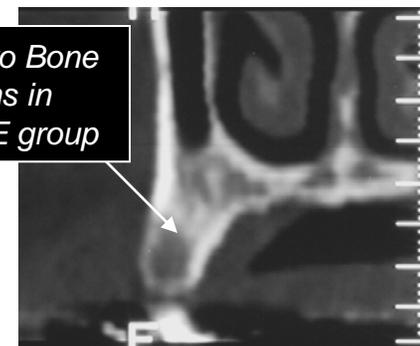
Unfilled defect 16 weeks post extraction

INFUSE[®] Bone Graft



INFUSE[®] defect at time of placement

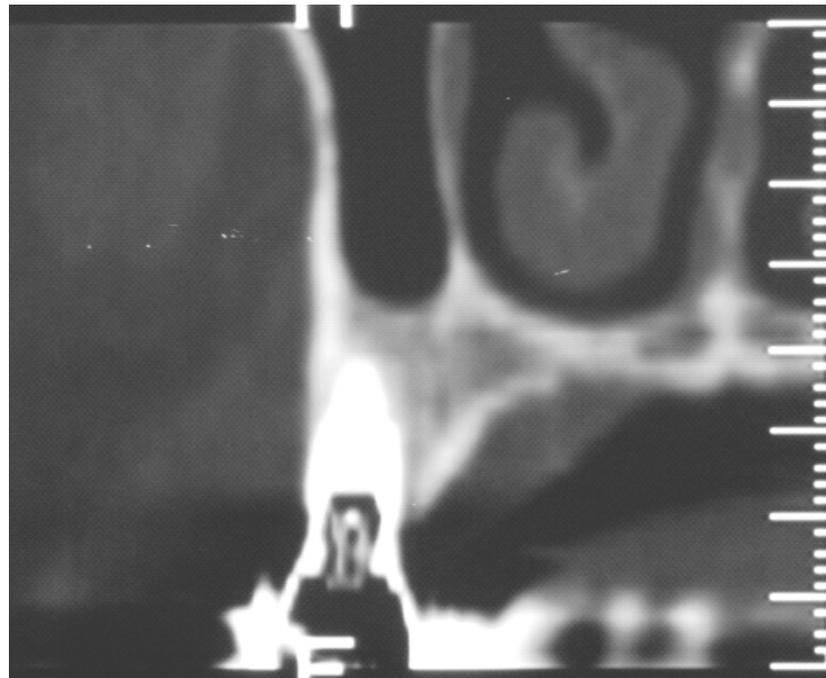
De Novo Bone
forms in
INFUSE group



INFUSE[®] defect 16 weeks post placement

Patient Therapeutic Benefit

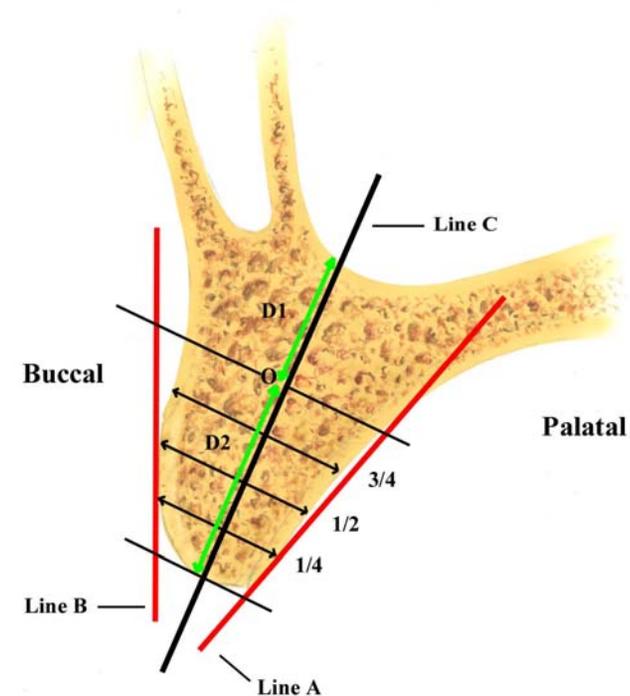
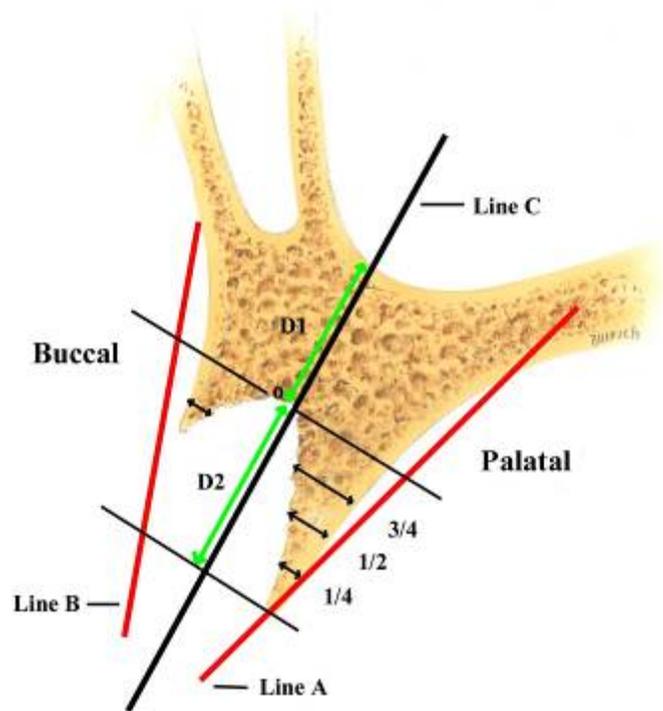
- **Demonstrated**
- **Dental implant placed in *de novo* bone.**



Extraction Socket Augmentation CT Scan Measurement Methodology

Pre-op

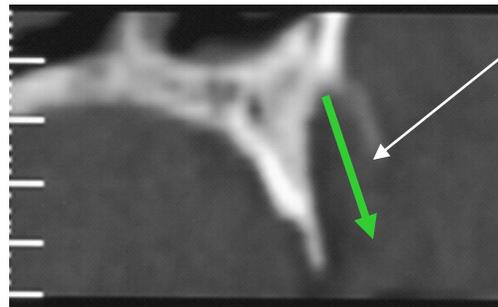
16-week post rhBMP-2/ACS



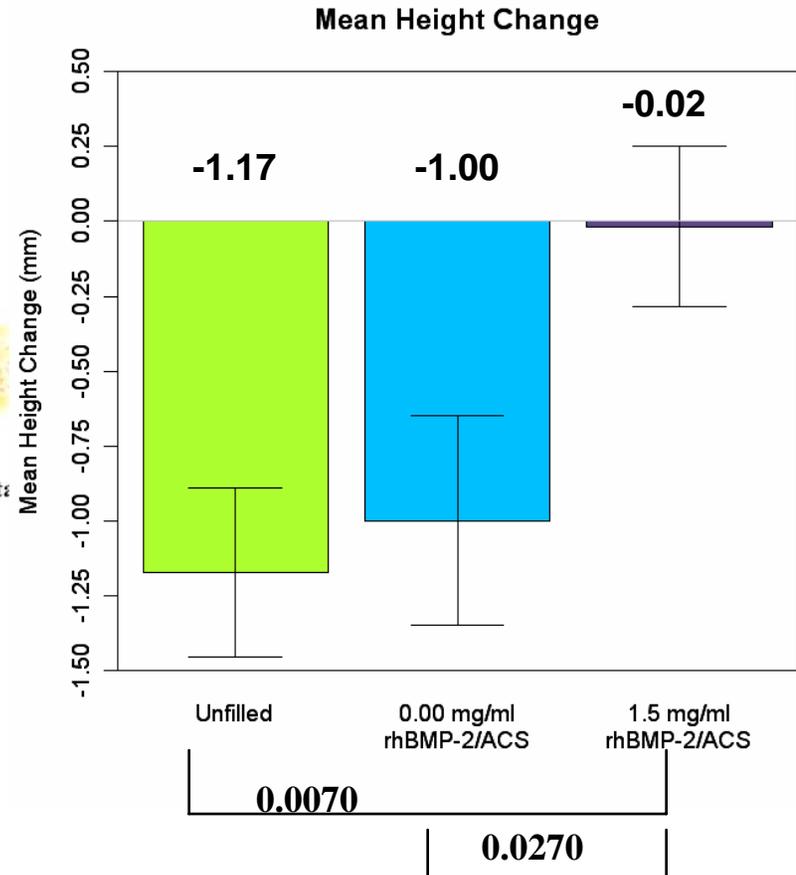
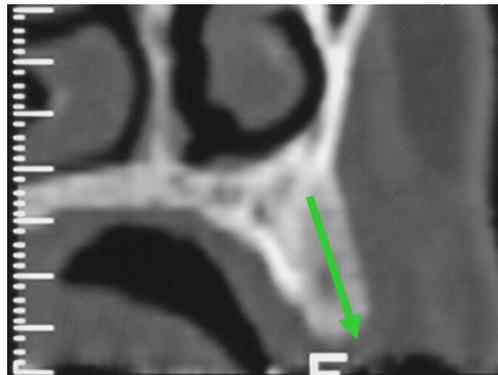
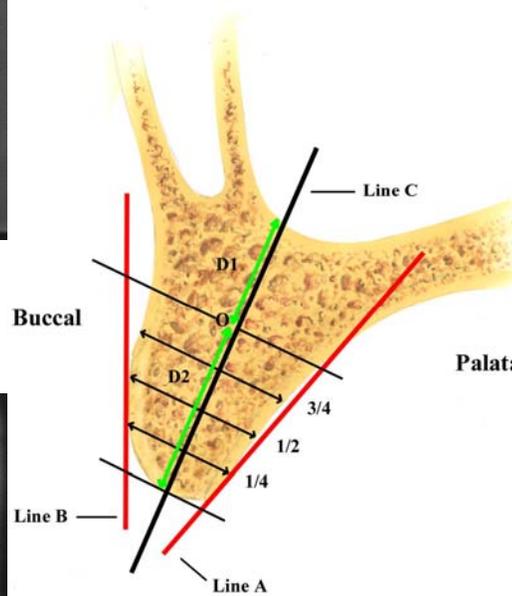
Alveolar ridge height = D1 + D2

Width: perpendicular to line D2 at 1/4, 1/2, and 3/4

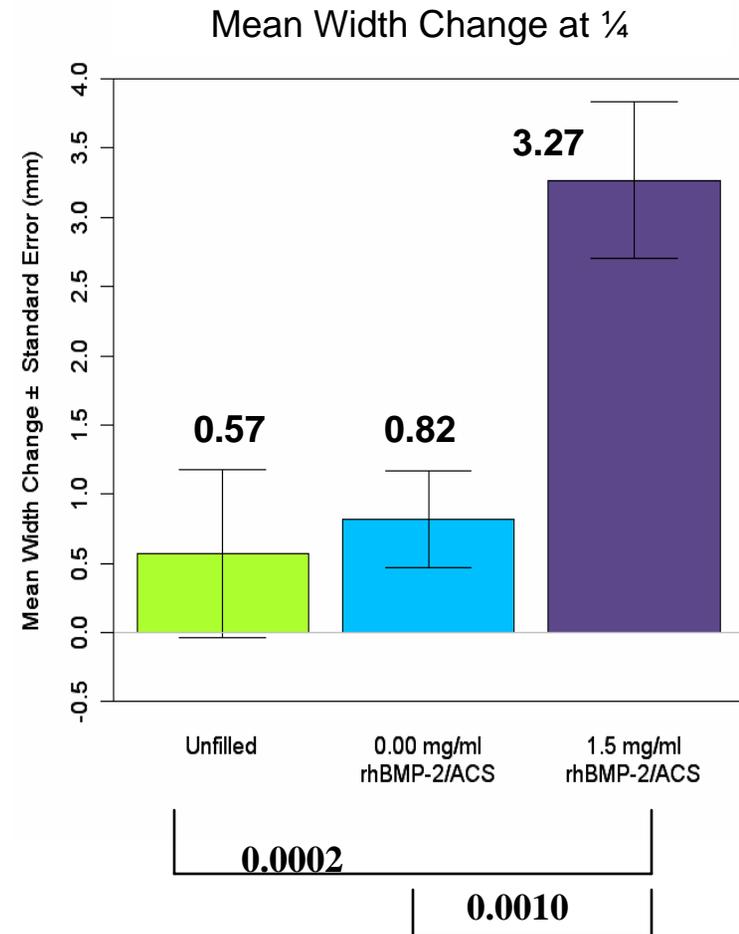
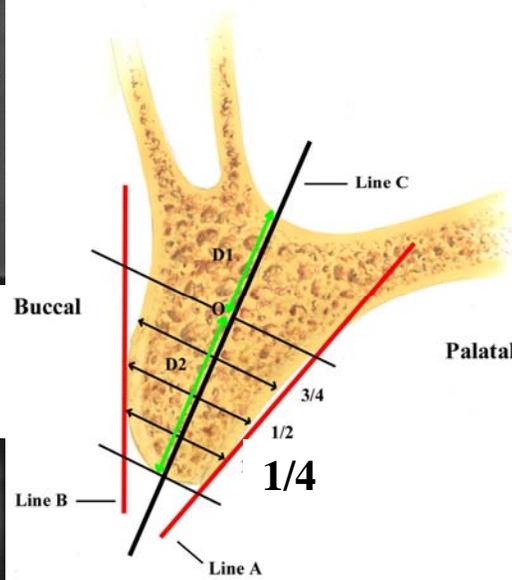
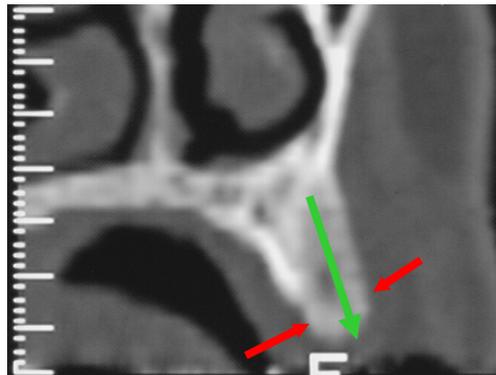
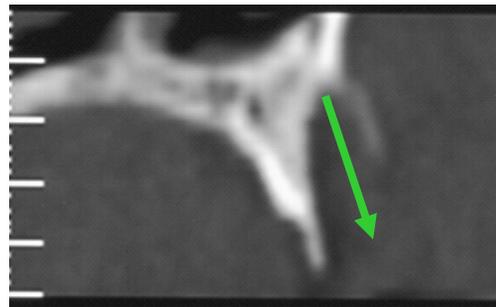
Height Change (Loss) at 4 months



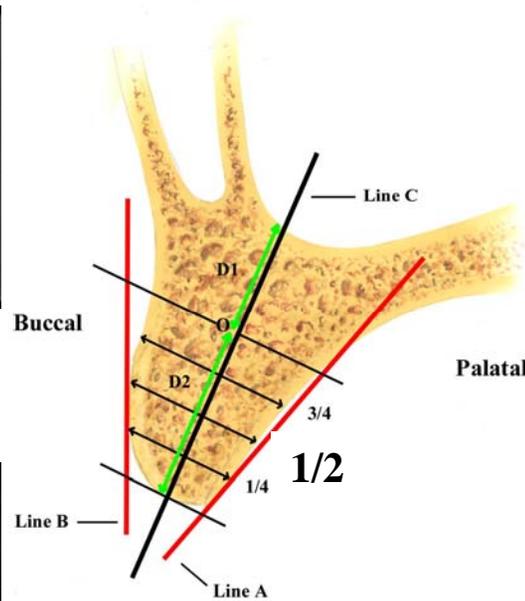
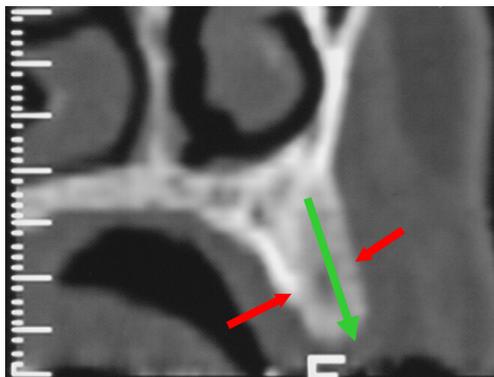
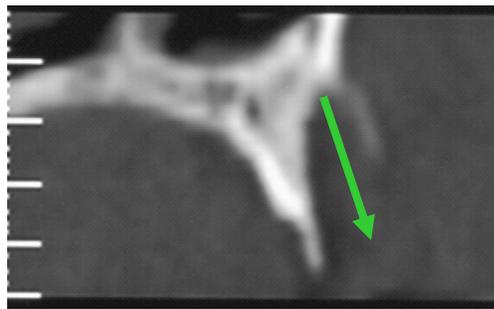
D1 + D2



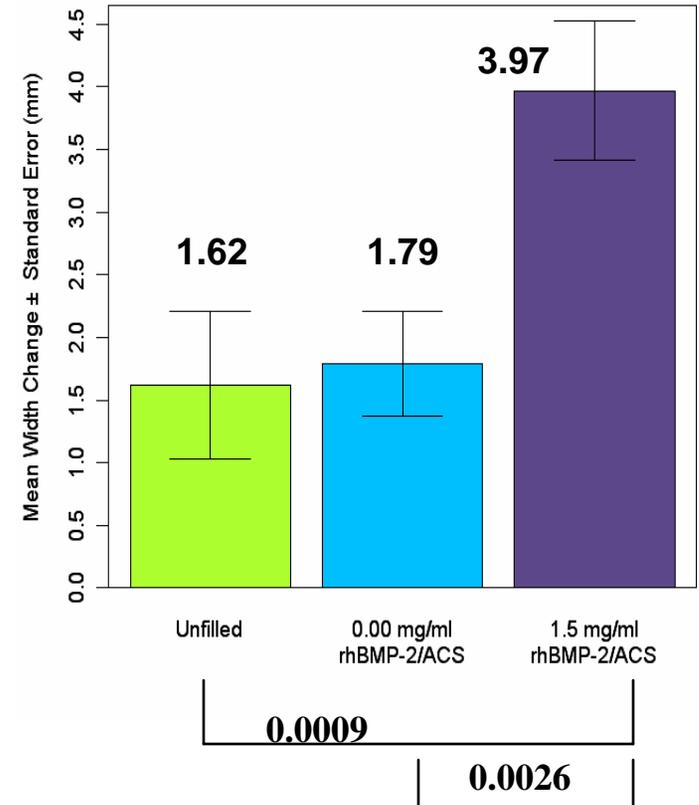
Width Change at 1/4 at 4 Months



Width Change at 1/2 at 4 Months



Mean Width Change at 1/2



INFUSE® Extraction Socket Augmentation Bone Growth and Implant Placement

Mean Change (mm) ± SD			
	No Implant	Implant	P Value
Height	-1.21 ± 1.34	-0.36 ± 1.28	0.0085
Width at ¼	0.74 ± 1.76	2.17 ± 2.45	0.0049
Width at ½	1.79 ± 1.80	2.89 ± 2.37	0.0280
Width at ¾	2.12 ± 1.61	2.06 ± 1.56	0.8862

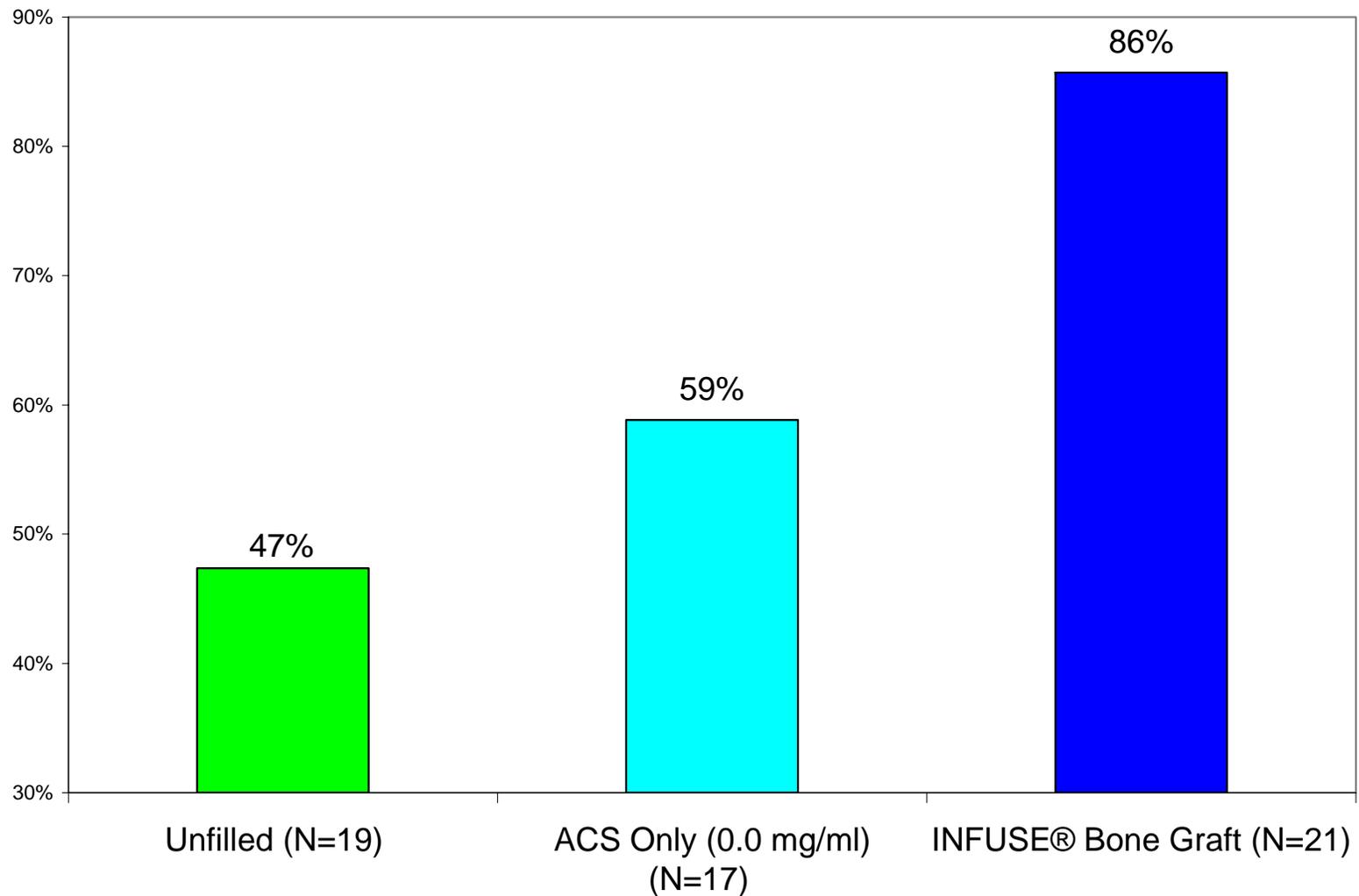
**Greater bone growth is associated with
greater implant placement.**

Functional Loading Endpoint, By Patient

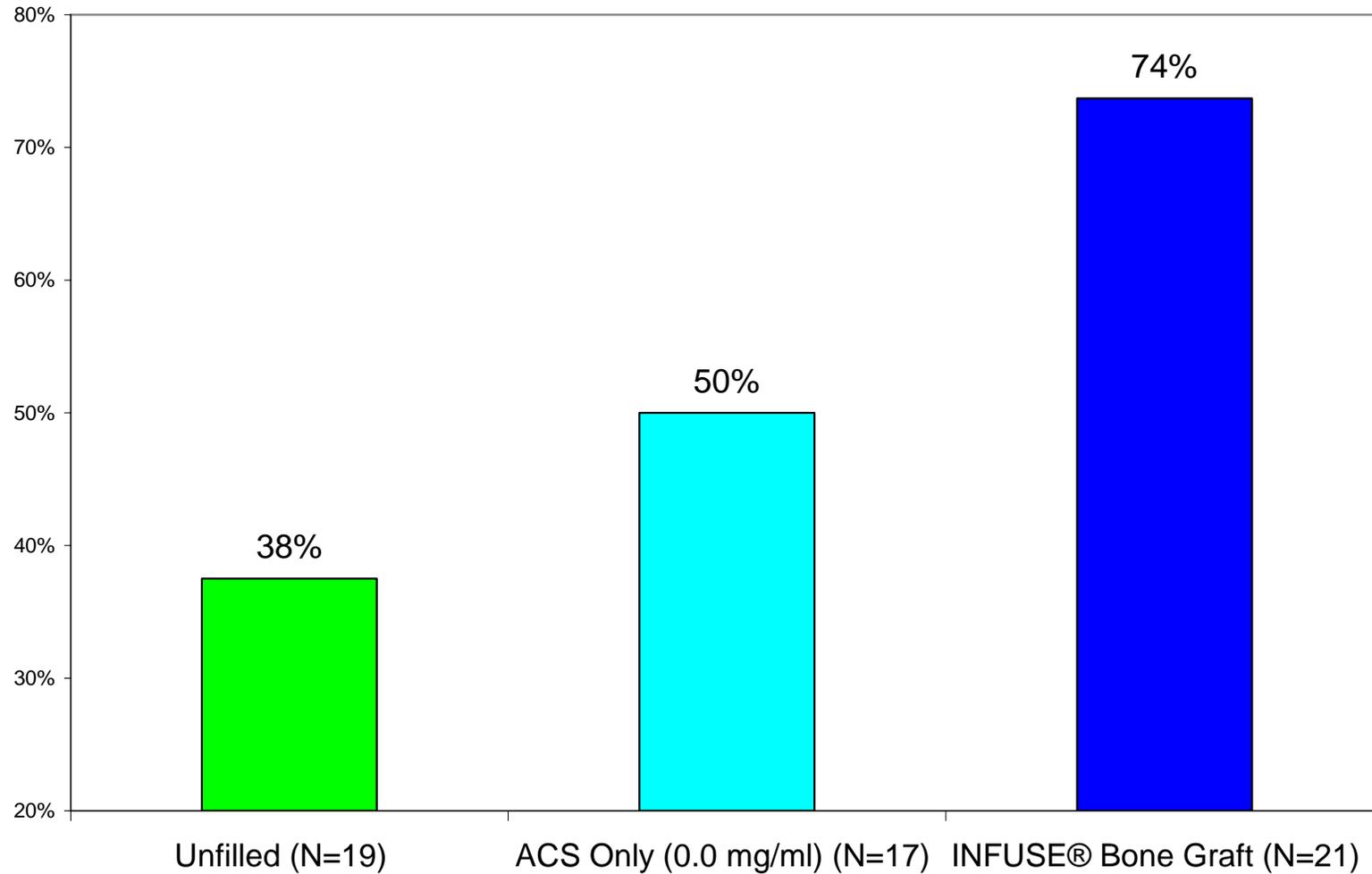
Time Post Functional Loading	Unfilled	ACS Only (0.0 mg/ml)	INFUSE [®] Bone Graft	P Value Unfilled / ACS Only vs. INFUSE [®] Bone Graft
Dental Implant Placement	47% (9/19)	59% (10/17)	86% (18/21)	0.0171 / 0.0780
Received prosthesis	41% (7/17)	56% (9/16)	76% (16/21)	0.0458 / 0.2913
6 month	38% (6/16)	50% (7/14)	74% (14/19)	0.0442 / 0.2728
12 month	38% (6/16)	50% (7/14)	72% (13/18)	0.0824 / 0.2769
18 month	38% (6/16)	50% (7/14)	69% (11/16)	0.1556 / 0.4572
24 month	38% (6/16)	50% (7/14)	67% (10/15)	0.1556 / 0.4621

INFUSE[®] Bone Graft is more successful.

Dental Implant Placement w/o Augmentation: INFUSE[®] Bone Graft vs. ACS only vs. Unfilled by Patient



6 month Functional Loading: INFUSE[®] Bone Graft Compared with ACS only and Unfilled by Patient



Same Histology for Both Indications

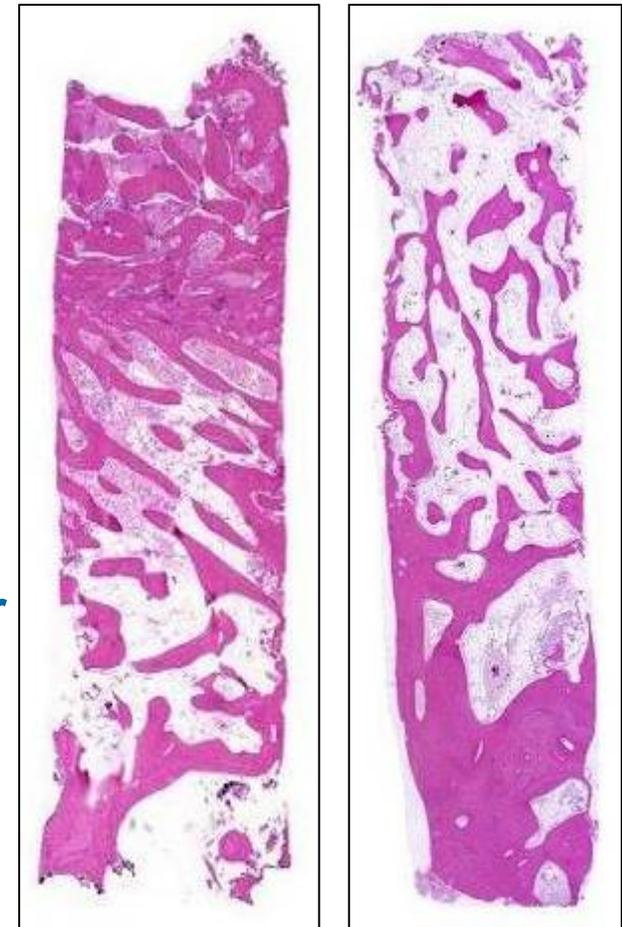
Sinus

Extraction Socket



- **INFUSE[®] BONE GRAFT**
- **Samples taken approx. 7 months post-op**
- **Similar Qualitative Parameters including Trabecular Volume, Thickness, and Number**

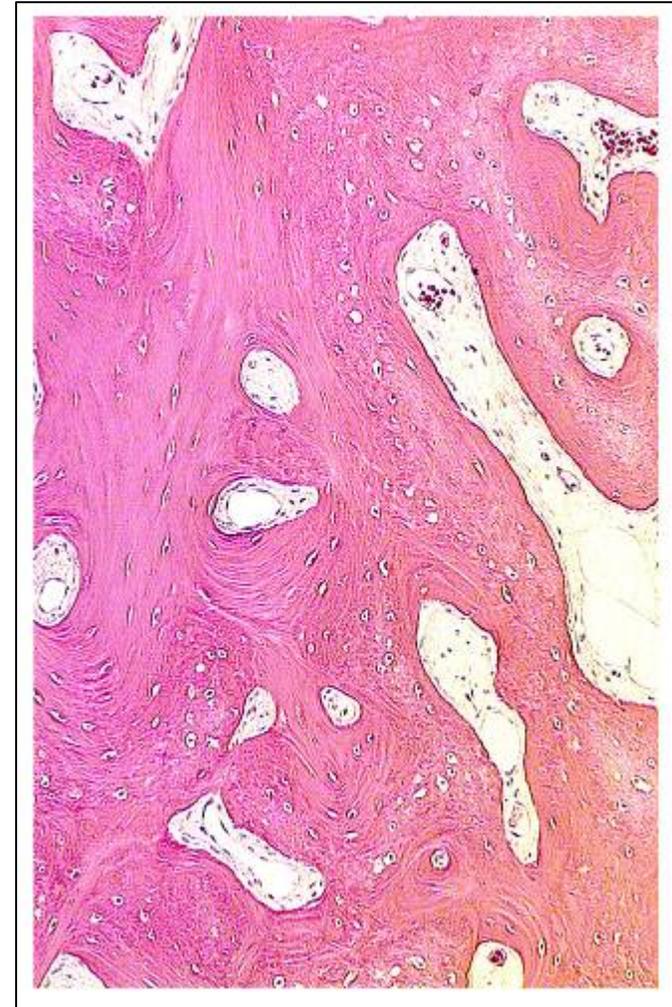
Augmentation



Extraction Socket Representative Histology

rhBMP-2/ACS induced bone

- **Vascular marrow space**
- **Lamellar and immature bone**
- **Similar to the bone formed in the sinus studies**

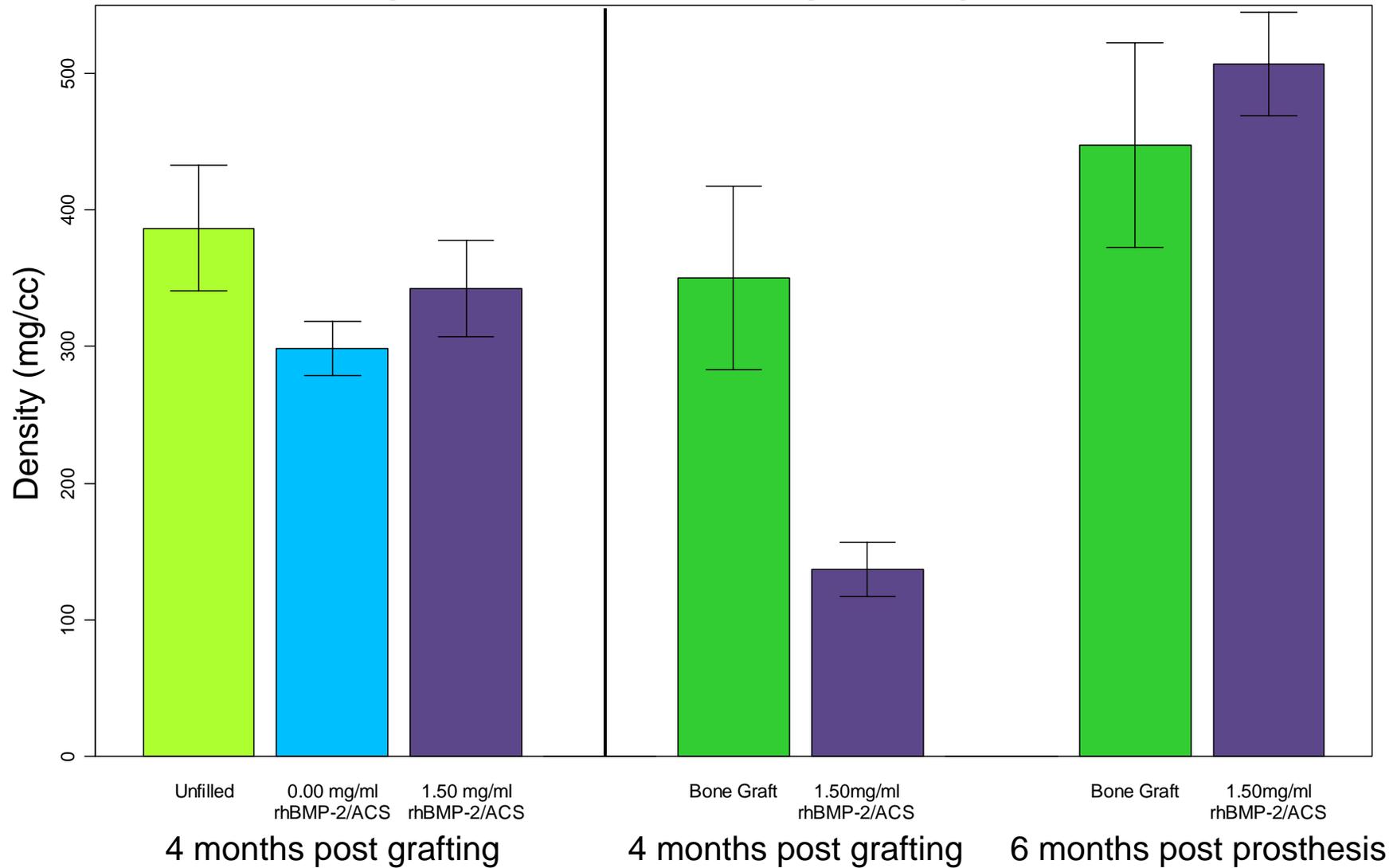


H & E stain, 10 X magnification

Density Comparison

Extraction Socket

Sinus Studies



Summary of Clinical Effectiveness: Extraction Socket Augmentation

INFUSE[®] Bone Graft:

- Induced *de novo* bone formation
- Is clinically effective following tooth extraction for:
 - Preservation of the alveolar ridge and
 - Dental restoration



SAFETY OF INFUSE[®] Bone Graft

Safety Profile

- **Two PMA approvals**
 - **More than 300,000 kits distributed worldwide**
 - **437 patients received rhBMP-2/ACS in IDE clinical trials which supported two PMAs**
- **More Level I clinical evidence than any other bone grafting agent**
 - **1,070 patients studied in FDA clinical trials**

Prospective, Controlled IDE Studies (N=312) Safety Data

<ul style="list-style-type: none"> ▪ Sinus Augmentation (N=220) – rhBMP-2/ACS (1.5 mg/ml) – Bone Graft – rhBMP-2/ACS (0.43; 0.75 mg/ml) 	<p><u>N</u></p> <p>99</p> <p>91</p> <p>30</p>	}	<p>Safety:</p> <p>All</p> <p>rhBMP-2/ACS</p> <p>N= 184</p> <hr style="width: 100%;"/> <p>1.5 mg/ml</p> <p>rhBMP-2/ACS</p> <p>N=120</p>
<ul style="list-style-type: none"> ▪ Extraction Socket (N=92) – rhBMP-2/ACS (1.5 mg/ml) – Unfilled Control Treatment – rhBMP-2/ACS (0.43; 0.75 mg/ml) – ACS Alone (0.0mg/ml) 	<p>21</p> <p>20</p> <p>34</p> <p>17</p>		

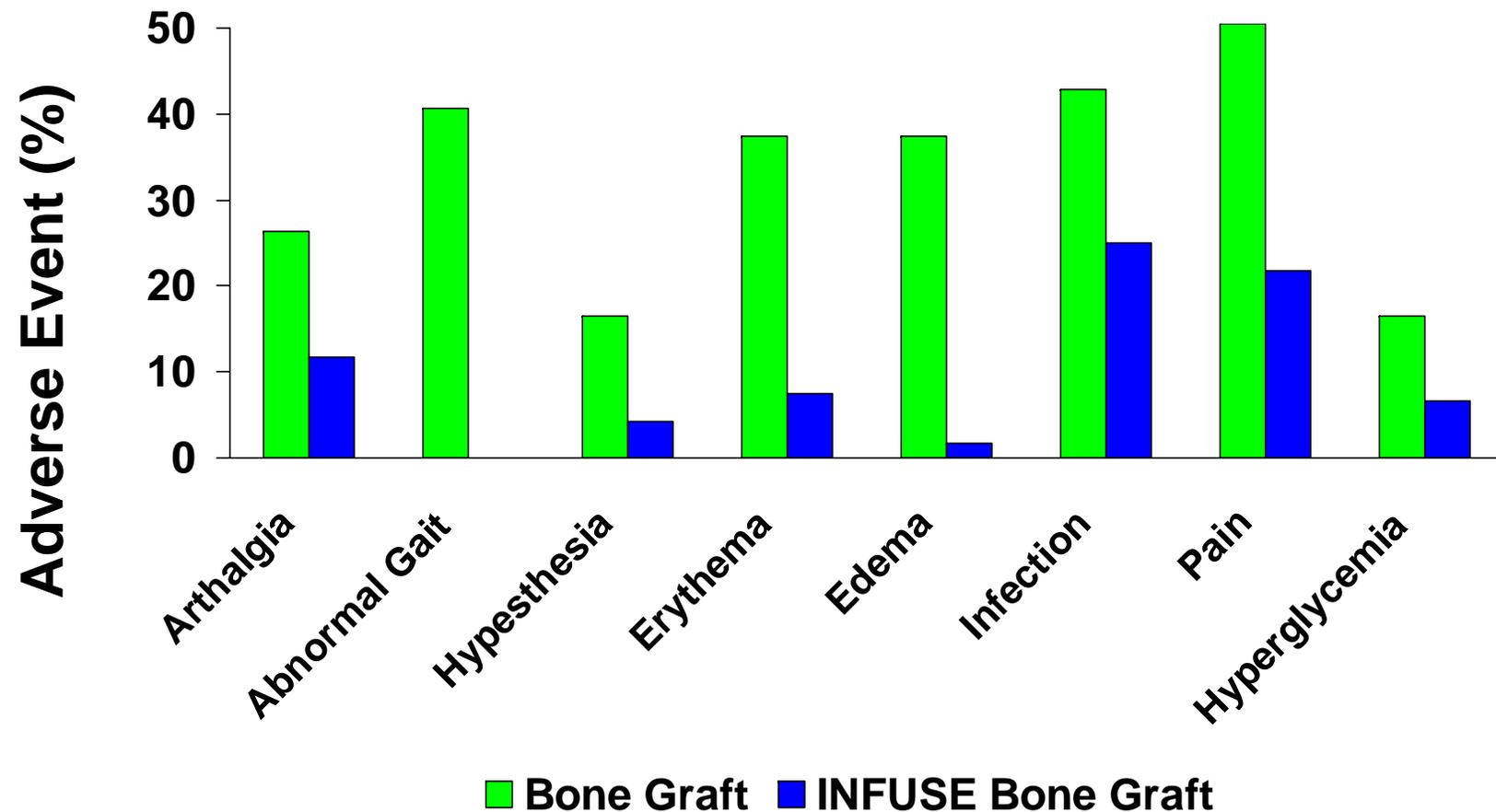
Adverse Events > 10% Patients

COSTART TERM	Bone Graft (n=91)	INFUSE[®] Bone Graft (n=120)
EDEMA	37.4%	1.7%
FACE EDEMA	57.1%	67.5%
INFECTION	42.9%	25.0%
PAIN	50.5%	21.7%
ORAL EDEMA	64.8%	67.5%
ORAL ERYTHEMA	61.5%	47.5%
MOUTH PAIN	83.5%	85.0%
ECCHYMOSIS	23.1%	15.8%

Adverse Events > 10% Patients (cont.)

COSTART TERM	Bone Graft (n=91)	INFUSE[®] Bone Graft (n=120)
HYPERGLYCEMIA	16.5%	6.7%
ARTHRALGIA	26.4%	11.7%
BONE DISORDER	12.1%	11.7%
ABNORMAL GAIT	40.7%	0
HYPESTHESIA	16.5%	4.2%
SINUSITIS	16.5%	9.2%
ERYTHEMA	37.4%	7.5%

Adverse Events > 10% Patients (P<0.05)



Adverse Event Summary INFUSE[®] Bone Graft and Bone Graft

	Sinus Augmentation		Extraction Socket Augmentation
	Bone Graft N=91	rhBMP-2/ACS 1.5 mg/ml N=99	rhBMP-2/ACS 1.5 mg/ml N=21
At Least One Event	99%	100%	100%
rhBMP-2/ACS Procedure Related	Not Applicable	17%	24%
Grade 3 or 4	18%	10%	10%
Grade 3 or 4 rhBMP-2/ACS Procedure Related	Not Applicable	0	0

One death unrelated to INFUSE[®] Bone Graft at 3 years post-implantation

rhBMP-2 and Collagen Antibodies

- Immune response evaluated in 184 rhBMP-2/ACS patients and 91 bone graft patients

Antibody	Bone Graft	rhBMP-2/ACS
Anti-rhBMP-2	0.0%	2.2%*
Anti-bovine Type I collagen	31%	20%
Anti-human Type I collagen	None	None

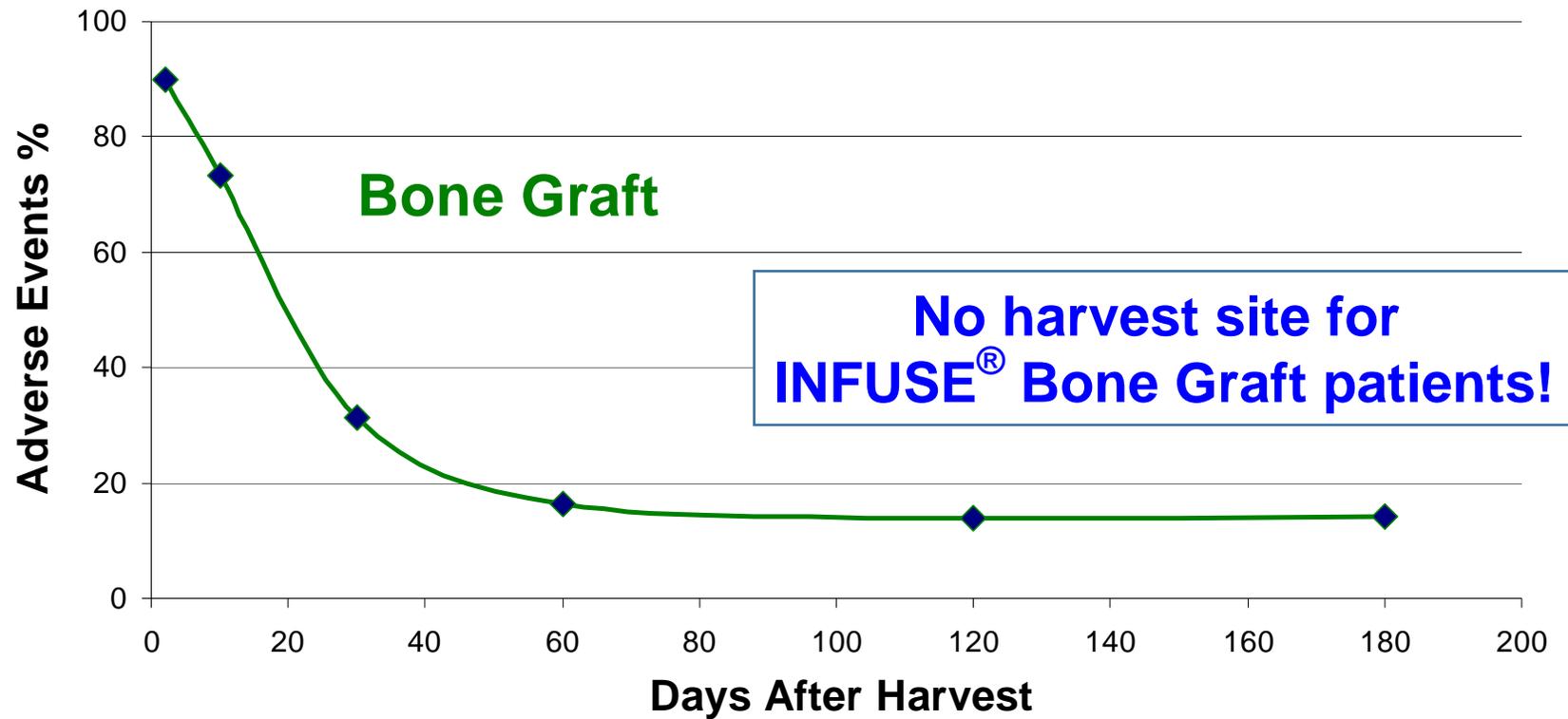
*Low titers, transient effect, clinically insignificant

Bone Graft Patients: Harvest Site Pain and Morbidity

N=91

Harvest Site		Conditions	2 days	10 days	6 months
Iliac Crest (n=18)		Pain	89.9%	44.4%	0%
		Sensory Loss	0%	0%	11.1%
		Gait Disturbance	55.6%	44.4%	5.6%
Tibial Plateau (n=33)		Pain	66.7%	51.5%	3.1%
		Sensory Loss	0%	3%	0%
		Gait Disturbance	72.7%	45.5%	3.1%
Intra-Oral Bone (n=30)		Pain	58.6%	27.6%	0%
		Sensory Loss	27.6%	34.5%	17.2%
		Gait Disturbance	0%	0%	0%

Timeline of Harvest Site Adverse Events



Safety Summary

- **Established safety profile**
- **Thoroughly evaluated in these RCT**
- **Significantly fewer adverse events than bone graft**
- **Eliminates bone harvesting morbidity**

Conclusions

Ed Chin, DPh

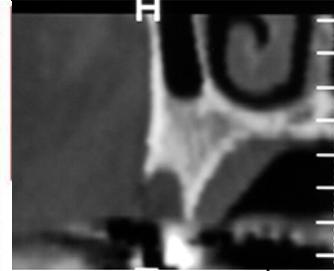
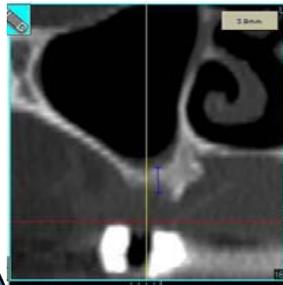
Group Director, Regulatory Affairs

Medtronic Spinal and Biologics

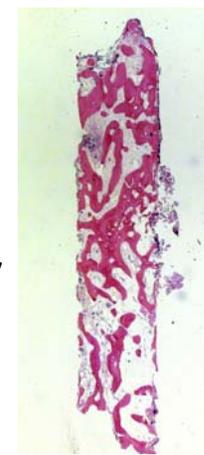
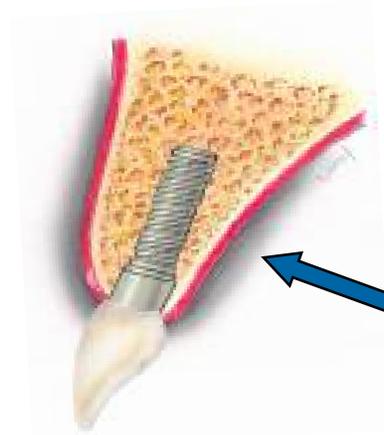
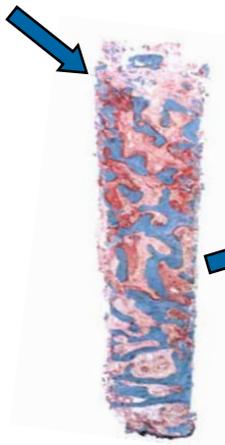
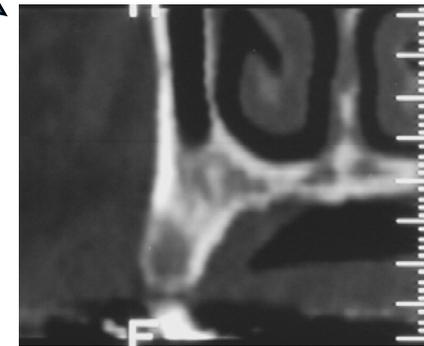
Proposed Indication For Use Statement

"INFUSE[®] Bone Graft is indicated as an alternative to autogenous bone graft for sinus augmentations and localized alveolar ridge augmentations for defects associated with extraction sockets."

Sinus Augmentation



Extraction Socket Augmentation



Implant and Tooth Restoration

Sinus Augmentation



Large bone loss on maxillary ridge

**Following INFUSE[®] Bone Graft,
multiple implants, and prosthetic
teeth replacement**



Extraction Socket Augmentation



Non restorable teeth

**Following INFUSE[®] Bone Graft,
dental implants, and prosthetic
teeth replacement**



SUMMARY

- **INFUSE induced new bone allowing for dental restoration in 2 separate IDE evaluations**
- **INFUSE is Safe and Effective for**
 - Sinus Augmentation and
 - Extraction Socket
- **INFUSE eliminates the need to harvest autogenous bone graft in oral maxillofacial procedures**

INFUSE[®] Bone Graft

SAFE and EFFECTIVE

Thank
You