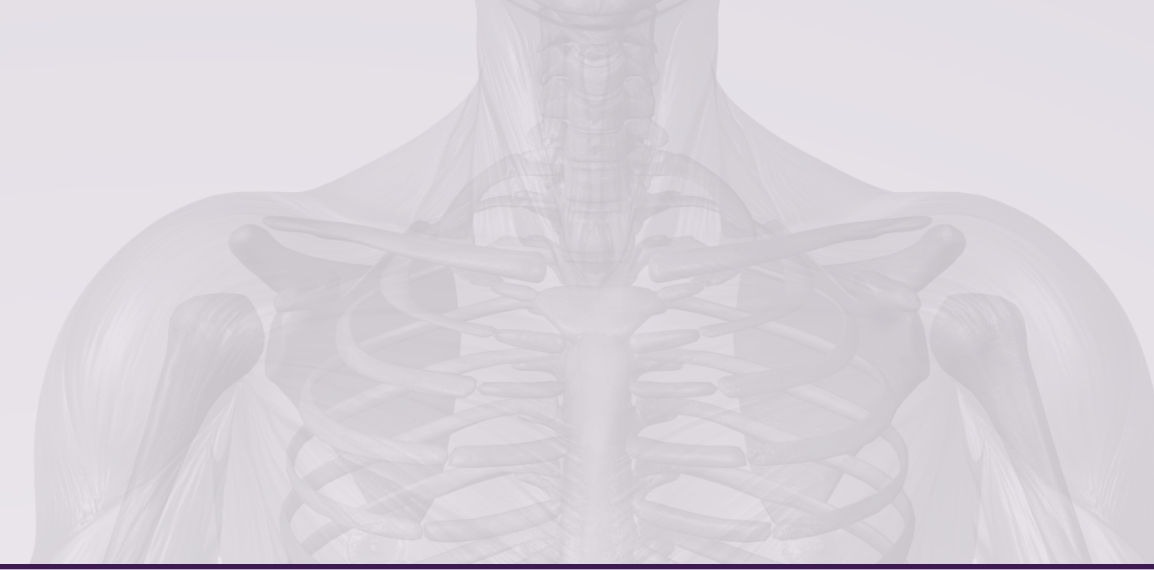


exogen[®]
ultrasound bone healing system

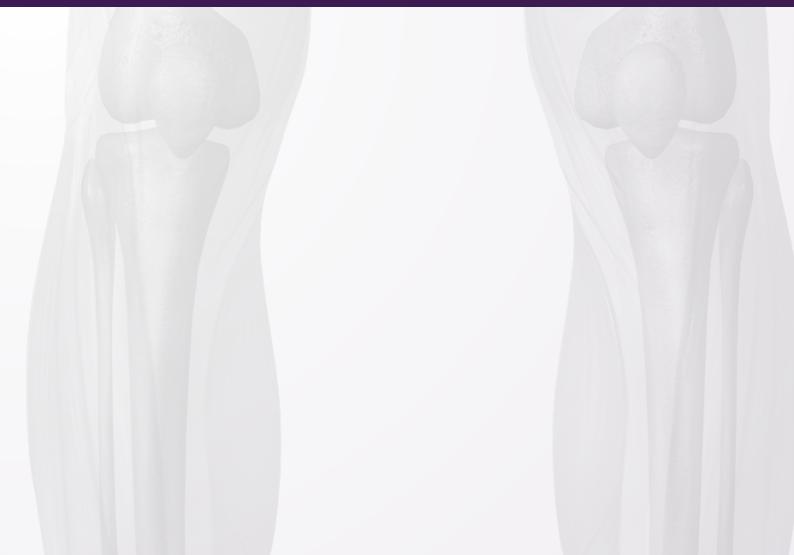
BONE HEALING.

PROVEN.





Ultrasound Bone Healing with EXOGEN



Product Overview

Ultrasound Bone Healing with EXOGEN.

Core Components of EXOGEN's Success

The EXOGEN Ultrasound Bone Healing System uses low-intensity pulsed ultrasound (LIPUS) technology to stimulate the body's natural bone healing process.¹

Proven Facts on EXOGEN

38%

faster healing of fresh fractures^{2,3}

86%

non-union fracture heal rate⁴

91%

treatment compliance⁵

20

minute daily treatment



Successful bone healing depends upon both effectiveness and treatment compliance.

EXOGEN delivers both.

Indications

Ultrasound Bone Healing with EXOGEN.

Summary of Indications for Use

EXOGEN is indicated for the non-invasive treatment of osseous defects (excluding vertebra and skull) that includes the treatment of delayed unions, non-unions[†], stress fractures and joint fusion. EXOGEN is also indicated for the acceleration of fresh fracture heal time, repair following osteotomy, repair in bone transport procedures and repair in distraction osteogenesis procedures.

[†] A non-union is considered to be established when the fracture site shows no visibly progressive signs of healing.

There are no known contraindications for the EXOGEN device. Safety and effectiveness have not been established for individuals lacking skeletal maturity, pregnant or nursing women, patients with cardiac pacemakers, on fractures due to bone cancer, or on patients with poor blood circulation or clotting problems. Some patients may be sensitive to the ultrasound gel. Full prescribing information can be found in product labeling, at www.exogen.com.



Treatment Tracking Calendar

Powered for Treatment Compliance

EXOGEN's built-in treatment tracking calendar tracks completed and missed treatments, making treatment compliance tracking convenient for patients and verifiable for physicians.

TREATMENT TRACKING CALENDAR
demonstrates higher compliance.⁶
Only EXOGEN has this feature.

MISSED TREATMENT

COMPLETED TREATMENT

COMPLIANCE SUMMARY



Powered for Treatment Compliance

EXOGEN Performance Program

EXOGEN Performance Program

The goal of the EXOGEN Performance Program is to provide added confidence in and adherence to EXOGEN treatment.

The EXOGEN Performance Program guarantees that radiographic healing progression will be shown in non-union fractures. If the requirements of the program are met and no healing progression is shown, out of pocket costs will be refunded to the patient.

20-minute Treatment

With treatments lasting just 20 minutes, EXOGEN fits conveniently into the patient's daily routine.



Important treatment compliance facts:

As many as 40% of patients fail to adhere to treatment recommendations⁷

Nonadherence reduces treatment benefits and can bias assessment of treatment effectiveness⁸

Compliance (synonym: adherence) is defined as the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen and is measured over a period of time and reported as a percentage⁹

Mechanism of Action

The EXOGEN Ultrasound Bone Healing System is a non-invasive treatment that works at the molecular level¹⁰

1. Stimulation

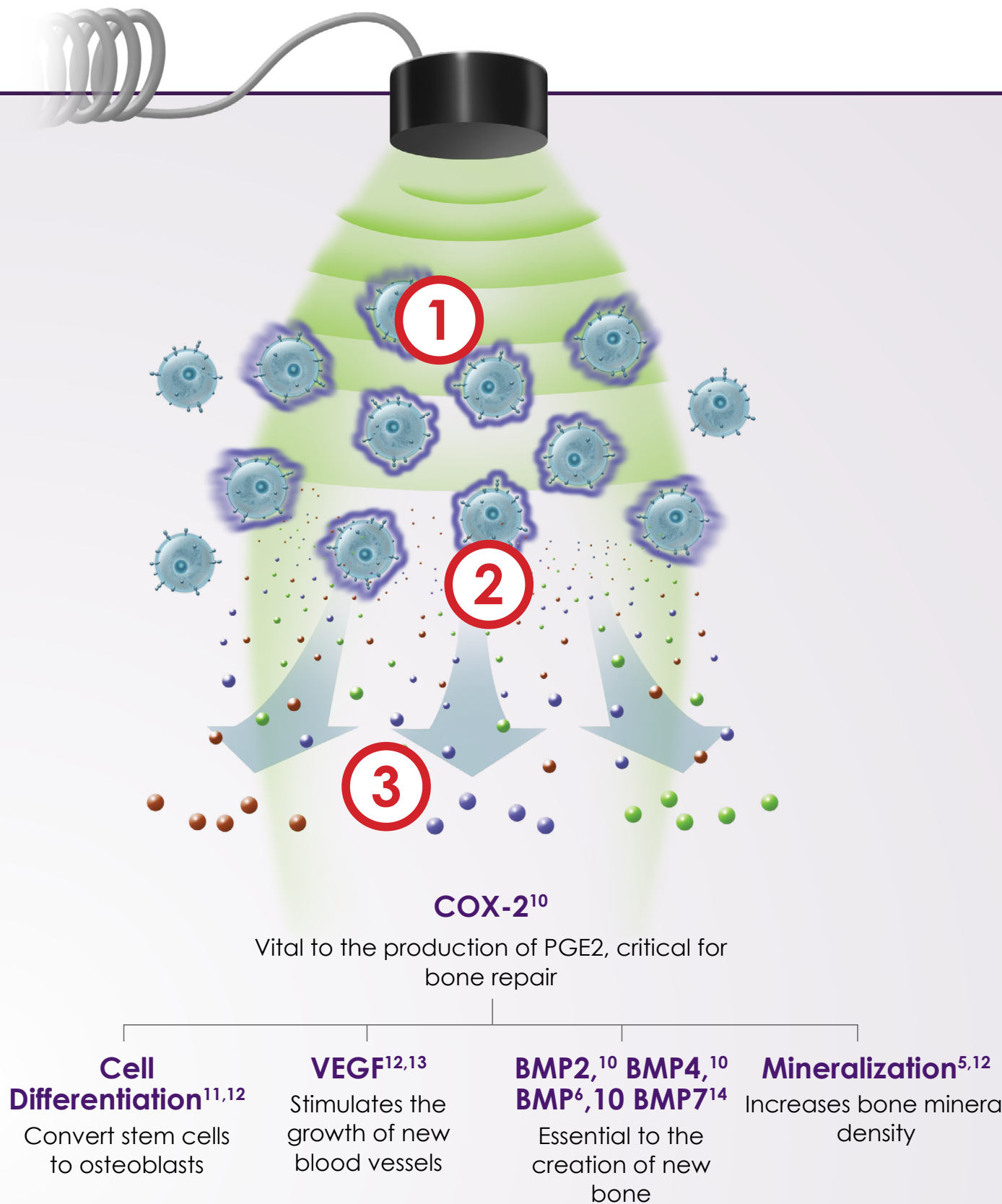
EXOGEN sends ultrasound waves through the skin and soft tissue to the fracture.

2. Activation

EXOGEN ultrasound activates cell surface mechanoreceptors called integrins, initiating an intracellular cascade that leads to upregulation.

3. Upregulation

EXOGEN ultrasound increases upregulation of genes and expression of proteins and growth factors critical to bone healing.



[Mechanism of Action Video](#)

[Go to video >](#)

Mechanism of Action

The EXOGEN Ultrasound Bone Healing System

EXOGEN can easily penetrate soft tissue to reach both deep and superficial fractures.

The depth and breadth of the EXOGEN signal enable it to treat superficial and deep indicated fractures, as well as non-union fractures with metal fixation or implants.^{15,16} Because the ultrasound waves travel easily through adipose tissue, it is suggested that EXOGEN therapy is effective for normally weighted and obese patients.¹⁷

Depth and breadth of penetration¹⁷:

- Beam reaches a depth of more than 260 mm
- Effective diameter of the ultrasound beam is more than 5 cm

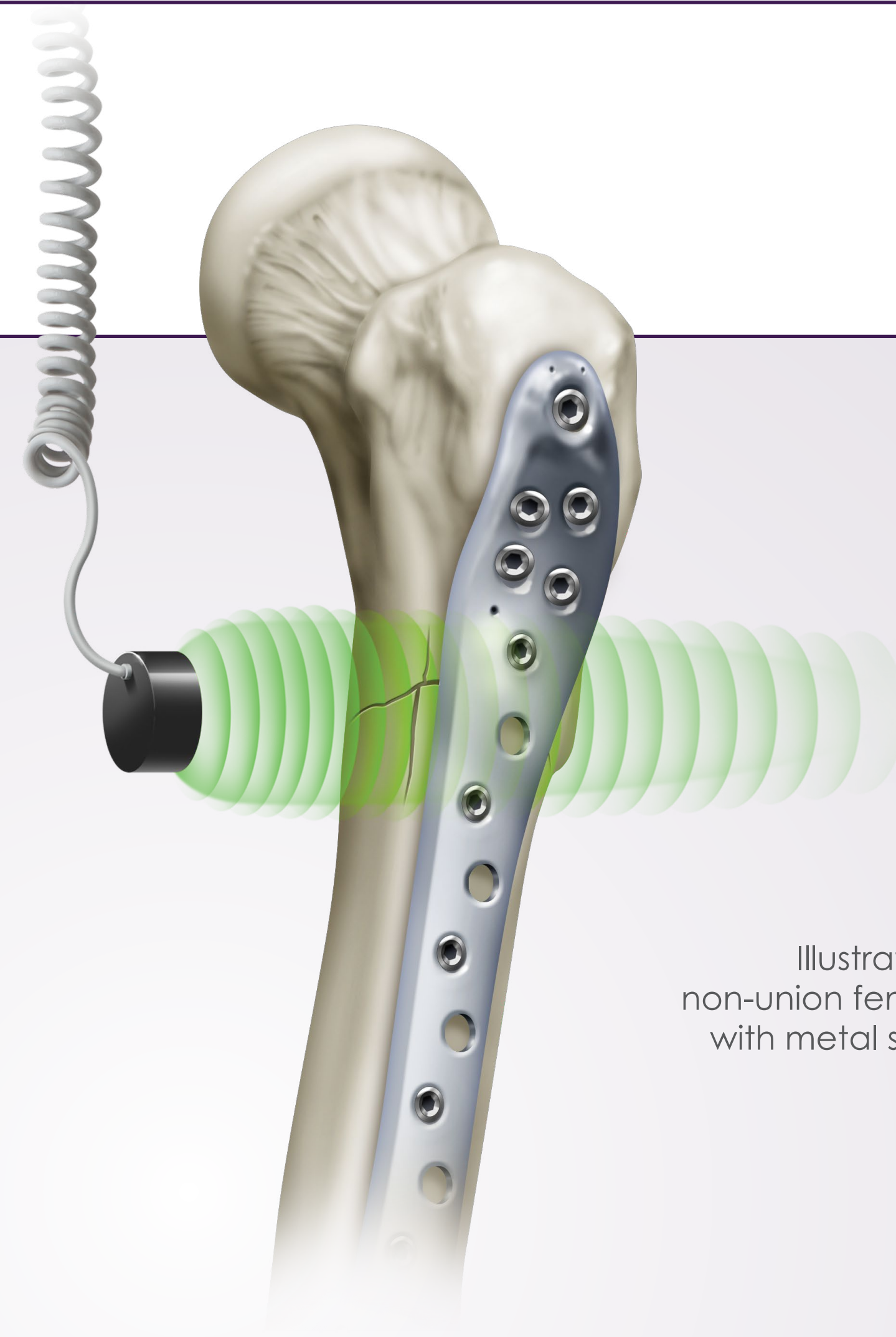


Illustration depicts non-union femur fracture with metal stabilization.

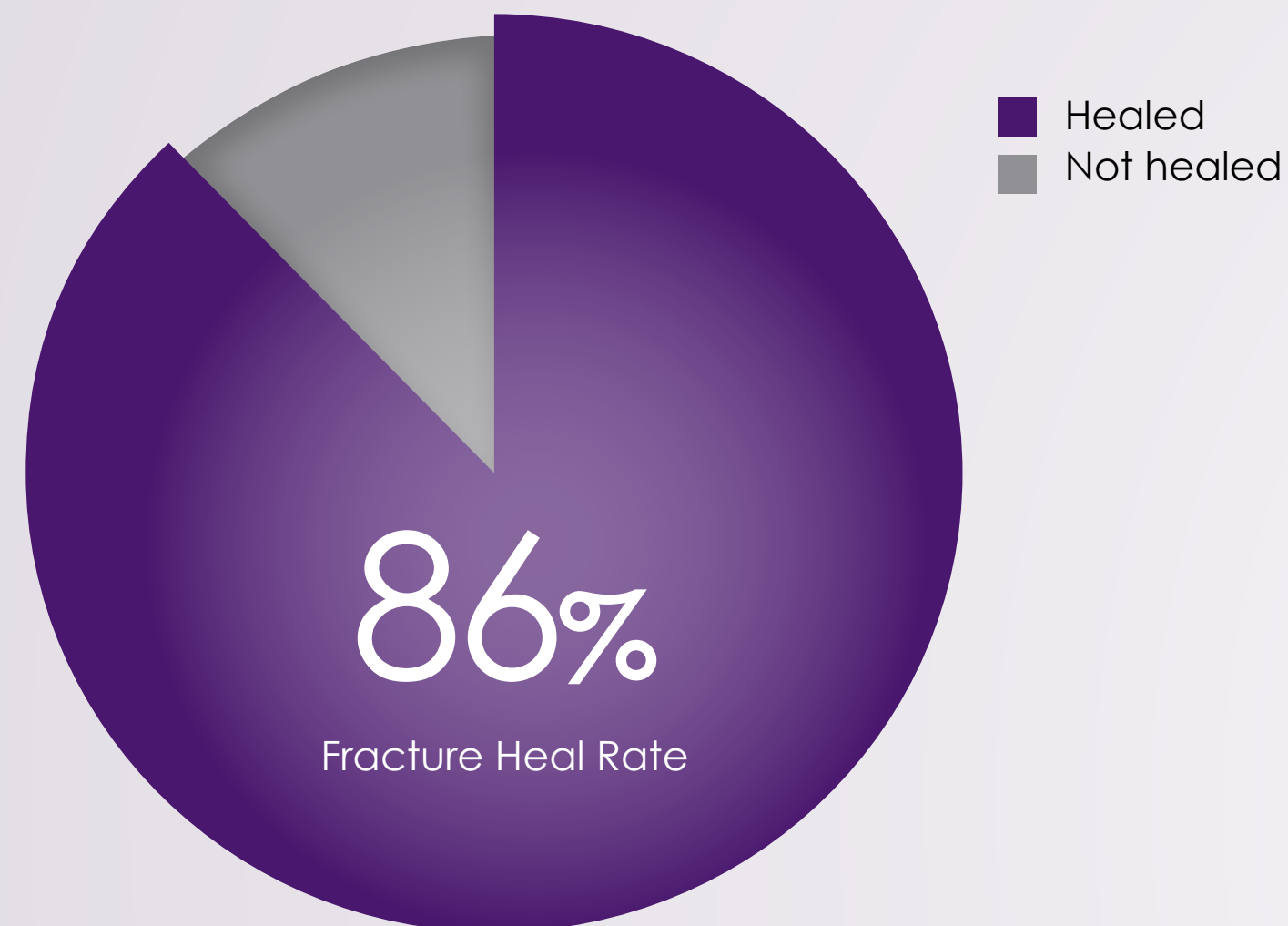


Non-Unions

Get high heal rates for non-union[†] fractures - 86%⁴

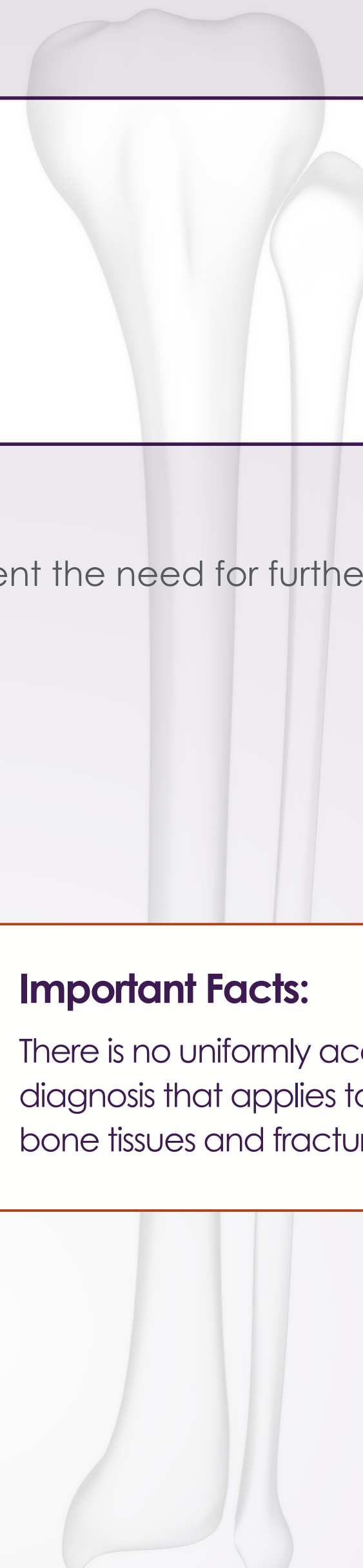
The EXOGEN Ultrasound Bone Healing System jump-starts the natural bone healing process¹ and may prevent the need for further surgery.⁴

Non-unions have no visual progression in healing without further intervention.¹⁸



Important Facts:

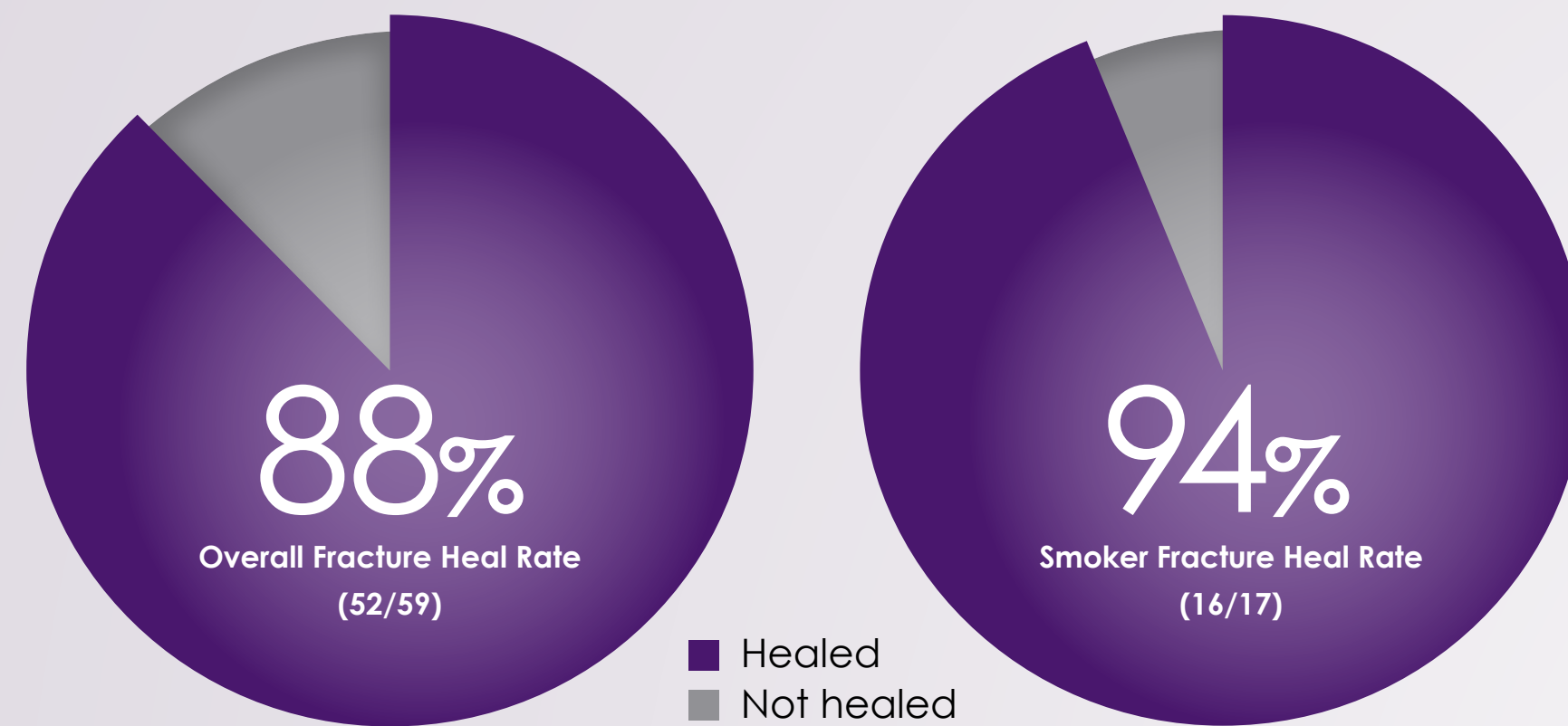
There is no uniformly accepted method of non-union diagnosis that applies to all fractures, given variations in bone tissues and fracture characteristics⁴



Evidence Based Medicine

Indications and results for the EXOGEN ultrasound system in the management of non-union:
a 59-case pilot study

Clinical study demonstrates 88% heal rate and >95% treatment compliance¹⁹



Considerations of Non-Union Therapy:

- Potential comorbidity associated with additional surgery (anesthesia, graft rejection, infection)
- Cost and effectiveness associated with EXOGEN - cost is lower than revision surgery with comparable efficacy¹⁹

Study facts:

- Retrospective case series of 59 non-unions[†]
- Inclusion criteria: stable fracture with first-line surgery, not consolidated at 6 months, fracture gap <10 mm (range: 2–10 mm, average 4 mm)
- Mean fracture age 9 months (271 days); 34% of patients had secondary/tertiary surgery prior to EXOGEN
- EXOGEN 20 min/day was the only change in treatment
- >95% treatment compliance rate**



Non-Unions — Heal Rates

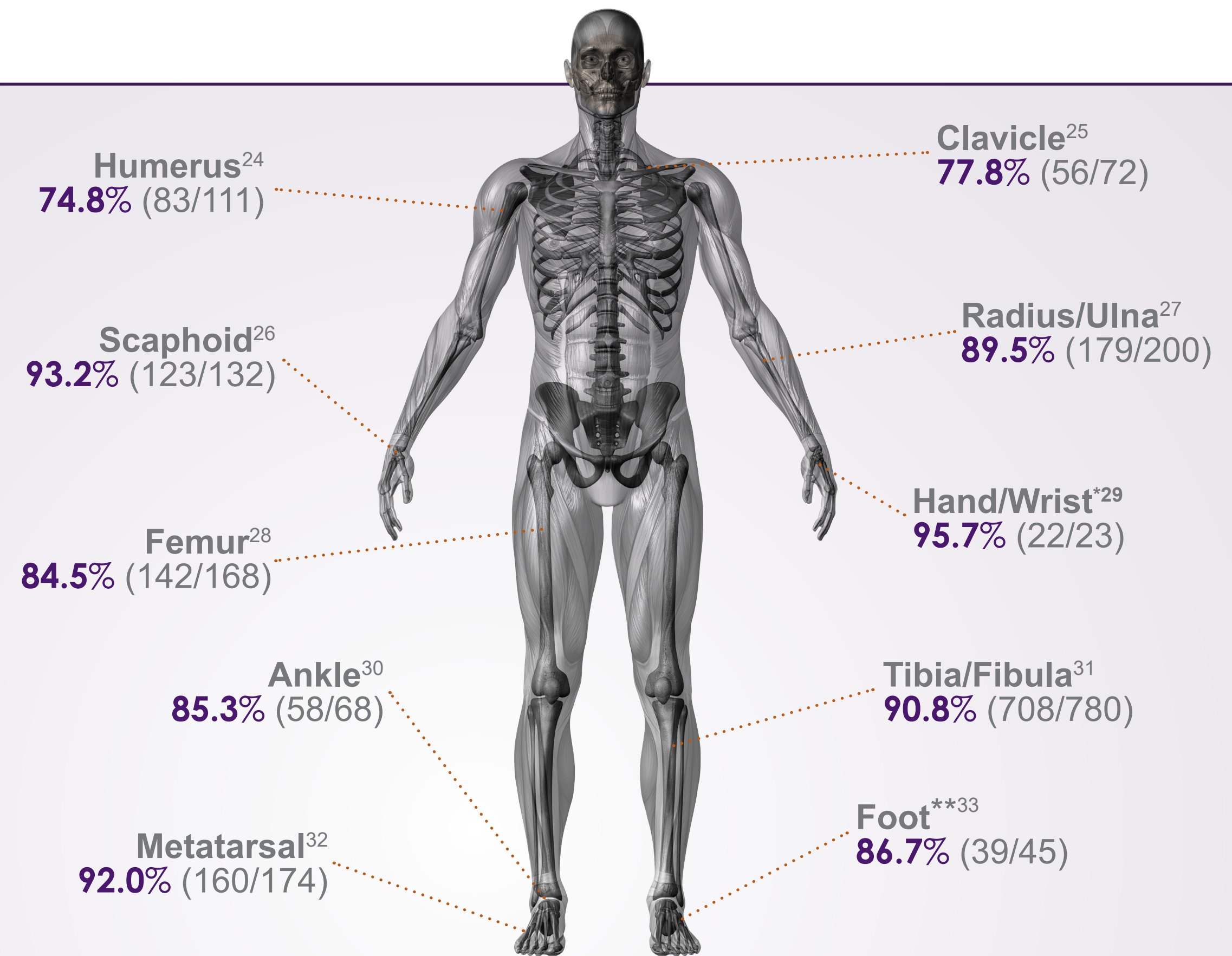
Numerous clinical studies with EXOGEN treatment show high non-union[†] heal rates.

Fracture management	Bone	Number of patients	Fracture heal rate
Conservative, internal fixation and external fixation	ankle, clavicle, femur, hip and rib, humerus, knee, metatarsal, patella, phalanges, radius, scaphoid, shoulder, tibia/fibula, ulna, other wrist and hand bones, other foot bones	3,685	84.1% ²¹
External fixation	femur, tibia, radius, ulna, humerus	18	89% ²⁰
Surgical	humerus, ulna, radius, metacarpal, femur, tibia, fibula, metatarsal	59	88% ¹⁹
Conservative, internal fixation and external fixation	clavicle, femur, humerus, metatarsal, radius, scaphoid, tibia/fibula, ulna	29	86% ⁴
Conservative, internal fixation and external fixation	clavicle, femur, foot, humerus, metatarsal, radius, scaphoid, tibia/fibula, ulna, other bones	366	86% ¹⁸
Conservative	clavicle, femur, radius, ulna, scaphoid, tibia	380	85.2% ²²
Conservative, internal fixation and external fixation	ankle, clavicle, femur, humerus, metatarsal, scaphoid, tibia/fibula, ulna	67	85% ²³



Common Fractures at Risk for Non-Unions†21

EXOGEN may prevent the need for further surgery in many cases.⁴



Heal rates based on fracture age of 91–180 days.²⁴⁻³³

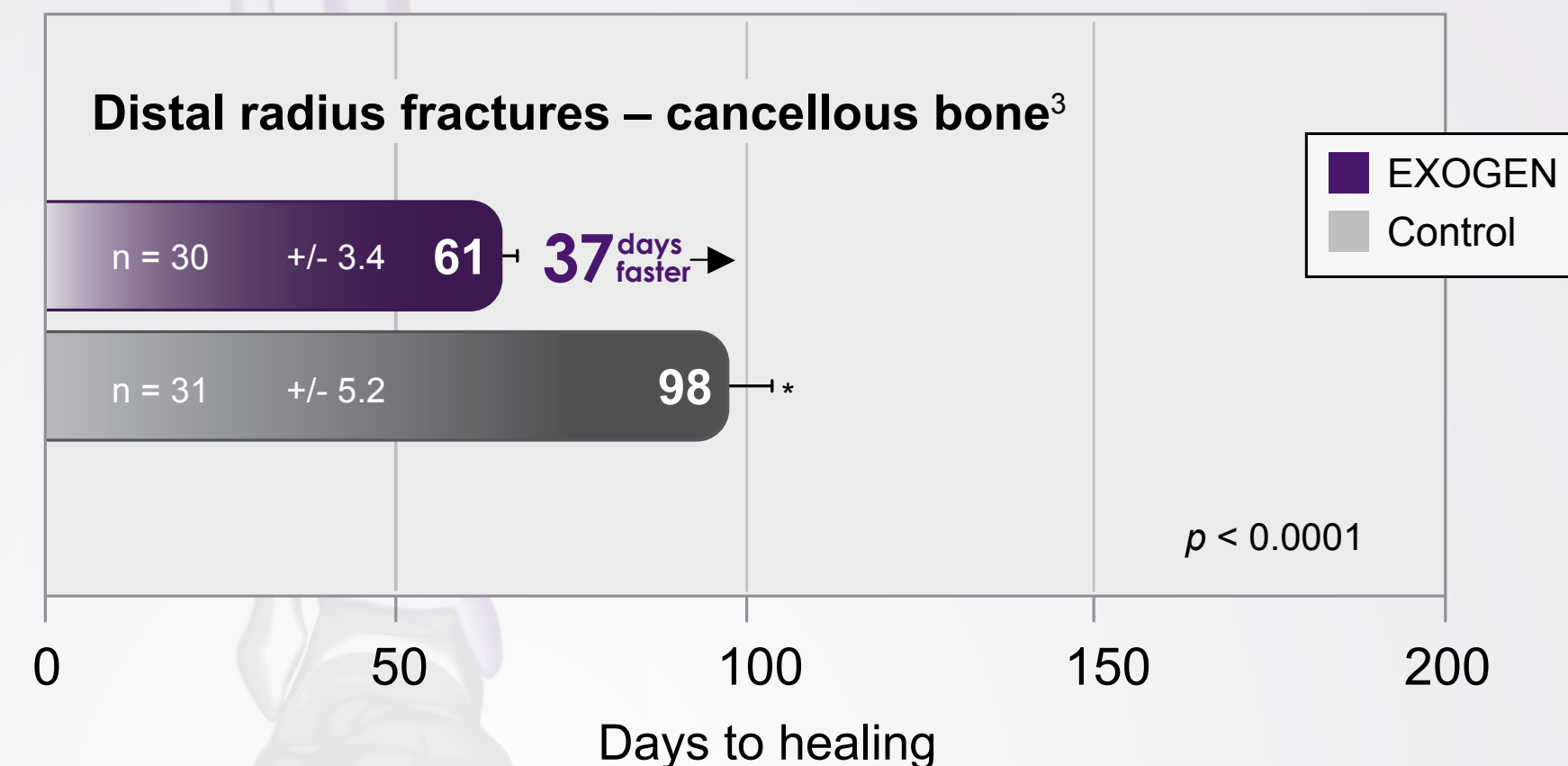
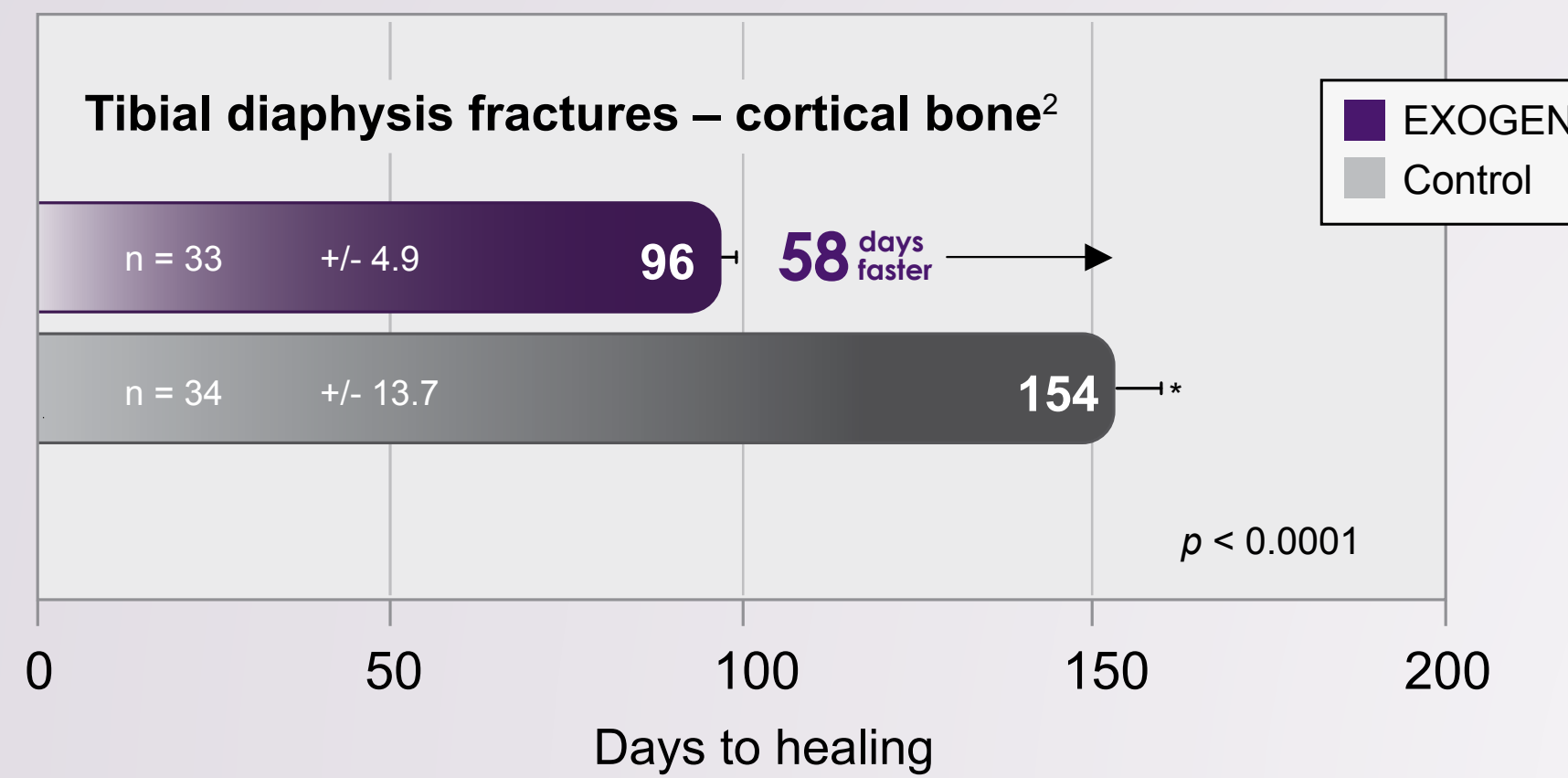
*Includes metacarpal, carpal and hamate

**Includes talus, calcaneus, tarsal navicular, cuboid and cuneiform

Fresh Fractures

EXOGEN accelerates healing of fresh fractures by 38%^{2,3}

EXOGEN treatment accelerates healing in both cortical and cancellous bone.^{2,3,34,35}

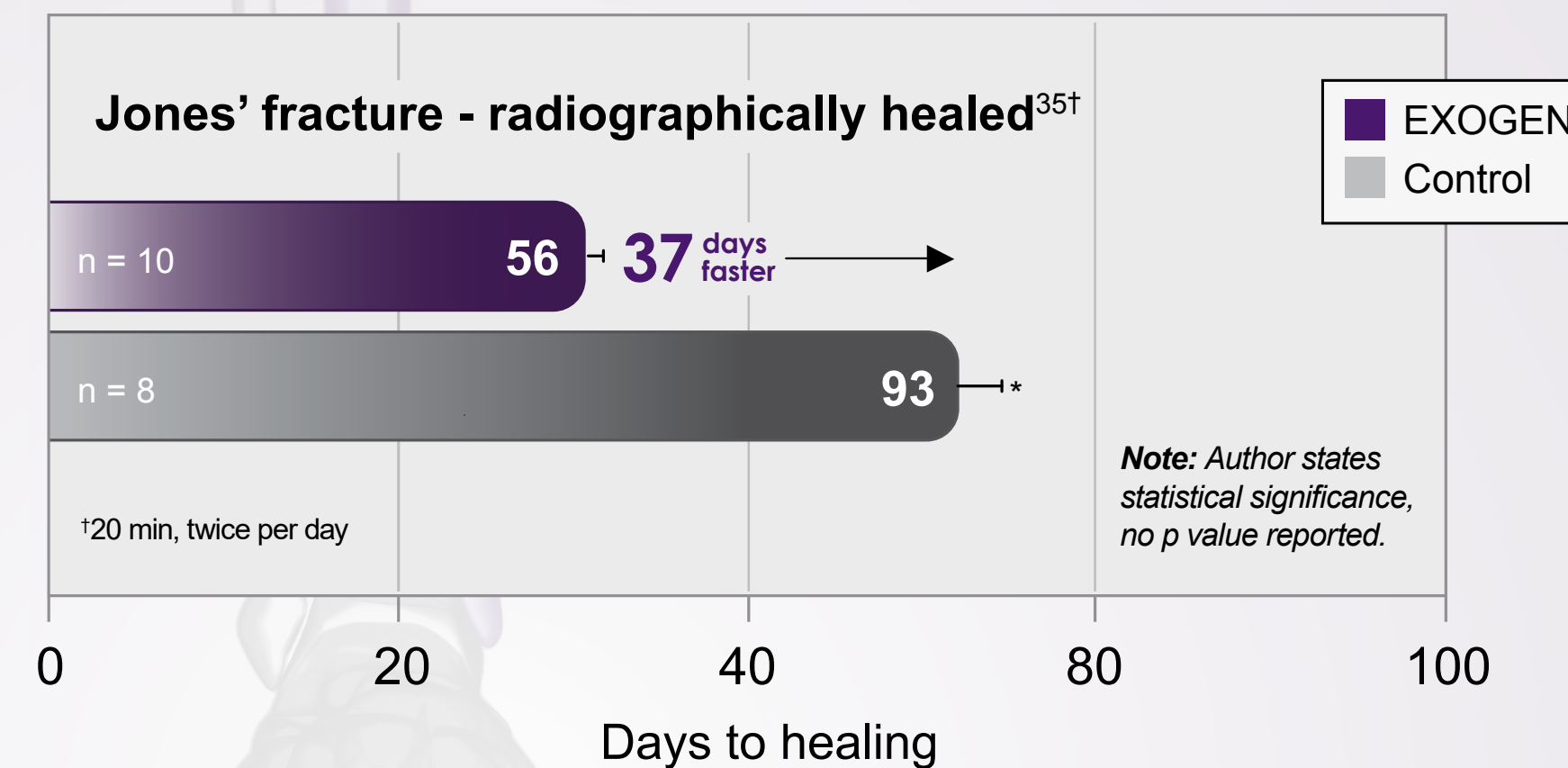
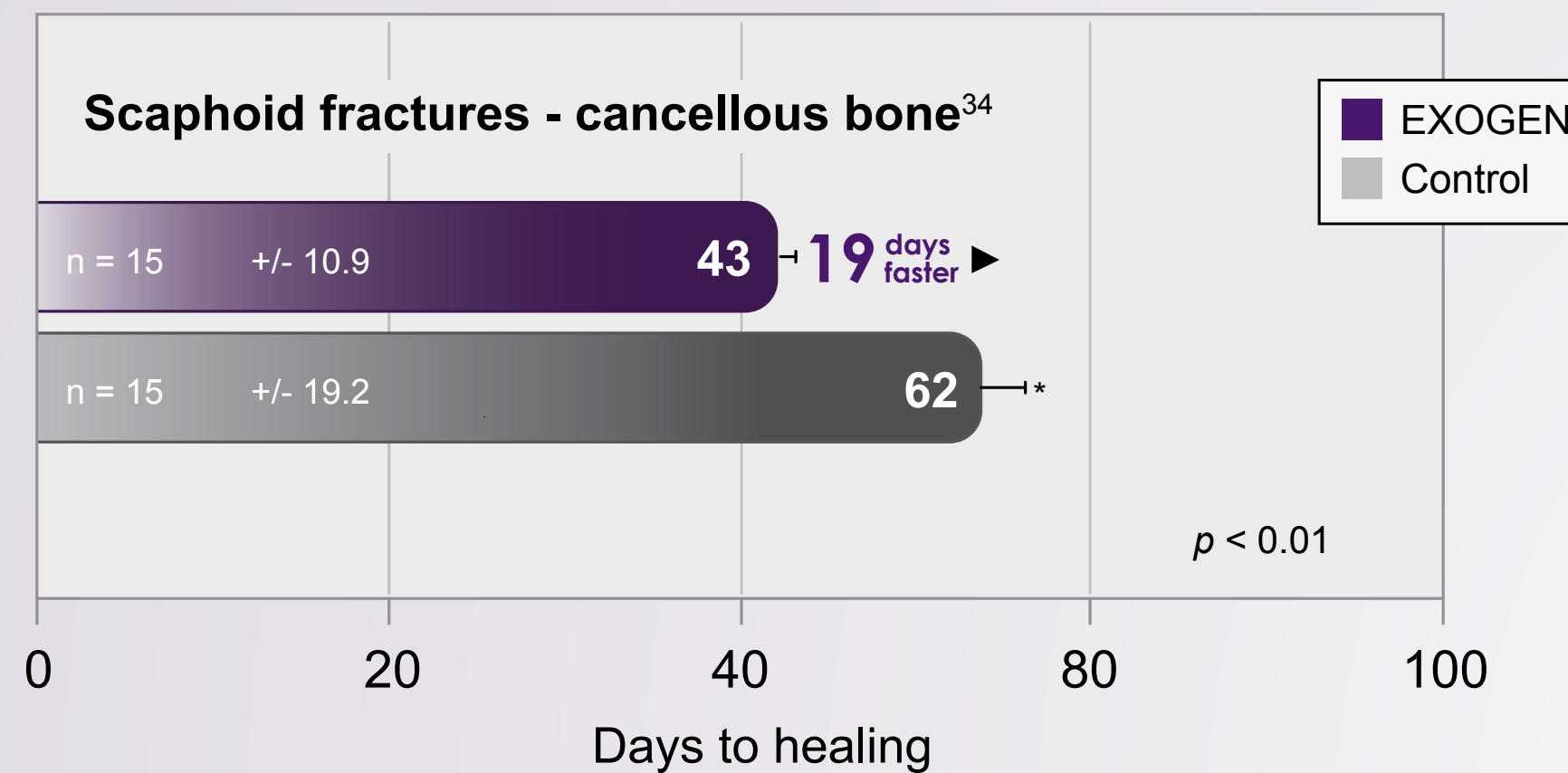


*Error bars represent standard error of the mean

Fresh Fractures

EXOGEN accelerates healing of fresh fractures by 38%^{2,3}

EXOGEN treatment accelerates healing in both cortical and cancellous bone.^{2,3,34,35}



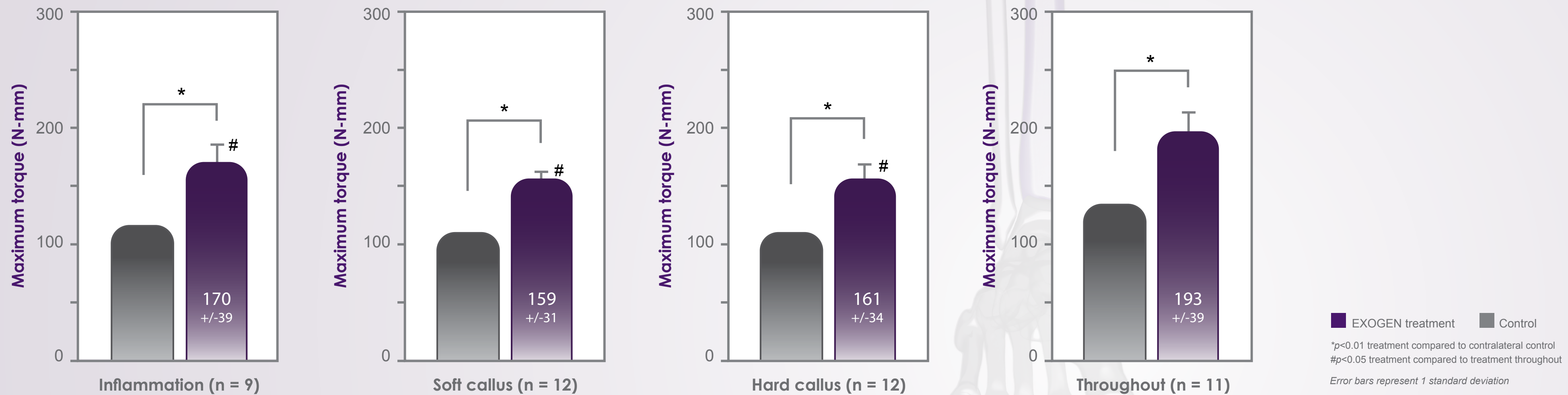
*Error bars represent standard error of the mean

Fresh Fractures

EXOGEN accelerates healing of fresh fractures by 38%^{2,3}

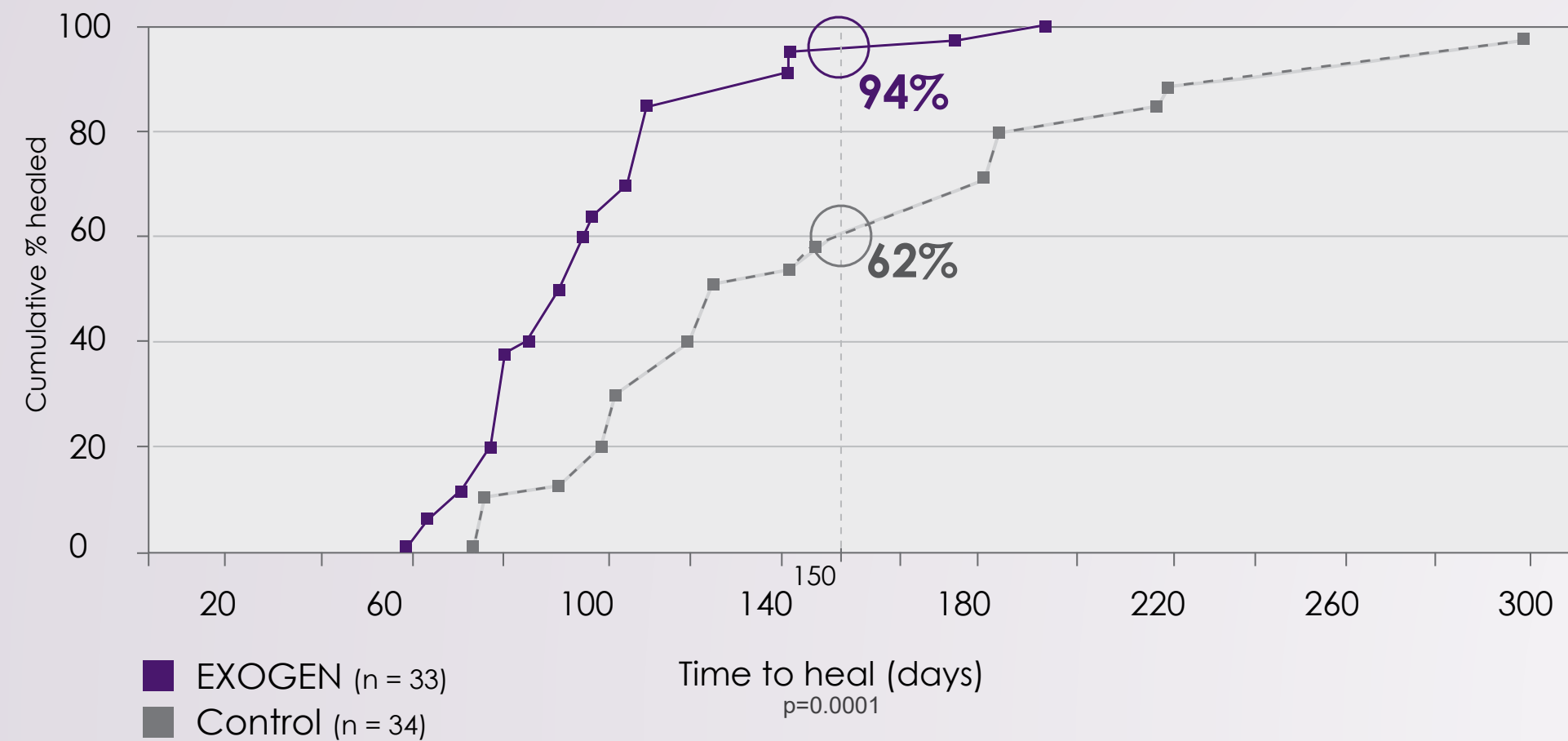
EXOGEN treatment accelerates fracture healing at every stage³⁶ with maximum impact being achieved when applied throughout the entire healing process.

Maximum torque of the EXOGEN-treated femurs was significantly greater than the placebo controls at each phase of fracture healing in an animal model.³⁶

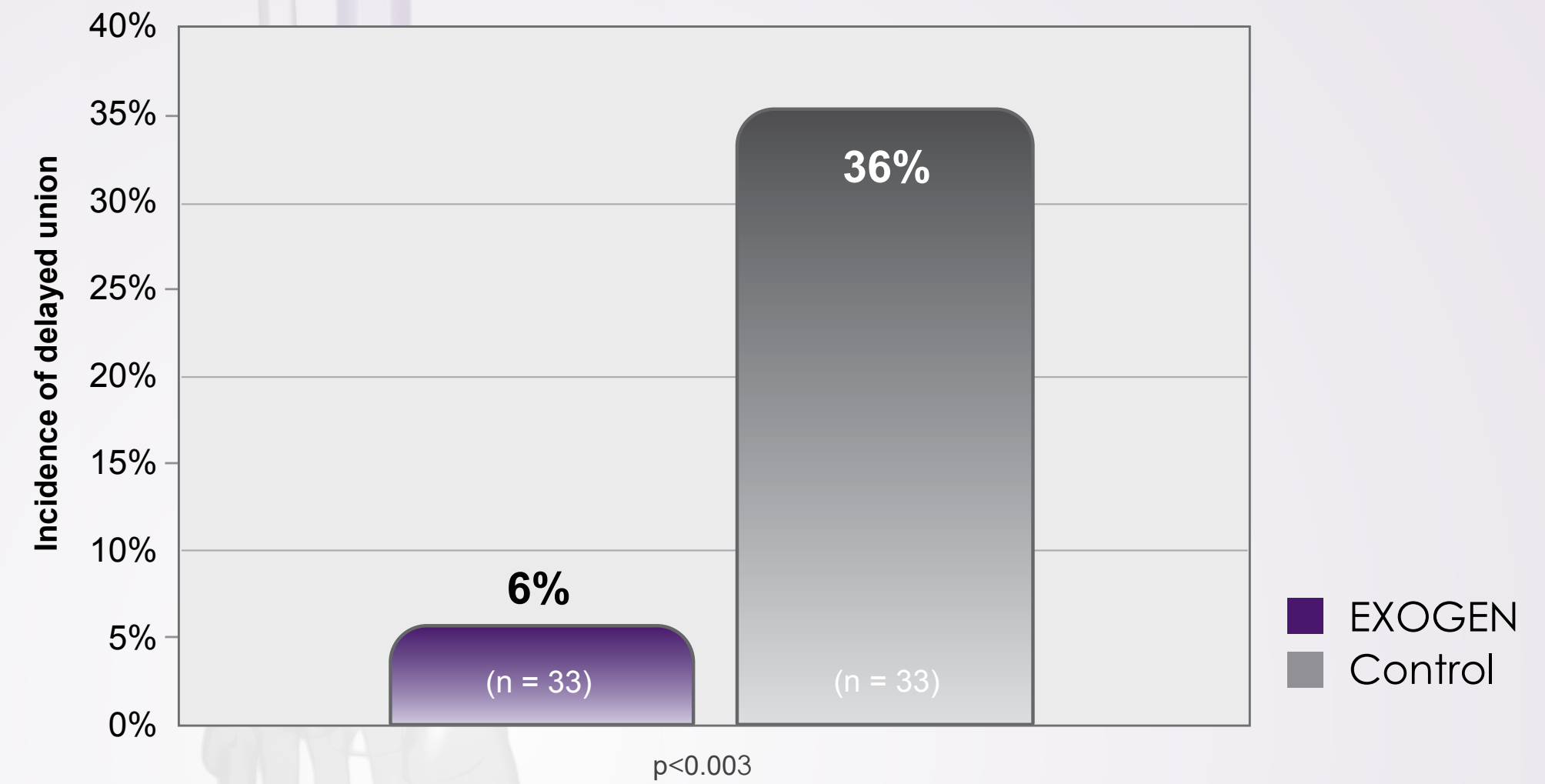


EXOGEN Accelerates Healing in Tibial Fractures

At 150 days, 94% of EXOGEN patients were healed while only 62% of placebo-treated patients healed.²



Early EXOGEN treatment reduced the incidence of delayed unions in tibial fractures (83% relative risk reduction) reducing the need for secondary procedures.³⁷



At-Risk Patients

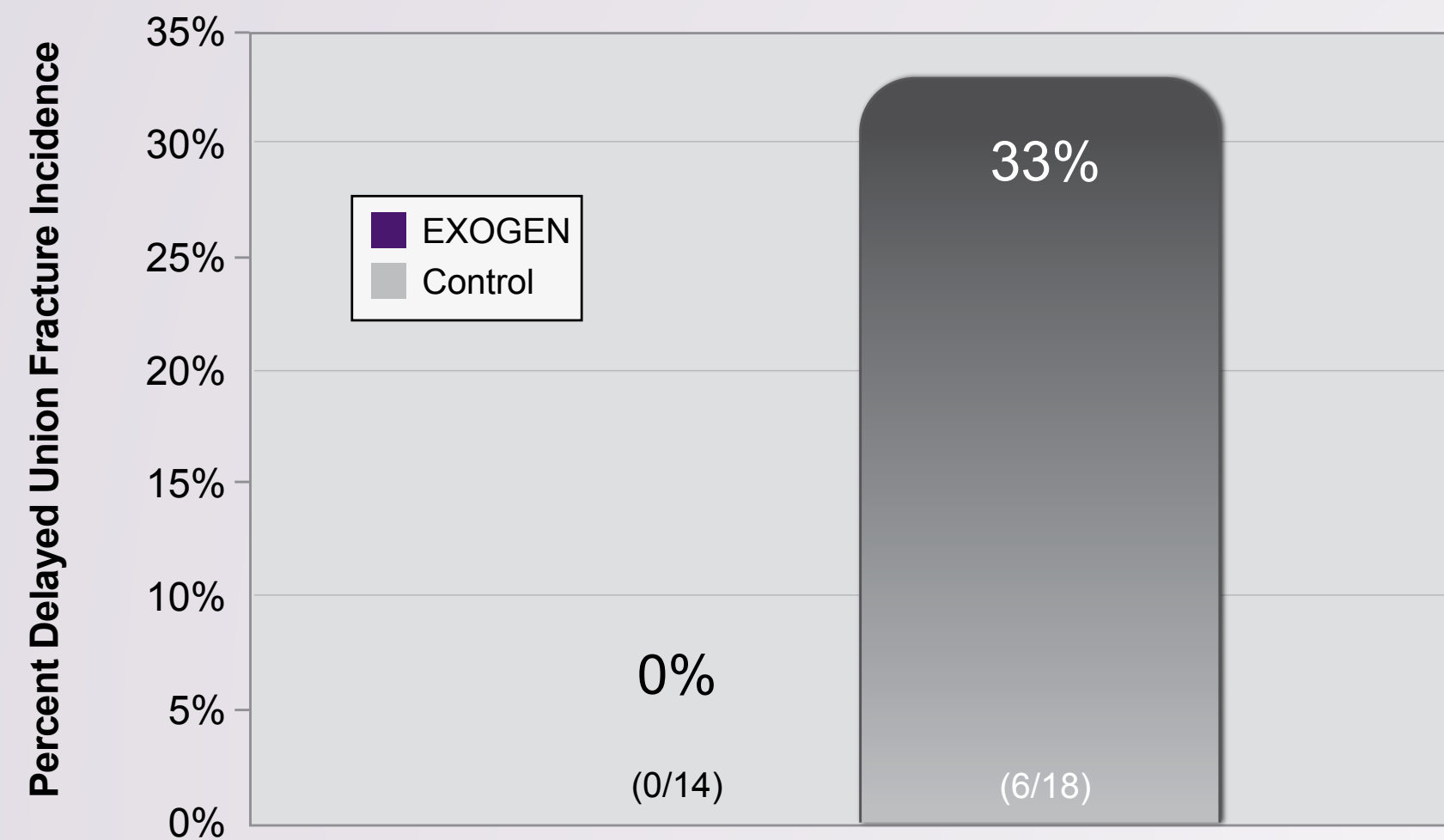
Smokers

EXOGEN treatment accelerates healing in patients who smoke³⁸

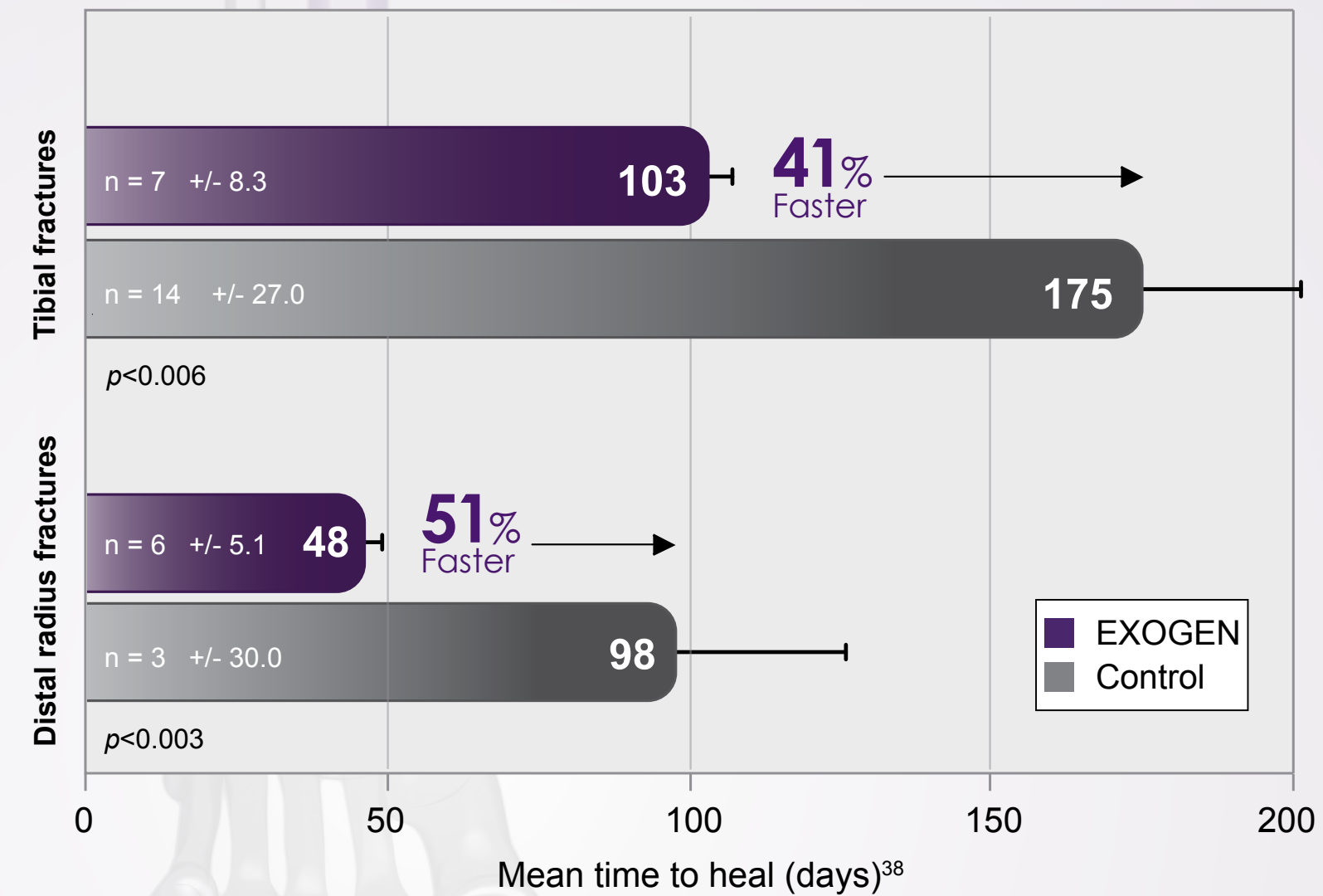
Effects of smoking on fracture healing:

- Reduces bone density and increases risk of fracture³⁸
- Hinders fracture healing by inhibiting vascularization at bone healing sites³⁹

0% of EXOGEN-treated smokers* developed a tibial delayed union.³⁸



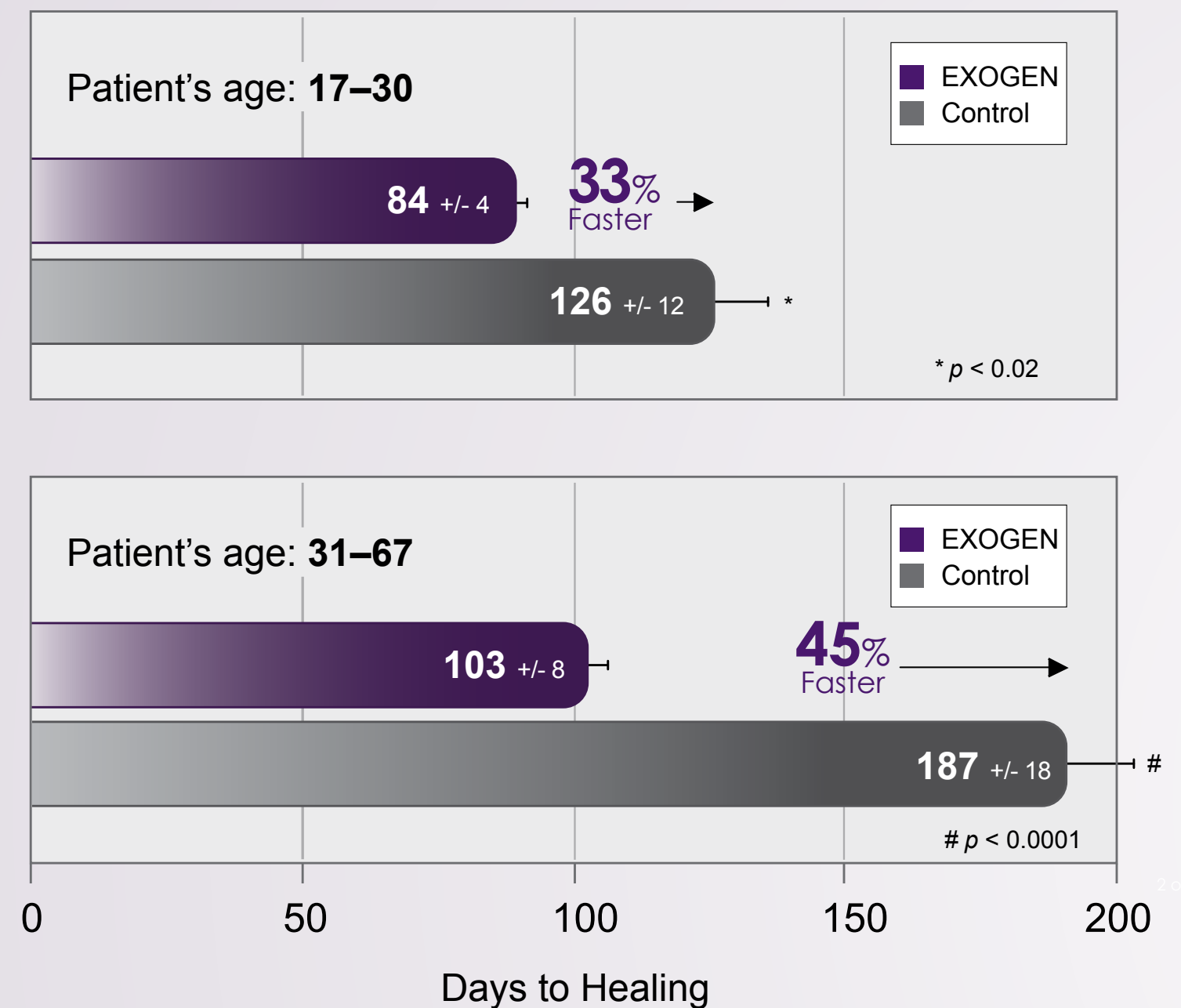
*Current smokers + stopped <10 years ago.



At-Risk Patients

Advanced Age

EXOGEN treatment accelerates healing of fresh fractures in younger and older patients.³⁷



Effects of advanced age on fracture healing:

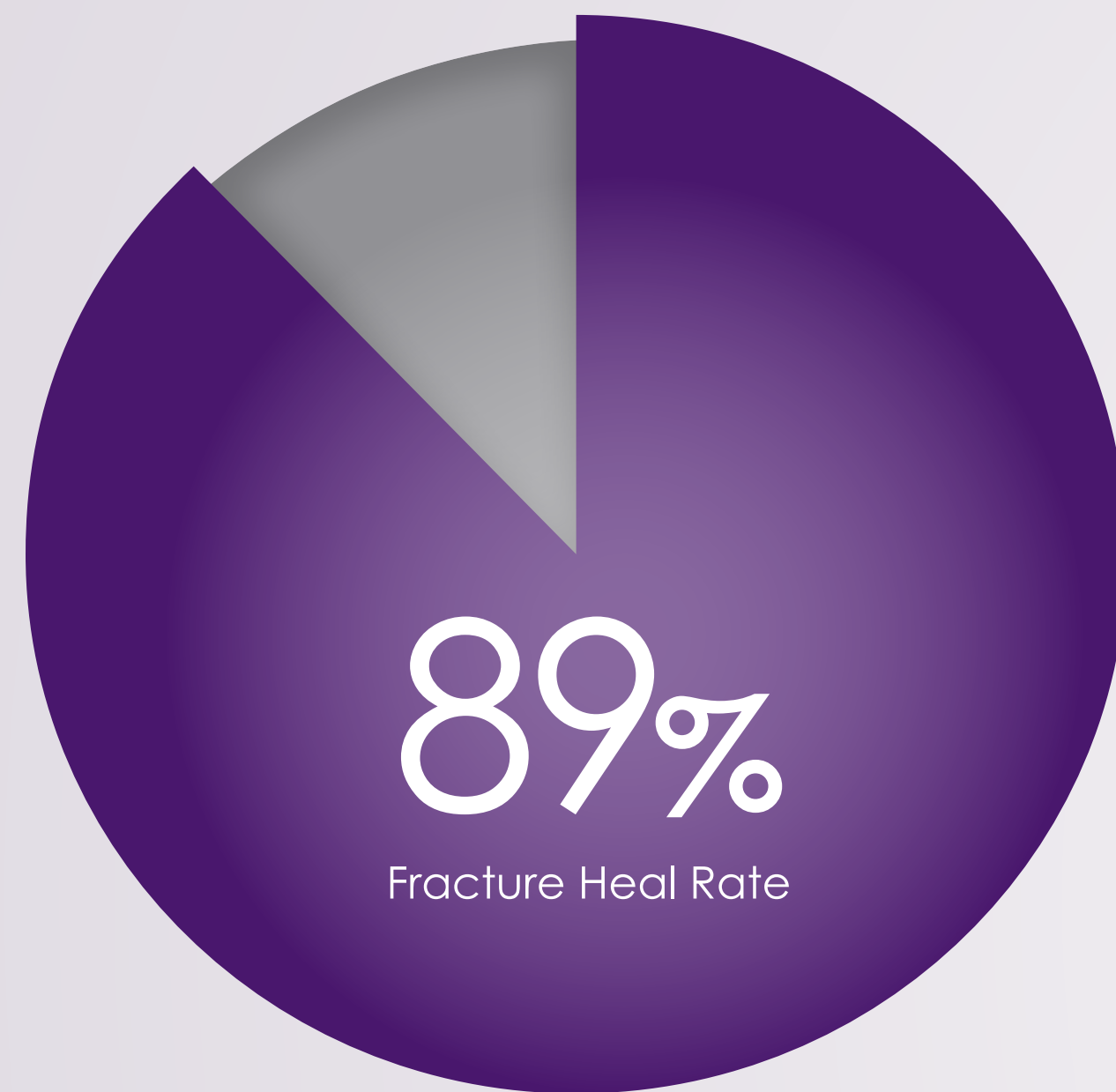
Number of bone marrow stem cells drops considerably during aging⁴⁰

Hinders fracture healing by inhibiting vascularization at bone healing sites⁴¹

At-Risk Patients

High-Energy Trauma

Fractures caused by high-energy trauma are more likely to develop a non-union.²⁰



- Healed
- Not healed

Important Fact:

A high degree of soft tissue damage is known to impair fracture healing^{20,42}

Study facts:

- 18 severe compound high-energy fractures
- Varying degrees of bone comminution
- Severe soft- and hard-tissue damage
- Previous treatment included either external fixation or IM nail



Patient Success

Clinical studies show that EXOGEN heals breaks not healing on their own at a high heal rate of up to 86%⁴ and speeds up healing of fresh fractures by 38%^{2,3}

> 53-year-old female school principal

History of non-union for prior midfoot deformity correction

> 20-year-old male college football player

- History of Jones' fracture
- Two prior surgeries
- No co-morbidities



Tibia Case Study

Clinical studies show that EXOGEN heals breaks not healing on their own at a high heal rate of up to 86%⁴ and speeds up healing of fresh fractures by 38%^{2,3}

53-year-old female school principal

History of non-union for prior midfoot deformity correction



INITIAL HISTORY

- Tibia fracture at external fixation pin site
- Closed reduction with long-leg cast
- Non-weight bearing

3 MONTHS

- No progression of healing
- Non-union diagnosis
- EXOGEN **prescribed**
- Remained in long-leg cast



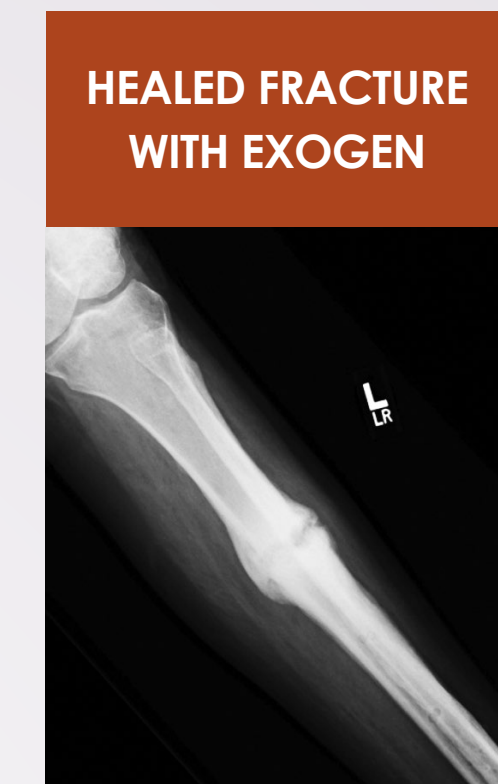
5 MONTHS

- Progressed to short-legged walking cast



6 MONTHS

- Significant bony healing



7 MONTHS

- **Non-union healed**
- Additional bone healing evident
- Surgery avoided

Tibia Case Study

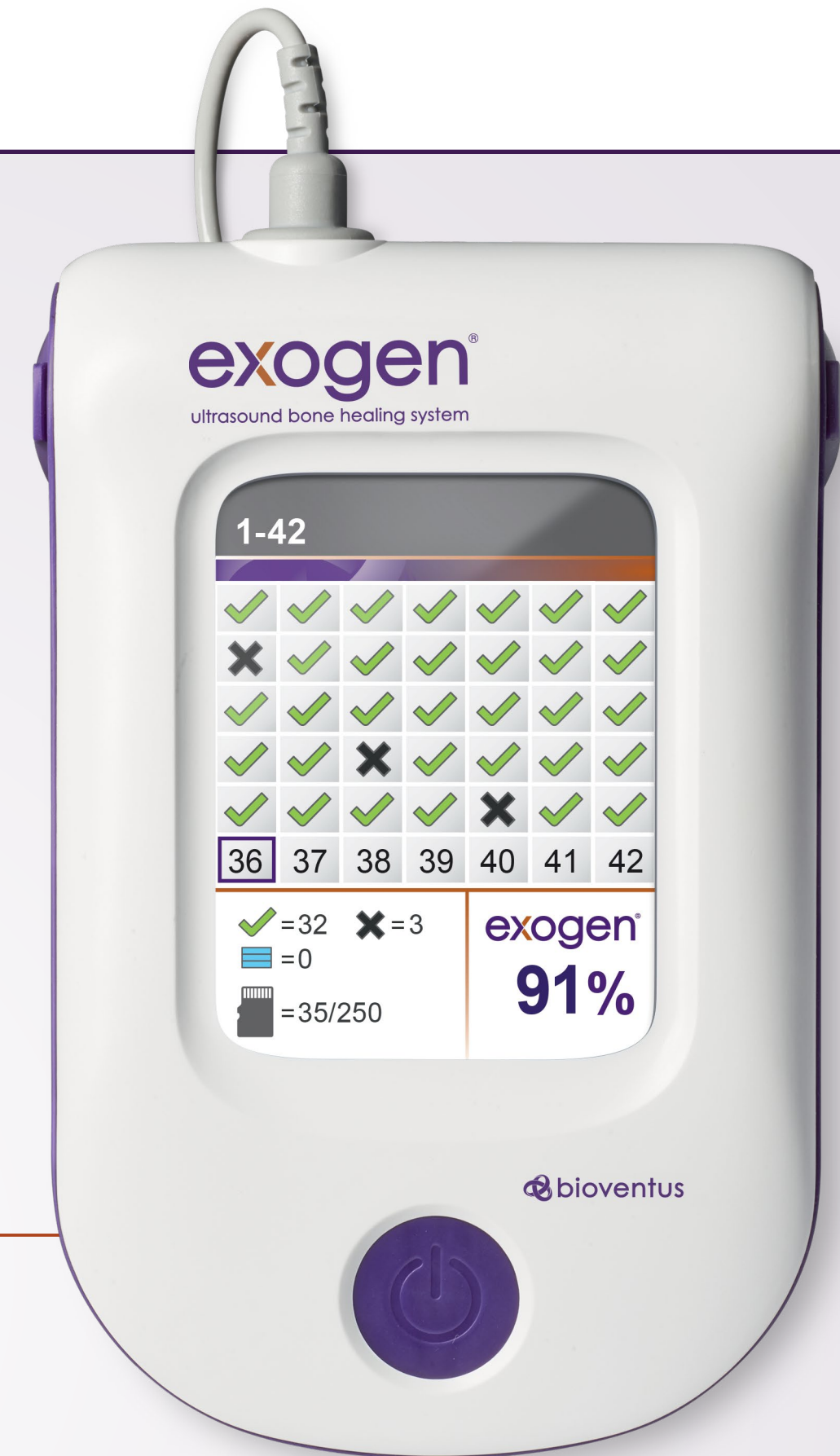
Clinical studies show that EXOGEN heals breaks not healing on their own at a high heal rate of up to 86%⁴ and speeds up healing of fresh fractures by 38%^{2,3}

53-year-old female school principal

History of non-union for prior midfoot deformity correction

Risks avoided by not doing surgery

- Infection
- Wound healing issues
- Nerve injury
- Deep vein thrombosis
- Pulmonary embolism
- Anesthesia-associated complications



Metatarsal Case Study

Clinical studies show that EXOGEN heals breaks not healing on their own at a high heal rate of up to 86%⁴ and speeds up healing of fresh fractures by 38%^{2,3}

20-year-old male college football player

- History of Jones' fracture + Two prior surgeries + No co-morbidities



INITIAL HISTORY

- Motor vehicle accident—re-fractured metatarsal on right foot
- Treated conservatively with cast and boot

3 MONTHS

- No progression with healing; non-union diagnosis
- Screw from prior surgery is bending
- EXOGEN **prescribed**
- Boot with weight bearing continued

HEALED FRACTURE 17 WEEKS EXOGEN USE



SUCCESS WITH EXOGEN

7 MONTHS

- Complete union noted 17 weeks after initiating EXOGEN
- Patient asymptomatic
- Additional surgery avoided

8 MONTHS

- Patient returned to football

Metatarsal Case Study

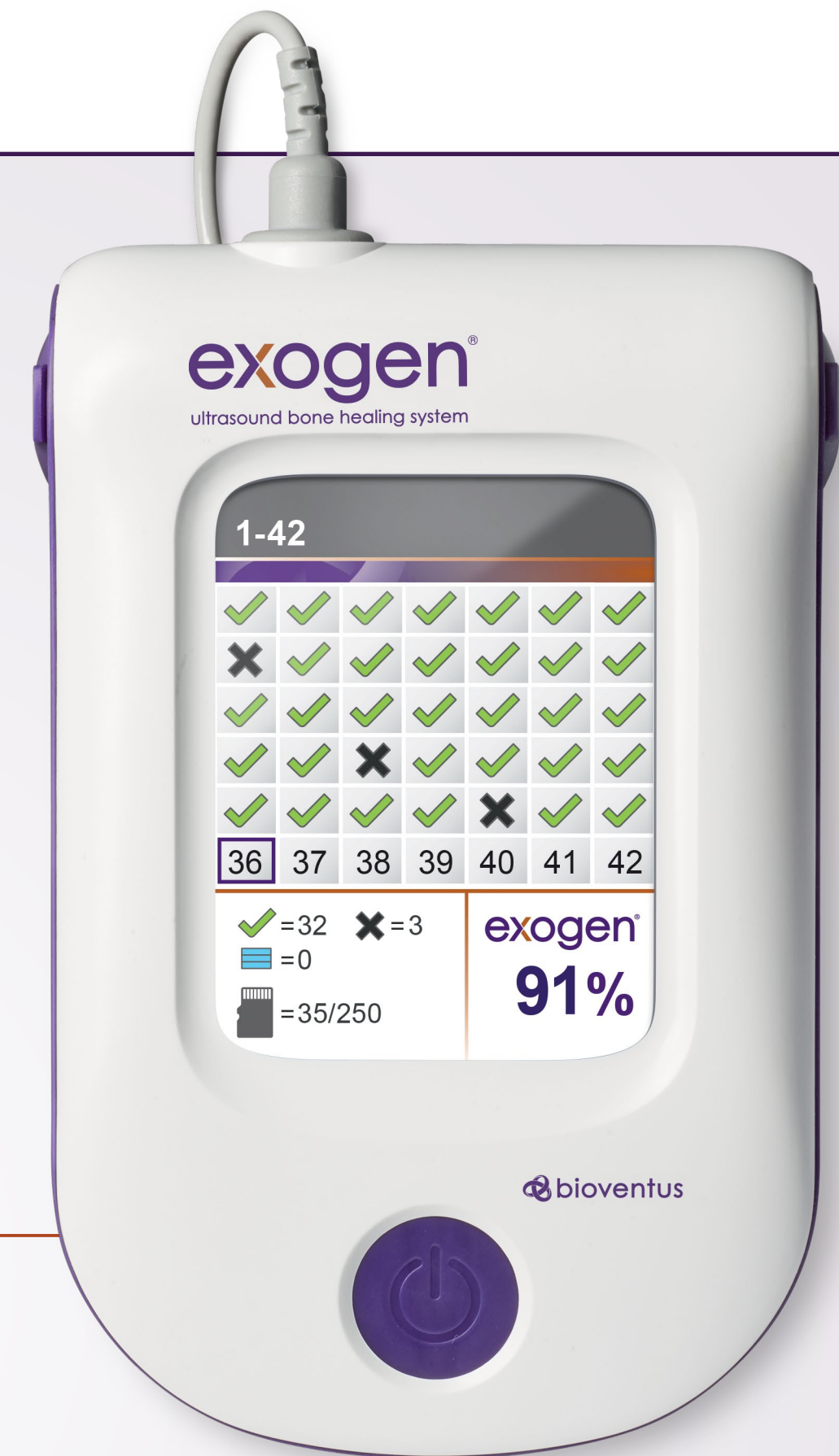
Clinical studies show that EXOGEN heals breaks not healing on their own at a high heal rate of up to 86%⁴ and speeds up healing of fresh fractures by 38%^{2,3}

20-year-old male college football player

- History of Jones' fracture + Two prior surgeries + No co-morbidities

Risks avoided by not doing ADDED surgery

- Infection
- Wound healing issues
- Nerve injury
- Deep vein thrombosis
- Pulmonary embolism
- Anesthesia-associated complications



Patient Support

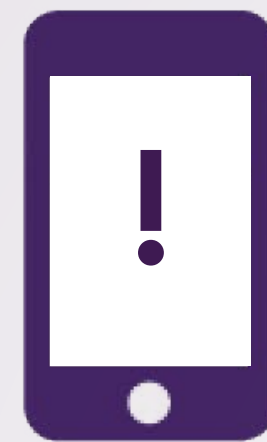
EXOGEN provides patients with tools for success

exogen[®]
connects



1. Download

The EXOGEN CONNECTS app, available on the App Store and Google Play Store, is easy to download and activate.



2. Receive

Patients receive daily treatment reminders on their smartphone.



3. Treat

Automated reminders encourage patients to complete their daily 20-minute treatment.



4. Heal

Using EXOGEN as prescribed can help put patients on the road to faster healing.



Patient Support

EXOGEN provides patients with tools for success

Benefits of EXOGEN

38%

EXOGEN accelerates the time to healing of fresh fractures by 38%^{2,3}

91%

EXOGEN has demonstrated a 91% treatment compliance rate⁵

Safe

Non-invasive treatment with no contraindications^{4,3}

20min.

Effective in just 20 minutes a day

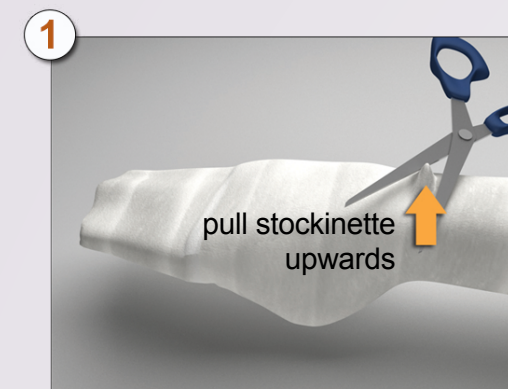


Casting & Ports

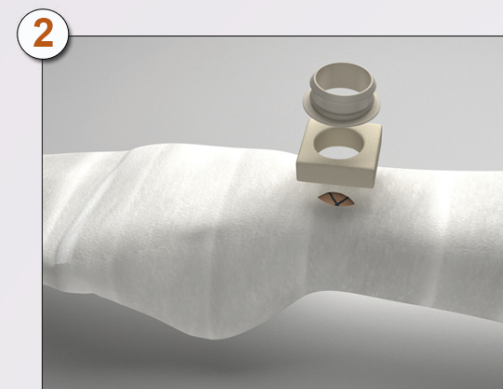
EXOGEN easily incorporates into casts

Built into cast method

Building the EXOGEN treatment port into a cast is the recommended method of preparing a patient to use EXOGEN.



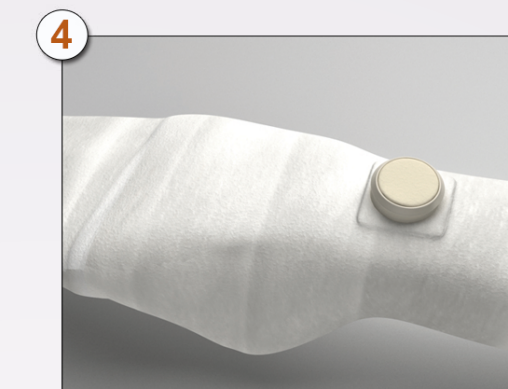
- Mark treatment area and put on stockinette
- Cut hole in stockinette over treatment site, make certain marked area is open to skin



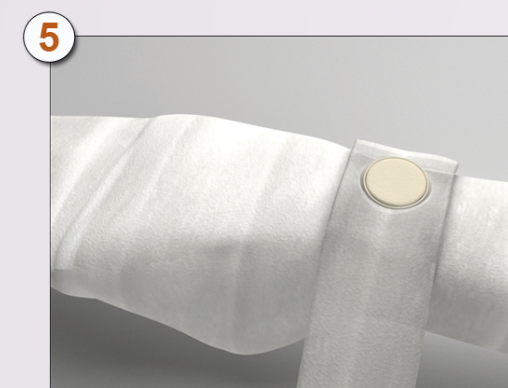
- Peel off adhesive backing from off-white square pad and stick to bottom of RAF
- Insert assembly into stockinette



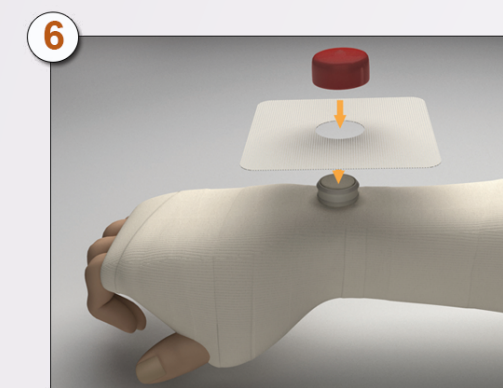
- Illustration of correct placement under padding



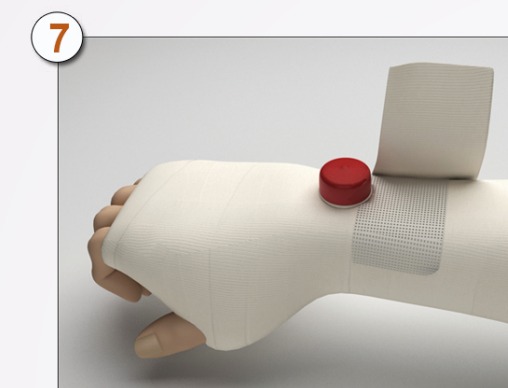
- Insert round felt plug to hold RAF in place



- Apply cast felt – split or cut hole to fit over RAF
- Apply rest of cast padding. Putting RAF through hole will help hold it in place when finishing the cast



- Apply one layer of synthetic cast material
- Place mesh square onto plastic port to ensure solid construct



- Put the red cap on the RAF
- Finish building cast to cover mesh around RAF



- Install RAF cap



Casting & Ports

EXOGEN easily incorporates into casts

In cast installation with square pad

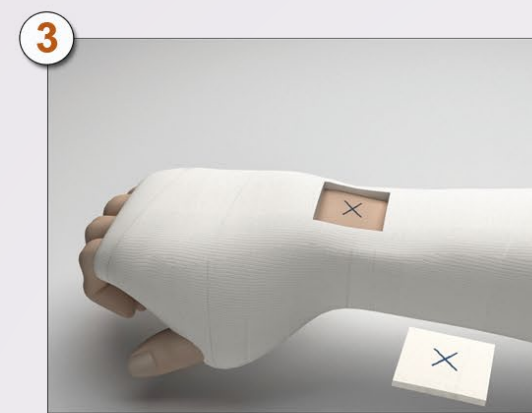
Any cast can be prepared for an EXOGEN treatment port by using the windowing cast installation technique.



- Locate fracture site using X-Ray
- Mark treatment area on cast with an X



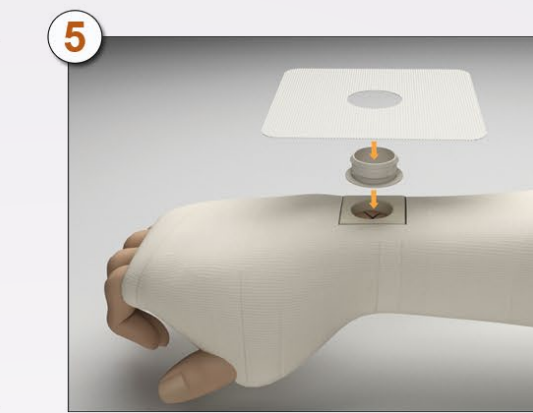
- Use standard cast saw
- Cut window out of cast



- Remove newly created window
- Remove excess padding and cut stockinette with scissors



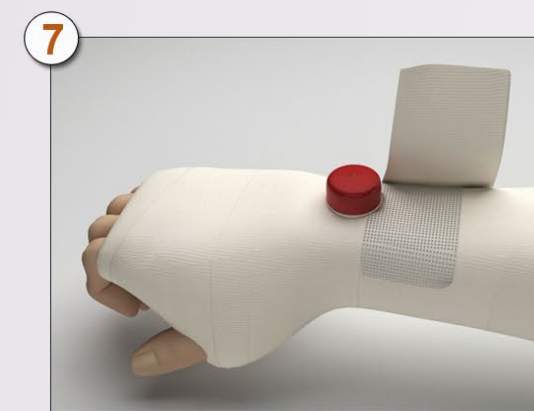
- Remove layers of square felt pad until pad is same thickness as cast
- Use only square pad when cutting square hole



- Insert RAF into mesh until mesh sits over lower lip
- Peel off adhesive backing from off-white square pad and stick to bottom of RAF



- Insert assembly into the square window
- Put the red cap on the RAF



- Finish building cast to cover mesh around RAF



- Completed in cast build



- Install felt plug to prevent window edema



- Install RAF cap



Casting & Ports

EXOGEN easily incorporates into casts

On cast method

Place the assembly strap over the cast window and secure into place.



- Position RAF of strap assembly securely over cast window



- Place round felt plug into RAF



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

Selected clinical studies in non-union[†] fractures

- 1998 – [Charcot neuroarthropathy](#)
- 1999 – [Septic pseudoarthrosis](#)
- 2001 – [Established non-unions in various locations](#)
- 2002 – [Established non-unions in various locations](#)
- 2004 – [Compound high energy delayed/non-unions in various locations](#)
- 2005 – [Delayed union and non-unions in various locations](#)
- 2010 – [Improved healing response in delayed unions of the tibia](#)
- 2012 – [Treatment of non-union fractures in various locations](#)

Clinical studies supporting healing of fresh fractures

- 1994 – [Tibial fracture healing](#)
- 1997 – [Tibial and distal radius fracture](#)
- 1997 – [Distal radial fractures](#)
- 1998 – [Jones' fracture](#)
- 2000 – [Scaphoid fracture](#)



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

1998 – Charcot neuroarthropathy

Level IV study: Single-center case series

Study Title	Objective	Conclusions
Adjunct low intensity ultrasound in Charcot neuroarthropathy. Strauss E, Gonya G. <i>Clin Orthop Relat Res.</i> 1998;349:132-138.	To review the potential for lowintensity ultrasound and to heal difficult non-union cases of Charcot neuroarthropathy, a rapidly progressive deterioration of weightbearing joints.	Strauss and Gonya described the effects of EXOGEN on two difficult cases of Charcot non-unions with multiple prior failed surgical procedures. Both cases healed within 5.5 months when treated with the EXOGEN bone healing system. » Click here to view abstract



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

1999 – Septic pseudoarthrosis

Level IV study: Single-center case series

Study Title	Objective	Conclusions
Romano C, Messina J, Meani E. Low-intensity ultrasound for the treatment of infected nonunions. In: Agazzi M, Bergami PL, Cicero G, Gualdrini G, Mastorillo G, Meani M, Mintina S, Soranzo ML, editors. <i>Guarderni di Infezione Osteoarticolari</i> . 1999;83-93.	To examine the clinical effects of low-intensity pulsed ultrasound for the treatment of septic non-unions.	Romano et al. reported on prospective longitudinal studies in infected non-unions and pseudoarthrosis respectively, suggesting high success rates with EXOGEN in both situations.



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

2001 – Established non-unions in various locations

Level II study: Multi-center consecutive case series, self-pairing controling high success rates with EXOGEN in both situations.

Study Title	Objective	Conclusions
Low-intensity pulsed ultrasound in the treatment of non-unions. Nolte PA, van der Krans A, Patka P, Janssen IM, Ryaby JP, Albers GH. <i>J Trauma</i> . 2001;51(4):693-703.	To evaluate the effect of low-intensity ultrasound for the treatment of established non-unions in a consecutively enrolled patient population from various trauma departments.	25 of 29 non-union cases (86%) healed in an average treatment time of 22 weeks (median 17 weeks), leading the authors to conclude that EXOGEN can be useful in the treatment of challenging, established non-unions. » Click here to view abstract



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

2002 – Established non-unions in various locations

Level II study: Single-center consecutive prospective case series, self-pairing control

Study Title	Objective	Conclusions
<p>Is low intensity ultrasound effective in treating disorders of fracture healing?</p> <p>Mayr E, Möckl C, Lenich A, Ecker M, Rüter A. <i>Unfallchirurg.</i> 2002;105(2):108-115.</p>	<p>To examine the effectiveness of pulsed low-intensity ultrasound for treatment of fracture healing disorders.</p>	<p>The authors found an overall healing rate of 86% among 64 delayed unions and 36 non-unions. The healing rate in femur fractures was 64%; among tibial fractures, it was 96%; and among scaphoid fractures, 75%.</p>

[» Click here to view abstract](#)



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

2004 – Compound high energy delayed/non-unions in various locations

Level IV study: Single-center retrospective case series

Study Title	Objective	Conclusions
Compound high-energy limb fractures with delayed union: our experience with adjuvant ultrasound stimulation (EXOGEN).	To study the effectiveness of low intensity pulsed ultrasound as adjuvant treatment for high energy limb fractures.	Among 18 high energy fractures, 16 of the fractures united within 13-52 weeks. This represents a 89% heal rate with patients that suffered severe high energy injuries with severe disruption in both soft and hard tissues. Previous prolonged treatment in these patients did not achieve bone healing.
Lerner A, Sten H, Soudry M. <i>Ultrasonics</i> . 2004;42:915-17.		» Click here to view abstract



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

2005 – Delayed union and non-unions in various locations

Level II study: Single-center, prospective, consecutive case study, self-pairing control

Study Title	Objective	Conclusions
<p>Low-intensity pulsed ultrasound: effects on nonunions.</p> <p>Gebauer D, Mayr E, Orthner E, Ryaby JP. <i>Ultrasound Med Biol.</i> 2005;31(10):1391-1402.</p>	<p>To study the effectiveness of low-intensity pulsed ultrasound as an alternative to surgery, electrical bone growth stimulation, and extracorporeal shock-wave therapy for treating non-unions.</p>	<p>Among the 67 cases that met the study criteria, mean fracture age was 39 ± 6.2 months, 85% of the non-union cases were clinically and radiographically healed after daily 20-min EXOGEN treatment at home for an average of 168 days. The authors conclude, based on their study and a review of literature reports on studies that used a similar design, that their results demonstrate that EXOGEN can affect heal rates similar to those achieved by surgery (without the associated risks and complications), and similar to those achieved by electrical bone growth stimulation or extracorporeal shock-wave therapy. This study demonstrated a highly significant treatment effect for EXOGEN by healing 85% of non-unions that had the ideal comparative group (i.e. their own prior failed orthopedic treatments). Patient treatment compliance averaged 89% with EXOGEN.</p>

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Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

2010 – Improved healing response in delayed unions of the tibia

Level I study: Multi-center randomized sham controlled

Study Title	Objective	Conclusions
Improved healing response in delayed unions of the tibia with low-intensity pulsed ultrasound: results of a randomized sham-controlled trial.	To determine the effectiveness of LIPUS in accelerating the healing process in delayed unions of the tibial shaft.	Among the 101 study subjects, findings demonstrate significantly greater progress toward bone healing after EXOGEN treatment compared to no EXOGEN treatment with established delayed unions of the tibia, as measured by a mean improvement in bone mineral density (BMD) of 1.34 based on log transformed data and a reduction in fracture gap area. Overall treatment compliance was 91% based on median total time of device use divided by total possible time.
Schofer MD, Block JE, Aigner J, Schmelz A. <i>BMC Musculoskelet Disord.</i> 2010;11(1):229		» Click here to view abstract



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

2012 – Treatment of non-union fractures in various locations

Level IV study: A continuous retrospective study conducted from 2004 to 2009

Study Title	Objective	Conclusions
Indications and results for the EXOGEN ultrasound system in the management of non-union: A 59-case pilot study. Roussignol X, Currey C, Duparc F, Dujardin F. <i>Orthop Traumatol Surg Res.</i> 2012;98(2):206–213.	To assess the use of external ultrasound stimulation (EXOGEN) in the treatment of femoral or tibial non-union.	External EXOGEN treatment offers an alternative to traditional surgery and the procedure is non-invasive. The 88% EXOGEN heal rate is higher than in traditional surgery and supports first line use with grossly stable non-unions with < 10mm fracture gap. With the study population, EXOGEN cost was at least 60% lower versus traditional non-union surgery.

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Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

1994 – Tibial fracture healing

Level I study: Multi-center, prospective, randomized, double-blind, placebo-controlled

Study Title	Objective	Conclusions
Acceleration of tibial fracture-healing by non-invasive, low-intensity pulsed ultrasound. Heckman JD, Ryaby JP, McCabe j, Frey JJ, Kilcoyne RF. <i>J Bone Joint Surg Am.</i> 1994;76(1):26-34.	To evaluate the use of a new ultrasound-stimulating device as an adjunct to conventional treatment with a cast in a prospective, randomized, double-blind evaluation of closed or grade-I open fractures of the tibial shaft.	At the end of treatment, there was a statistically significant decrease in the time to clinical healing (96 ± 4.9 days for the EXOGEN-treatment group compared with 154 ± 13.7 days for the placebo treatment group ($p < 0.0001$)), representing a 38% improvement in healing time. There also was a significant decrease in the time to overall healing among the EXOGEN-treated group (86 ± 5.8 days for the EXOGEN-treatment group compared with 114 ± 10.4 days for the placebo-treatment group ($p < 0.03$)), confirming earlier clinical studies that demonstrated the effectiveness of EXOGEN in the acceleration of the normal fracture-repair process. Compliance with use of the device was excellent and there were no serious complications.

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Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

1997 – Tibial and distal radius fracture

Level I study: Multi-center, randomized prospective case series, placebo control

Study Title	Objective	Conclusions
Acceleration of tibia and distal radius fracture healing in patients who smoke. Cook SD, Ryaby JP, McCabe J, Frey JJ, Heckman JD, Kristiansen TK. <i>Clin Orthop Relat Res.</i> 1997;337:198-207.	To evaluate whether a low-intensity ultrasound device would act as an accelerator of cortical and cancellous bone fracture healing in smokers and nonsmokers.	EXOGEN reduced the time to attain a healed fracture with statistically significant reductions in healing time for smokers and nonsmokers in the tibial and distal radius fracture studies. » Click here to view abstract



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

1997 – Distal radial fractures

Level I study: Multi-center, prospective, randomized, double-blind, placebo-controlled

Study Title	Objective	Conclusions
<p>Accelerated healing of distal radial fractures with the use of specific, low-intensity ultrasound: a multicenter, prospective, randomized, double-blind, placebo-controlled study.</p> <p>KristiansenTK, Ryaby JP, McCabe J, Frey JJ, Roe, LR. <i>J Bone Joint Surg Am.</i> 1997;79(7):961-973.</p>	<p>To test the effectiveness of a specifically programmed, low-intensity, non-thermal, pulsed ultrasound medical device for shortening the time to radiographic healing of dorsally angulated fractures of the distal aspect of the radius that had been treated with manipulation and a cast.</p>	<p>Time to union was significantly shorter for the fractures treated with EXOGEN than for those treated with placebo. EXOGEN accelerated healing by thirty-seven days compared with the placebo device (38%; 61 ± 3.4 days compared with 98±5.2 days). Each radiographic stage of healing also was significantly accelerated in the EXOGEN group. The authors concluded that this specific ultrasound signal accelerated the healing of fractures of the distal radial metaphysis and decreased the loss of reduction during fracture healing.</p> <p>» Click here to view abstract</p>



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

1998 – Jones' fracture

Level 1 study: Single center, prospective, randomized, double-blind, placebo-controlled

Study Title	Objective	Conclusions
<p>Low-Intensity Ultrasound accelerates Jones' fracture healing.</p> <p>Strauss E, Ryaby JP, McCabe J, Poster presented at the International Society for Fracture Repair, Strausbourg France, Sept.23, 1998.</p>	<p>To investigate whether EXOGEN can enhance the rate of fracture healing and prevent delayed union or nonunion in Jones' fractures.</p>	<p>At the end of treatment there was a statistically significant decrease in the mean time to clinical and radiographic healing in EXOGEN treated active group patients. Healing was accelerated by an average of 40% in the active group compared to the healed fractures in the control group. The length of rehabilitation was only 28 days for the active group compared to 56 days for the control group.</p>



Clinical Summaries

Use of EXOGEN for acceleration of bone healing.

2000 – Scaphoid fracture

Level-I study: Randomised, blinded, placebo-controlled, single-center

Study Title	Objective	Conclusions
<p>Does pulsed low-intensity ultrasound accelerate healing in scaphoid fractures?</p> <p>Mayr E, Rudzki MM, Rudzki M, Borchardt B, Häusser H, Rüter A. <i>Handchir Microchir Plast Chir.</i> 2000;32(2):115-122.</p>	<p>To test the hypothesis that, in comparison to the standard treatment of casting of the forearm including the thumb and distal thumb joint, EXOGEN accelerates the healing of a stable, non-dislocated scaphoid fracture, as assessed by CT examination.</p>	<p>Results of this study show that EXOGEN significantly accelerated the healing of scaphoid fractures by 30% ($p=0.0055$) when used in combination with a cast (62 +/- 19.2 days in the 15 EXOGEN treated group compared to 43.2 +/- 10.9 days in the 15 control fractures group). At 4 weeks 61.1% of the fracture surface area was healed with EXOGEN compared to 32.2% in control fractures ($p<0.05$). All EXOGEN treated fractures were healed by 65 days; at this time point in the control group only 60% had healed. All control group patients were healed at 110 days.</p> <p>» Click here to view abstract</p>



References

1. Pounder NM, Harrison AJ. Low intensity pulsed ultrasound for fracture healing: A review of the clinical evidence and the associated biological mechanism of action. *Ultrasonics*. 2008;48:330–8.
2. Heckman JD, Ryaby JP, McCabe J, et al. Acceleration of tibial fracture-healing by non-invasive, low-intensity pulsed ultrasound. *J Bone Joint Surg [Am]*. 1994;76(1):26–34.
3. Kristiansen TK, Ryaby JP, McCabe J, et al. Accelerated healing of distal radial fractures with the use of specific, low-intensity ultrasound. A multicenter, prospective, randomized, double-blind, placebo-controlled study. *J Bone Joint Surg [Am]*. 1997;79(7):961–973.
4. Nolte PA, van der Krans A, Patka P, et al. Low-intensity pulsed ultrasound in the treatment of nonunions. *J Trauma*. 2001;51(4):693–703.
5. Schofer MD, Block JE, Aigner J, Schmelz A. Improved healing response in delayed unions of the tibia with low-intensity pulsed ultrasound: results of a randomized sham-controlled trial. *BMC Musculoskelet Disord*. 2010;11(1):229.
6. Pounder NM, Jones JT, Tanis KJ. Design evolution enhances patient compliance for low-intensity pulsed ultrasound device usage. *Medical Devices: Evidence and Research*. 2016; 9: 423-427.
7. Martin LR, Williams SL, Haskard KB, DiMatteo MR. The challenge of patient adherence. *Ther Clin Risk Manag*. 2005;1(3):189–199.
8. McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: *Scientific Review*. JAMA. 2002;288(22):2868–2879.
9. Cramer JA, Roy A, Burrell A, et al. Medication compliance and persistence: terminology and definitions. *Value Health*. 2008;11(1):44–47.
10. Naruse K, Sekiya H, Harada Y, et al. Prolonged endochondral bone healing in senescence is shortened by low-intensity pulsed ultrasound in a manner dependent on COX-2. *Ultrasound Med Biol*. 2010;36(7):1098–1108.
11. Lai CH, Chen SC, Chiu LH, et al. Effects of low-intensity pulsed ultrasound, dexamethasone/TGF- β 1 and/or BMP-2 on the transcriptional expression of genes in human mesenchymal stem cells: chondrogenic vs. osteogenic differentiation. *Ultrasound Med Biol*. 2010;36(6):1022–1033.
12. Leung KS, Cheung WH, Zhang C, et al. Low intensity pulsed ultrasound stimulates osteogenic activity of human periosteal cells. *Clin Orthop Relat Res*. 2004;418:253–259.
13. Coords M, Breitbart E, Paglia D, et al. The effects of low-intensity pulsed ultrasound upon diabetic fracture healing. *J Orthop Res*. 2011;29(2):181–188.
14. Sant'Anna EF, Leven RM, Viridi AS, Sumner DR. Effect of low intensity pulsed ultrasound and BMP-2 on rat bone marrow stromal cell gene expression. *J Orthop Res*. 2005;23(3):646–652.
15. Lehmann JF, Brunne GD, Martinis AJ, McMillan JA. Ultrasonic effects as demonstrated in live pigs with surgical metallic implants. *Arch Phys Med Rehabil*. 1959;40:483–488.
16. Premarket Approval P900009/ Supplement 6, Summary of Safety and Effectiveness Data.
17. Data on File. RPT-000368. EXOGEN ultrasound signal depth and penetration. DOS 12000.04.
18. Mayr E, Frankel V, Rüter A. Ultrasound—an alternative healing method for nonunions? *Arch Orthop Trauma Surg*. 2000;120(1):1–8.
19. Roussignol X, Currey C, Duparc F, Dujardin F. Indications and results for the EXOGEN ultrasound system in the management of non-union: a 59-case pilot study. *Orthop Traumatol Surg Res*. 2012;98(2):206–213.
20. Lerner A, Stein H, Soudry M. Compound high-energy limb fractures with delayed union: our experience with adjuvant ultrasound stimulation (EXOGEN). *Ultrasonics*. 2004;42(1):915–917.
21. Data on file: RPT-000438. Postmarket patient registry for the period of October 17, 1994 to June 15, 1998. DOS 12000.01.
22. Duarte R, Xavier M, Choffie M, McCabe JM. Review of nonunions treated by pulsed low-intensity ultrasound. In: Proceedings of the 1996 Meeting of the Societe Internationale de Chirurgie Orthopaedique et de Traumatologie (S-COG). 1996:110.
23. Gebauer D, Mayr E, Orthner E, Ryaby JP. Low-intensity pulsed ultrasound: effects on nonunions. *Ultrasound Med Biol*. 2005;31(10):1391–1402.
24. Data on file: RPT-000396 Humerus Nonunion Claims based on EXOGEN Registry
25. Data on file: RPT-000409 Clavicle Nonunion Claims based on EXOGEN Registry
26. Data on file: RPT-000398 Scaphoid Nonunion Claims based on EXOGEN Registry
27. Data on file: RPT-000410 Radius/Ulna Nonunion Claims based on EXOGEN Registry
28. Data on file: RPT-000395 Femur Non Union Claims based on EXOGEN Registry
29. Data on file: RPT-000411 Hand/Wrist Nonunion Claims based on EXOGEN Registry
30. Data on file: RPT-000408 Ankle Nonunion Claims based on EXOGEN Registry
31. Data on file: RPT-000391 Tibia/Fibula Non Union Claims based on EXOGEN Registry
32. Data on file: RPT-000389 Metatarsal Non Union Claims based on EXOGEN Registry
33. Data on file: RPT-000412 Foot Nonunion Claims based on EXOGEN Registry
34. Mayr E, Rudzki MM, Rudzki M, Borchardt B, Hausser H, Rüter A. Does low intensity, pulsed ultrasound speed healing of scaphoid fractures? *Handchir Mikrochir Plast Chir*. 2000;32(2):115-122.
35. Strauss E, Ryaby JP, McCabe J. Low-intensity ultrasound accelerates Jones' fracture healing. Poster presented at the International Society for Fracture Repair, Strasbourg France, Sept. 23, 1998.
36. Azuma Y, Ito M, Harada Y, et al. Low-intensity pulsed ultrasound accelerates rat femoral fracture healing by acting on the various cellular reactions in the fracture callus. *J Bone Miner Res*. 2001;16(4):671–680.
37. Heckman and Sarasohn-Kahn. The Economics of Treating Tibia Fractures; The Cost of Delayed Unions. 1997. Bulletin Hospital for Joint Diseases 56(1):63–72.
38. Cook SD, Ryaby JP, McCabe J, et al. Acceleration of tibia and distal radius fracture healing in patients who smoke. *Clin Orthop Relat Res*. 1997;337:198–207.
39. Castillo RC, Bosse MJ, MacKenzie EJ, Patterson BM. Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures. *J Orthop Trauma*. 2005;19(3):151–157.
40. Pilitsis JG, Lucas DR, Rengachary SR. Bone healing and spinal fusion. *Neurosurg Focus*. 2002;13(6):1–6.
41. Lu C, Hansen E, Sapozhnikova A, et al. Effect of age on vascularization during fracture repair. *J Orthop Res*. 2008;26(10):1384–1389.
42. Karladani AH, Granhed H, Kärrholm J, Styf J. The influence of fracture etiology and type on fracture healing: a review of 104 consecutive tibial shaft fractures. *Arch Orthop Trauma Surg*. 2001;121(6):325–328.
43. EXOGEN User Guide

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Summary of Indications for Use:

EXOGEN is indicated for the non-invasive treatment of osseous defects (excluding vertebra and skull) that includes the treatment of delayed unions, non-unions[†], stress fractures and joint fusion. EXOGEN is also indicated for the acceleration of fresh fracture heal time, repair following osteotomy, repair in bone transport procedures and repair in distraction osteogenesis procedures.

[†]A non-union is considered to be established when the fracture site shows no visibly progressive signs of healing.

There are no known contraindications for the EXOGEN device. Safety and effectiveness have not been established for individuals lacking skeletal maturity, pregnant or nursing women, patients with cardiac pacemakers, on fractures due to bone cancer, or on patients with poor blood circulation or clotting problems. Some patients may be sensitive to the ultrasound gel. Full prescribing information can be found in product labeling, at www.exogen.com.

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