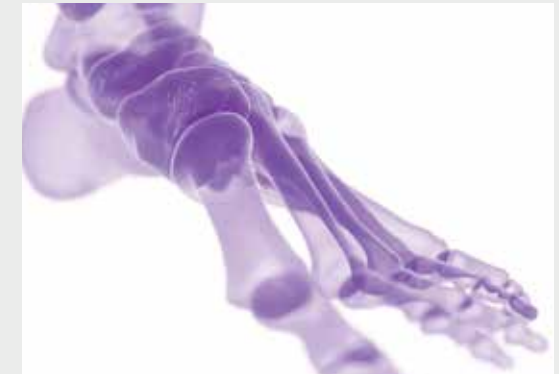


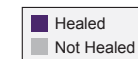
Reduced Vascularity Places Fractures at Greater Risk of Non-Union

Vascularization is essential for bone healing, directly affecting chondrogenesis and thus ossification.¹ Certain fractured bones are at risk of reduced vascularity, often progressing to delayed union or non-union.^{2,3}

- Two examples are the scaphoid and fifth metatarsal bones. The scaphoid bone, especially the proximal pole, has a peculiar vascular anatomy that is vulnerable to posttraumatic ischemia.⁴ Research has reported scaphoid nonunion rates up to 15%.⁵
- The fifth metatarsal, particularly in the proximal diaphysis, has reduced intrasosseous vascular anatomy which contributes to poor fracture healing.⁶ For the Jones fractures of the proximal 5th metatarsal, the non-union rate may be as high as 28%.⁷



EXOGEN Heals Scaphoid and Metatarsal Non-Unions



Scaphoid Non-Union
Heal Rate

100%
(16/16)¹²

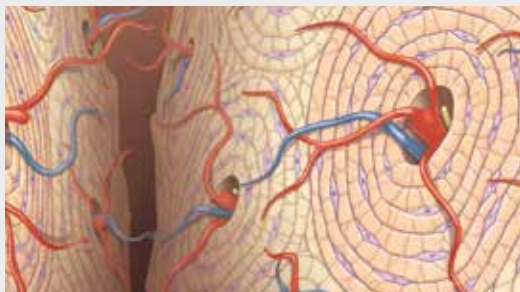
Metatarsal Non-Union
Heal Rate

90%
(75/83)¹³



EXOGEN Upregulates VEGF, Angiogenesis, and Chondrogenesis

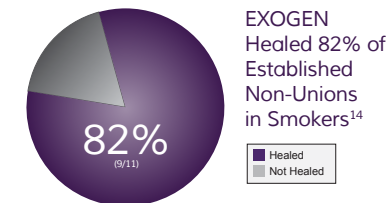
- VEGF-mediated angiogenesis is essential during the chondrogenic phase of healing, when cartilage resorption and primary bone remodeling are initiated.^{8,9}
- In vitro and in vivo studies show EXOGEN upregulates the expression of VEGF in osteoblasts and periosteal cells, leading to increased aggrecan and proteoglycan synthesis in chondrocytes.^{10,11}



EXOGEN Promotes Angiogenesis

- In an animal model of diabetic fracture healing, EXOGEN was shown to enhance angiogenesis and restore a normal density of new blood vessels at the fracture site.¹
- In vitro and in vivo studies suggest EXOGEN upregulates the expression of vascular endothelial growth factor (VEGF) in osteoblasts and periosteal cells.^{10,11}

EXOGEN Heals Established Non-Unions¹⁴

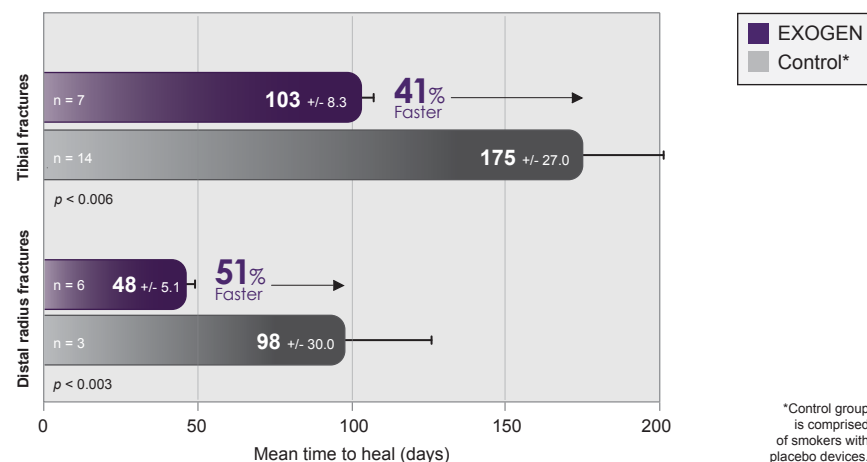


Smoking Delays Bone Healing

- Cigarette smoking is one of the conditions that prolongs the healing time for bone fractures, delaying or preventing union.
- Nicotine directly affects an array of genes responsible for angiogenesis and osteoblast differentiation.¹⁵
- A recent systematic review showed smokers have more than double the risk of long bone non-union compared with non-smokers.¹⁶
- Smoking had a correlated cumulative odds ratio of 2.32 for developing a long bone non-union as compared to nonsmokers. (n=1121, p<0.001)¹⁶

Non-Union Risk Greater than 2x in Smokers

EXOGEN Significantly Reduced Time to Bone Healing for Smokers¹⁷



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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. 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, or at www.exogen.com.

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