Distributor Representative Training

Introduction to Biocomposites and genex®

Biocomposites®

Training objectives

At the end of this session you will have the knowledge to:

- ✓ Speak confidently about Biocomposites and gene**x**
- ✓ Discuss the cost of trauma and sell the value of gene**x**
- ✓ Demonstrate how gene**x** has the power to restore™
- ✓ Ask probing questions and successfully handle objections
- ✓ Describe why gene**x** is superior to competitor products
- ✓ Grow your business
- ✓ Utilize resources effectively

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Training agenda

- ✓ Introduction to Biocomposites
- ✓ Trauma and non-unions
- ✓ Introduction to gene**x**
- ✓ How to prepare gene**x**
- ✓ Power to restore - applications and case studies
- ✓ Selling gene**x**
- ✓ Frequently asked questions
- ✓ Competitor comparison
- ✓ Supporting evidence
- ✓ Useful resources

Biocomposites®


Introduction to Biocomposites

Biocomposites

bringing Ca 20 calcium to life®

- Innovative approaches to void management at infected sites
- Singular focus on calcium compound technologies
- Deep expertise
- Dedicated to quality
- Based in Keele, UK – with companies in the USA and China, and a presence in Canada, Europe and India

Trauma and non-unions

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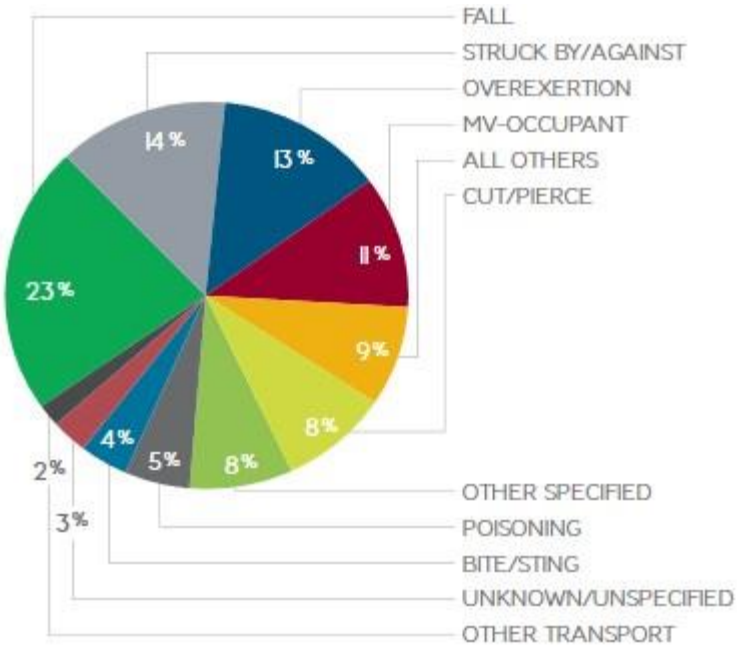
Trauma and non-unions

Trauma has a significant and ever increasing impact on healthcare systems

- In the USA, there are over 41 million emergency department visits and 2.3 million hospital admissions[1]
- In the USA, trauma has an estimated economic burden of $671 billion a year, including both healthcare costs and lost productivity[1]



Leading causes of non-fatal unintentional injuries (age 15-65), in USA[2]

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POWER TO RESTORE WITHOUT LEAVING A TRACE

The only remaining
evidence of the trauma

genex®

Treatment goals

- ✓ Restores natural bone structure
- ✓ Completely absorbed and leaves no artifact to impair structural integrity
- ✓ Reduce avoidable complications
- ✓ Improve patient outcomes
- ✓ Improve treatments while decreasing overall treatment cost

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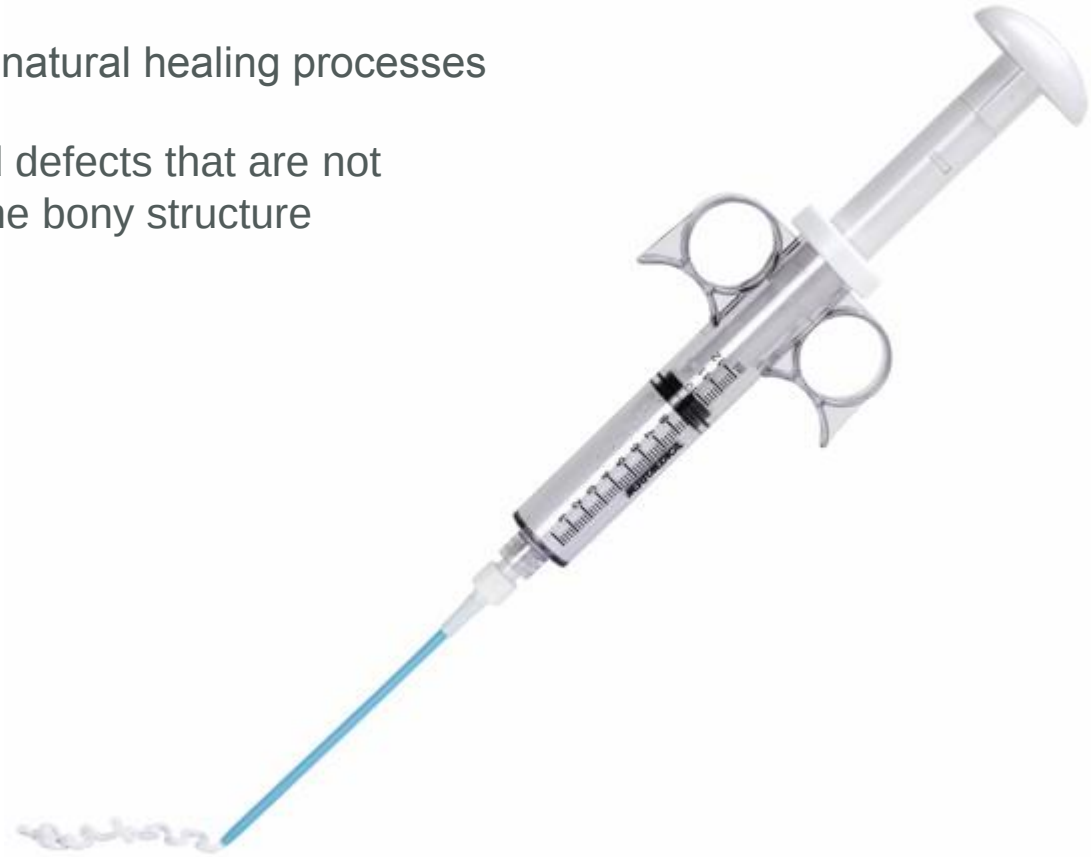
Perfect partner for your trauma and non-unions

- ✓ gene**x** is a catalyst for bone healing
- ✓ It complements the body's natural healing processes
- ✓ Cleared for bony voids and defects that are not intrinsic to the stability of the bony structure



genex®

Designed to be completely absorbed and leave no trace

genex is a precisely balanced β-tricalcium phosphate/calcium sulfate hemihydrate (50/50) compound with distinct design properties:

- ✓ Contains no hydroxyapatite (HA)
- ✓ Negatively charged surface chemistry

genex provides a powerful scaffold for accelerated bone restoration and helps to hinder soft tissue ingrowth:

- ✓ Fully absorbed within 12 months
- ✓ Enhances osteogenic response
- ✓ Restores strong healthy bone

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Why do we use β-TCP rather than hydroxyapatite (HA)?

- ✓ Bioceramics made of more soluble forms of calcium phosphate are preferable for biomedical purposes[3]
- ✓ β-TCP has superior osteoconductivity over HA[4]
- ✓ Osseointegration of β -TCP is faster than HA (6 weeks vs 4 months) [5]
- ✓ The full absorption of β -TCP allows for the restoration of the original bone architecture[5,6]
- ✓ Hydroxyapatite (HA) is hardly absorbed, which blocks the formation of new bones and remodeling, and results in poor local stability or permanent stress concentration[4,7]
- ✓ Only β-TCP is relatively balanced between scaffold absorption and bone formation[7]

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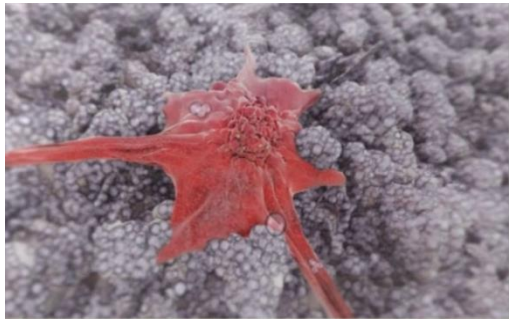
Advantages of negatively charged surface chemistry

genex utilizes a negative surface charge to attract osteogenic (bone forming) proteins to the graft surface and direct cell response, thereby accelerating bone growth

- Proven to increase the concentrations of key markers of osteoblast activity

Stage 1: Protein and cellular attachment

- Negatively charged genex attracts osteogenic proteins to its surface
- Proteins trigger osteogenic cell differentiation and attachment to the surface of genex



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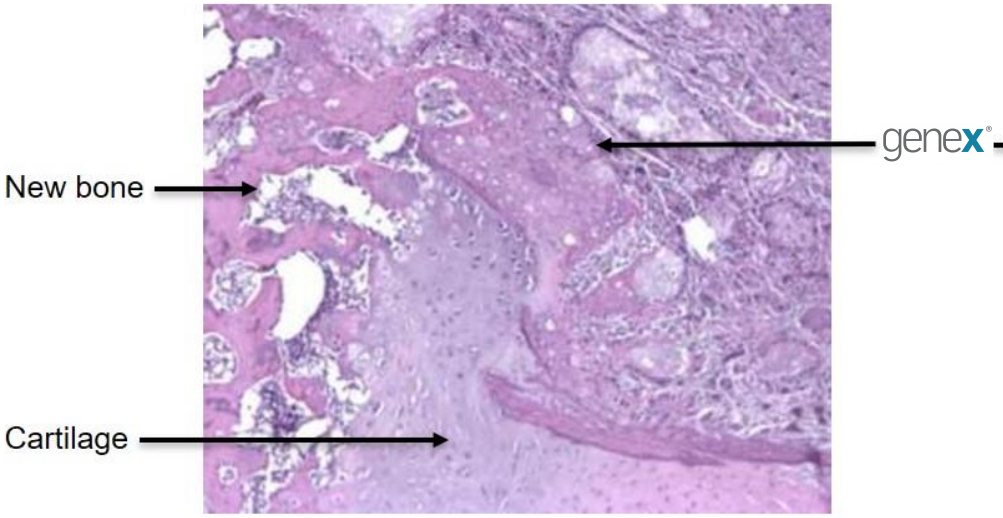
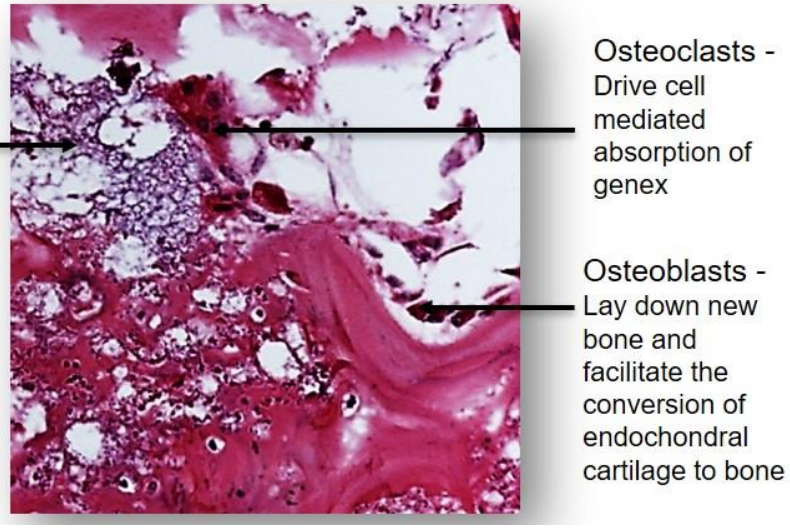
Advantages of negatively charged surface chemistry

Stage 2: Bone formation and genex absorption

- Promotes both endochondral and intramembranous bone formation



genex implantation site showing cartilage and bone formation at 4 weeks. (Light microscopy x 400 magnification, H&E stain)



genex implantation site showing bone formation and graft absorption at 16 weeks. (Light microscopy x 400 magnification, H&E stain)

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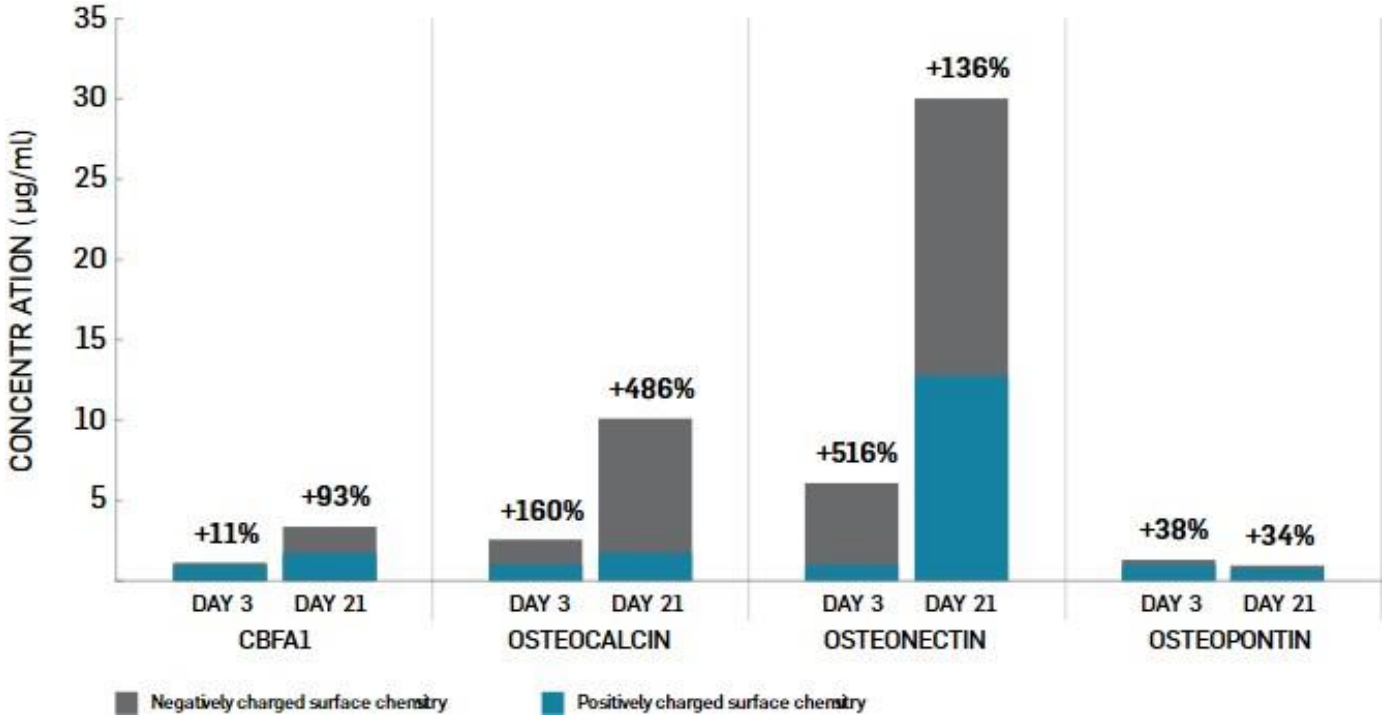
Enhances the osteogenic response to accelerate bone growth – up to 5x normal levels[8]



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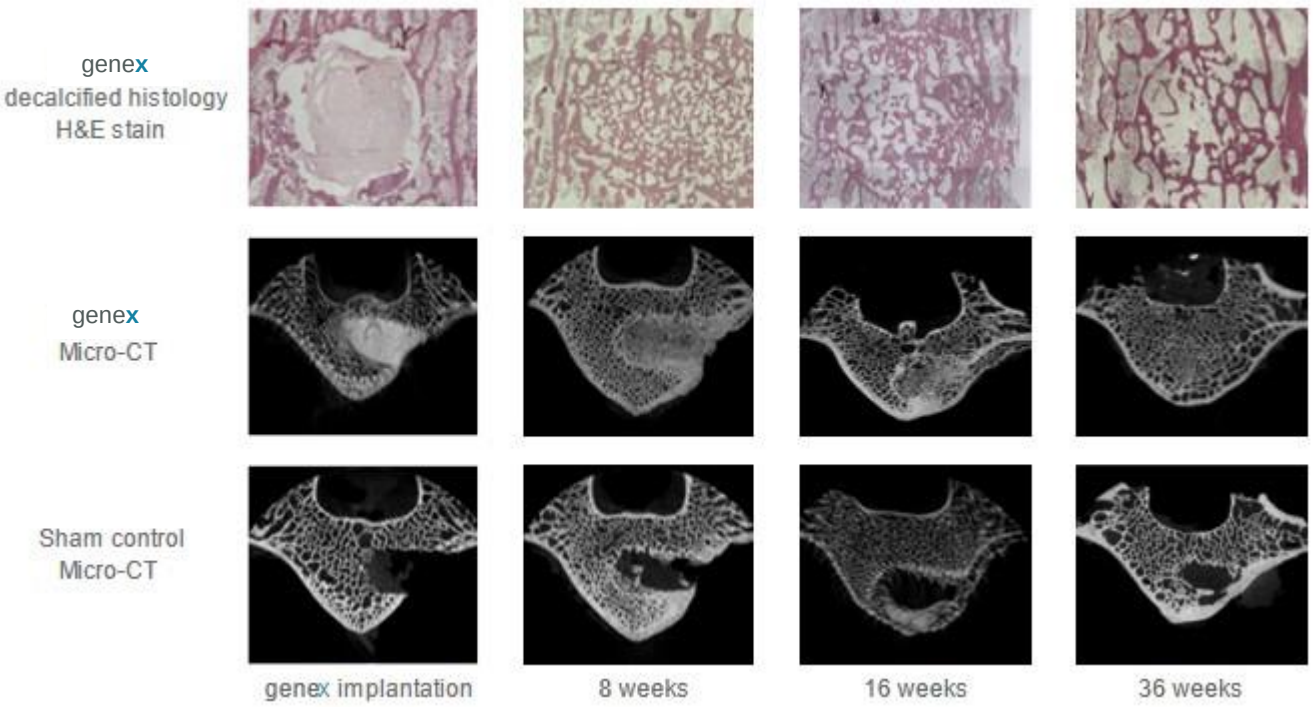
Completely absorbed within 12 months[9,10]

genex contains no hydroxyapatite. HA can only be absorbed at 1-2% per year[11]



Large animal model

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Restores strong healthy bone within a clinically relevant timeframe[7]

Tibial plateau fracture

Post-operative

15 months

genex restores bone to normal trabecular structure in 36 weeks[3]

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genex®

Versatility at your fingertips

- ✓ Versatile and easy to prepare
- ✓ Can be digitally implanted or injected in difficult-to-reach sites or minimally invasive procedures
- ✓ Can be placed before or after hardware implantation
- ✓ Sets within 15 minutes at body temperature
- ✓ Working time of 3 minutes, drillable after 15 minutes

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Pack components

- ✓ Powder: 50% β – tricalcium phosphate, 50% calcium sulfate hemihydrate
- ✓ Mixing liquid: Sterile water
  - 5cc paste: 4ml mixing liquid
  - 10cc paste: 7.6ml mixing liquid
- ✓ Included accessories:
  - Mixing bowl
  - Luer lock syringe
  - Plastic cannula
  - Spatula
- ✓ Optional accessories:
  - OsteoPrecision™ Graft Delivery Device

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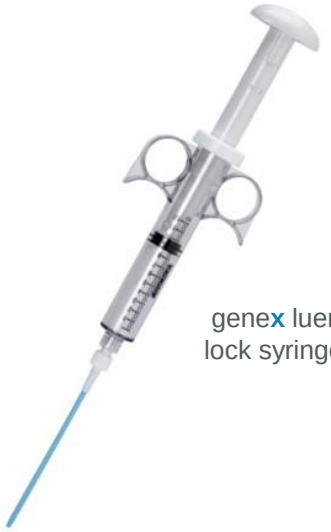
Injection flexibility

- ✓ For hard-to reach defects:
  - genex luer lock syringe with a narrow plastic cannula
  - Cannula is radiopaque for visibility under fluoroscopy
  - 2mm inside diameter, 80mm long, 11 gauge
- ✓ To withstand insertion pressure:
  - OsteoPrecision™ Graft Delivery Device with a syringe and wider metal cannula
  - Allows for faster injection of high product volumes
  - 3.4mm inside diameter, 100mm long, 8 gauge



genex luer lock syringe

OsteoPrecision™ Graft Delivery Device

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Ordering information

Product	Pack size	Order code
genex Bone Graft Substitute	5cc	910-005
	10cc	910-010
OsteoPrecision™ Graft Delivery Device	One size	990-001
genex demo pack	5cc	910-005D

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Power to restore without leaving a trace

- ✓ Perfect partner for your trauma and non-unions
- ✓ Designed to be completely absorbed and leave no trace
- ✓ Versatility at your fingertips

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How to prepare genex

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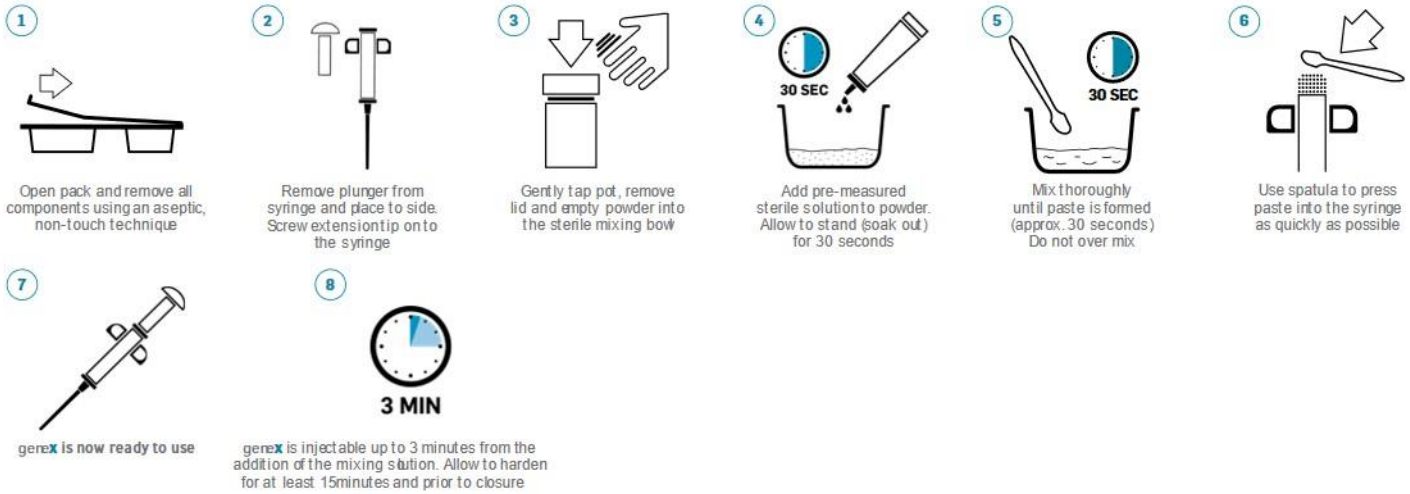
Preparation guide

Preparation of genex takes only a few careful moments. Use only the mixing solution provided. Do not add any additional substances to the paste.

genex



SURGEON'S TIPS

1. Only start to prepare genex after the surgical site has been prepared
2. If implanting digitally, the genex paste can be used after completion of step 5
3. Once implanted, do not disrupt the genex for at least 15 minutes while it is setting

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Mixing tips

- ✓ Allow to ‘soak out’ for 30 seconds
- ✓ Mix for 30 seconds
- ✓ Working time of 3 minutes
- ✓ Sets within 15 minutes
- ✓ Drillable after 15 minutes

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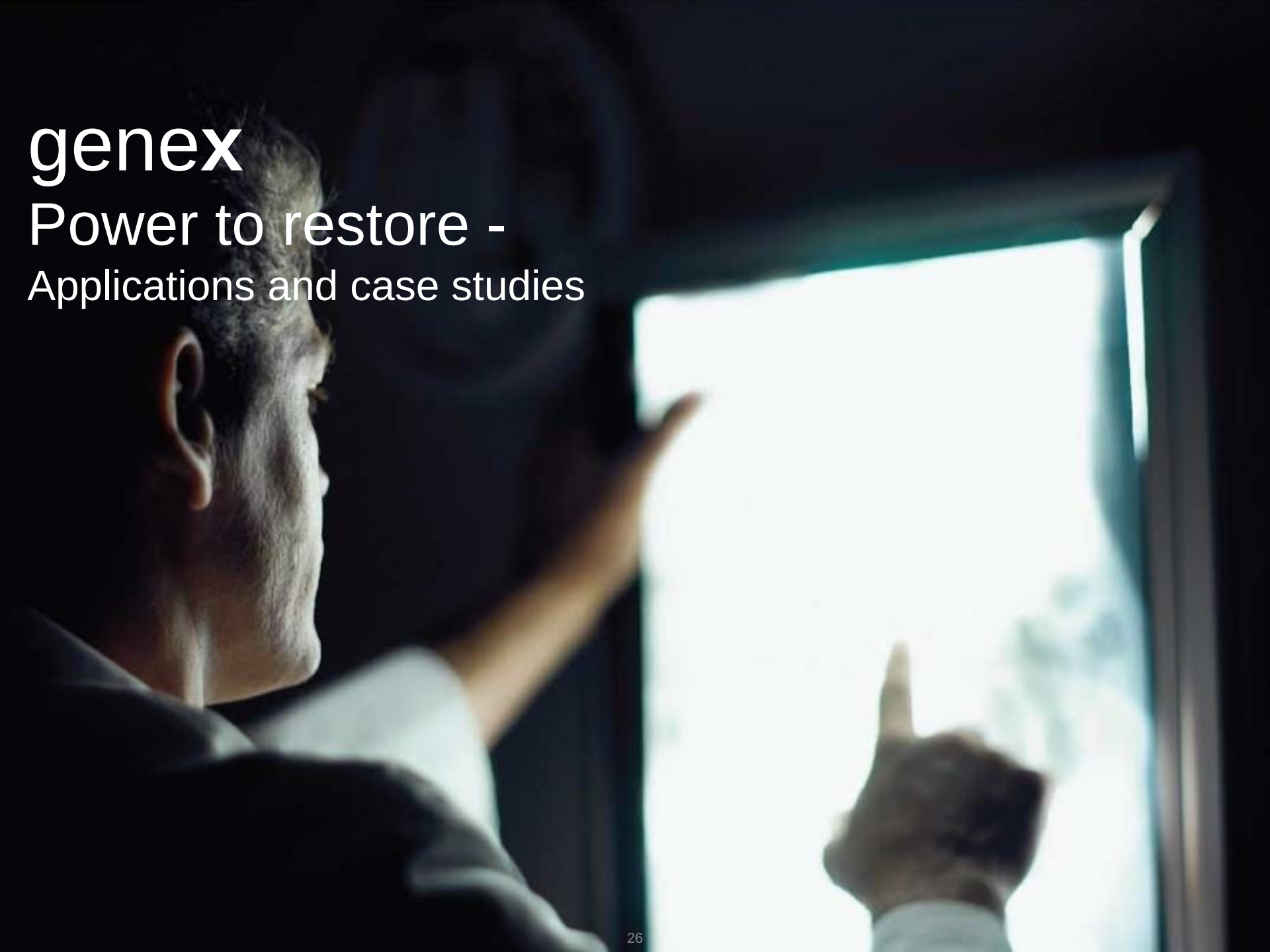

genex

Power to restore -

Applications and case studies

genex®

What is genex indicated for?

INTENDED USE

- ✓ genex injectable paste provides a bone graft substitute that resorbs and is replaced with bone during the healing process

INDICATIONS FOR USE

- ✓ genex is indicated only for bony voids or defects/gaps that are not intrinsic to the stability of the bony structure
- ✓ genex is indicated to be gently packed into voids or defects of the skeletal system (i.e. long bones, extremities, spine and pelvis)
- ✓ genex resultant paste can be injected, digitally packed into the bone void to cure in situ or molded into solid implants that are to be gently packed into the defect
- ✓ The bony defects or cavities may be surgically created or the result of traumatic injury. genex provides a bone graft substitute that resorbs and is replaced with bone during the healing process

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What is genex contraindicated for?

CONTRAINDICATIONS

- ✓ Filling of defects which are intrinsic to the stability of the bony structure
- ✓ Severe vascular or neurological disease
- ✓ Uncontrolled diabetes
- ✓ Severe degenerative bone disease
- ✓ Pregnancy
- ✓ Uncooperative patient who can’t or won't follow post-operative instructions including individuals who abuse drugs or alcohol
- ✓ Hypercalcaemia

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Target audience

- ✓ Trauma surgeons
- ✓ Trauma surgeons that use or have used CERAMENT® (Bonesupport ™)
- ✓ Existing gene**x** paste and gene**x** ds users

genex® applications

Trauma - Non-unions - Fractures - Bone voids - Core decompressions	Ortho oncology - Avascular necrosis - Benign cystic voids
Foot and ankle - Calcaneus defects - Ankle fusions - Tarsal and metatarsal defects	Recon - Acetabular voids - Augments - Tibial plateau defects
Upper extremity - Distal radius fractures - Humeral head voids	Total joint revisions - Defects/lysis behind cup - Augments - Backfill screw holes

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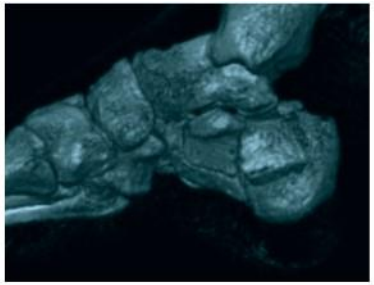
genex® - comminuted calcaneal fracture

Courtesy of Mr. A. Karladani, Gothenburg, Sweden

Pre-operative



Pre-operative - 3D CT

Post-operative

2 months

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genex® - ankle arthrodesis

Courtesy of Professor James B. Richardson, Oswestry, UK

Pre-operative

Post-operative

5 months – CT scan

12 months

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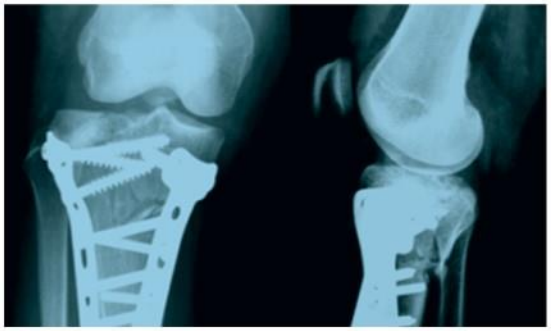
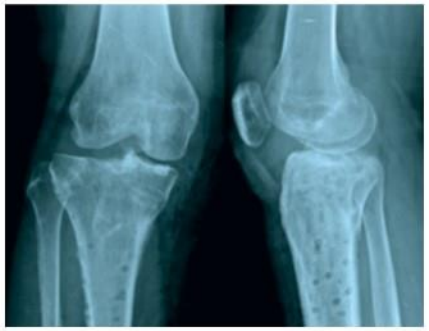
genex® - tibial plateau fracture

Courtesy of Mr. YS Chan, Taiwan, Republic of China



1 month

3 months



12 months

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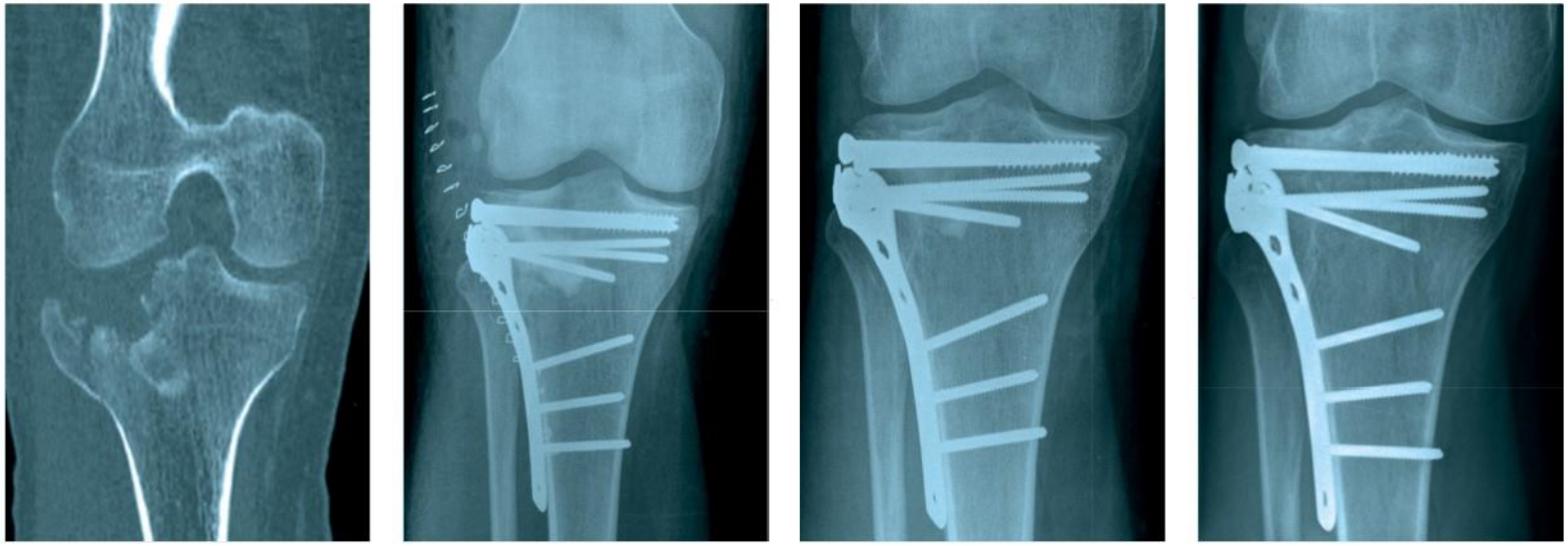
genex® - tibial plateau fracture

Courtesy of Mr. Hemant K Sharma, Hull, UK



Presentation – CT scan | Post-operative | 6 months | 15 months

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genex® - proximal femur fracture

Courtesy of Mr. Aamer Nisar & Mr. Shiva Gopal, Hull, UK

Presentation

Post-operative

4 months – screw backing out

4 months

1 year post revision

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Selling genex

How should I position genex to my customers?

genex is designed to be the perfect partner for trauma and non-unions; completely absorbing within 12 months and enhancing the osteogenic response to restore strong healthy bone.

It is easy to prepare, sets consistently and has the versatility to be digitally implanted or injected into difficult-to-reach sites or minimally invasive procedures.

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How do I generate interest in genex?

- ✓ Which products do you use for your fractures and non-union procedures?
- ✓ Have you used products that contain hydroxyapatite?
- ✓ Can you describe your experiences with products that contain hydroxyapatite?
- ✓ How important is product absorption to you?
- ✓ Do you ever use a bone graft substitute at infected sites?
- ✓ How important are handling properties to you when choosing a bone graft substitute?

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How do I respond to common objections?[13]

I prefer to use a product with hydroxyapatite as it remains in the body longer.

Hydroxyapatite (HA) absorbs at 1-2% per year and may leave behind artifacts that impair structural integrity. If present for prolonged periods of time, new bone will completely surround and embed the remaining HA particles. Embedded HA particles pose a burden to surgeons if product removal/revision is required. gene**x** contains no HA and completely absorbs within 12 months.

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How do I respond to common objections?[13]

I prefer to use a bone graft substitute that contains hydroxyapatite because of its strength.

Hydroxyapatite (HA) has a compressive strength of ~32 MPa. Because HA absorbs slowly, it's high compressive strength can interfere with normal forces that drive the bone remodeling process and cause stress shielding (or reduction in bone density) to occur. gene**x** has been shown to have a compressive strength of 15 MPa when fully set, which is 3x stronger than cancellous bone. As gene**x** is absorbed, its compressive strength reduces and does not interfere with the bone remodeling process.

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How do I respond to common objections?[13]

All bone graft substitutes are the same. I just use what is on the shelf at the hospital.

Some bone graft substitutes are designed to complement the body's natural healing processes and encourage normal bone structure to be restored at a steady rate. Over 12 months, gene**x** is completely absorbed and is replaced by bone. Other products that contain hydroxyapatite may be present longer than 12 months and are contraindicated for use where there is local infection at the site of implantation.

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How do I respond to common objections?[13]

Many bone graft substitutes are hard to prepare and are not drillable.

gene**x** is easy to prepare – simply mix in the bowl and transfer to a syringe. gene**x** has a working time of 3 minutes, sets consistently and is drillable after 15 minutes.

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Why should I sell gene**x**?

- ✓ Expand your product portfolio
- ✓ Sell within your current call pattern
- ✓ Provide another solution your customers
- ✓ Monetary rewards

Frequently asked questions

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FAQs

Who is using genex and in which hospitals?

genex is used in over 8,000 cases per year in a wide range of different indications. Biocomposites would be happy to introduce you to an appropriate surgeon if you would like to have a peer-to-peer conversation.

What are the working and setting times of genex?

genex is injectable up to 2 minutes from the addition of the mixing solution. genex should be allowed to harden for at least 15 minutes after mixing and prior to closure.

How is the setting time affected if I forget to soak out for 30 seconds during preparation?

The purpose of the 30 second ‘soak out’ step is to allow the mixing solution to soak through the powder ensuring a more efficient and thorough mixing process. If the ‘soak out’ step is missed, it is highly likely the mix may become dry and crumbly in consistency. This may result in genex becoming blocked in the syringe.

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FAQs

Can I mix genex with antibiotics?

genex is not currently FDA cleared or approved to be mixed with antibiotics. Specific questions relating to off label/physician directed use should be sent to the Biocomposites Compliance Department via the Unsolicited Request Process.

How much liquid is provided with the genex product?

genex is prepared using the pre-measured sterile solution provided; 4 ml for 5cc pack and 7.6ml for 10cc pack.

Can I substitute other mixing solutions or add additional solution when preparing genex?

You should only use the mixing solution provided. Using alternative mixing solutions and/or adding other substances to the mixture may alter the setting time significantly. Some substances such as bone marrow and blood will prevent the paste from setting.

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FAQs

How long does it take genex to absorb in bone?

genex is completely absorbed within 12 months.

What is the compressive strength of genex?

genex has been shown to have a compressive strength approximately 3x stronger than cancellous bone when fully set (15 MPa). The compressive strength reduces as genex is absorbed.

What supporting data do you have for genex?

Biocomposites has a variety of data ranging from pre-clinical laboratory testing, animal model data and clinical data. Biocomposites also has a growing number of case studies available that provide an overview of the use of genex in various clinical applications. Biocomposites would be happy to provide you with case studies for the clinical applications that you are most interested in.

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Competitor comparison

Cerament vs. genex[13,14]

Product Comparison	Cerament	genex
Composition	40% hydroxyapatite 60% calcium sulfate hemihydrate Iohexol	50% β – tricalcium phosphate 50% calcium sulfate hemihydrate Sterile water
Claimed absorption rate	6-12 months	Up to 12 months
Fully absorbs	No - HA may cause a long-term nidus for infection if not absorbed	Yes - Does not contain HA
Contraindicated for infected sites	Yes	No
Available sizes	5cc, 10cc, 18cc	5cc, 10cc
Versatility	Injectable, moldable, drillable	Injectable, digitally packed, moldable, drillable
Wait time before injection	3 minute wait time required after mixing for product to become viscous	None
Setting time	15 minutes	15 minutes
Drillable when fully set	Yes	Yes

Supporting evidence

genex®

genex publications

- Arthroscopically assisted use of injectable bone graft substitutes for management of scaphoid nonunions. *Po-June Chu; Jui-Tien Shih*. Arthroscopy: arthroscopic and related surgery 27(1): 31-27. 2011.
  - Key findings: genex used in conjunction with arthroscopically assisted treatment with percutaneous internal fixation is a reliable and minimally invasive method to achieve union and scaphoid healing

β-TCP articles

- Calcium Orthophosphate-Based Bioceramics and Biocomposites. *Sergey V. Dorozhkin* Published 2016 by Wiley – VCH Verlag GmbH & Co. KGaA
  - "…bioceramics made of more soluble forms of CaPO4 are preferable for biomedical purposes."
- Comparison of hydroxyapatite and beta tricalcium phosphate as bone substitutes after excision of bone tumors. *Ogose A, Hotta T, Kawashima H, Kondo N, Gu W, Kamura T, Endo N.* J Biomed Mater Res B Appl Biomater. 2005 Jan 15;72(1):94-101.
  - "Highly purified beta-TCP appears to be advantageous relative to HA for surgical intervention in bone tumors consequent to the nature of remodeling and superior osteoconductivity." "No obvious evidence of HA biodegradation was observed."

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β-TCP articles

- Osseointegration of hydroxyapatite and remodelling -resorption of tricalcium phosphate ceramics. Microscopy Research & Technique, 2013 *Draenert et al.* Microscopy Research & Technique, 2013
  - "HA yielded primarily a reinforcement of the recipient's cancellous-bone bed and full osseointegration after 4 months, whereas β-TCP-implants were fully osseointegrated after 6 weeks…. with a physiological architecture"
- Current application of β-tricalcium phosphate composites in orthopaedics. *Liu B, Lun DX.* Orthop Surg. 2012 Aug;4(3):139-44.
  - "Hydroxyapatite (HA) is hardly absorbed, which blocks the formation of new bones and remodeling, and results in poor local stability or permanent stress concentration. Only β-tricalcium phosphate (β-TCP) is relatively balanced between scaffold absorption and bone formation. "

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Useful resources

What resources can help you sell genex?

Distributor Hub

- Training materials
- Biocomposites and genex collateral
- Sales tools
- Case studies
- Mixing videos

Distributor Hub app

- Order form
- Unsolicited requests
- genex content

Biocomposites website

- Product information specific to clinical specialties
- Biocomposites overview
- Surgeon testimonial videos
- Mixing videos
- Education

Biocomposites®

genex®

Find out more at biocomposites.com

For indications, contraindications, warnings and precautions see Instructions for Use.

Patents granted: EP 1390086 B1, US 8632796, CN ZL02809194.9, US 8496955

“OsteoPrecision” is a trademark of Nordson Corporation

MA0287R1

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