MAGNEZIX

UNDERSTANDING INNOVATIONS

A CLOSER LOOK AT THE SPECIAL PROPERTIES OF MAGNEZIX®

Intelligent innovations for a better life.
www.syntellix.com

SYNTELLIX

STABILITY, DISSOLUTION AND OSTEOCONDUCTIVITY DEFINE A NEW STANDARD OF IMPLANTS!

Similar stability to comparable titanium implants.

Up to 5 times higher stability than PLA/PGA pins.

Metallic and bioabsorbable.
Osteoconductive.
Reduced risk of infection.

No remaining foreign material.

Practically no radiological artefacts.
Suitable for diagnostics in MRI and CT.

Free of aluminium, nickel, chromium and cobalt.
No known allergies and foreign body reactions.
Reduced risk of stress shielding.

TOP 100
Top-Innovator 2016

INNOVATIONSPREIS DER DEUTSCHEN WIRTSCHAFT
Sieger 2012/13

MAGNEZIX®

THE GAME CHANGER AND INNOVATION LEADER: MAGNEZIX®

Worldwide innovation leader

Most implants in the field of orthopedic surgery are made of non-resorbable materials such as steel or titanium which permanently remain in the body or have to be removed in a second surgery. These permanent implants can cause stress shielding, provoke inflammatory or foreign body reactions. In order to minimize these problems, resorbable, yet stable implants have become subject of extensive research. While there were many approaches to design a material that provides both adequate mechanical and degradation properties combined with excellent biocompatibility, MAGNEZIX® hit the market as **the globally first bioabsorbable metallic implant** approved for use in humans.

Inventing new technologies

There were good reasons to think about using magnesium in orthopedic surgery:

1. An implant consisting of a magnesium based alloy would initially be **as strong as a traditional bone implant** made of steel or titanium and would, additionally, gradually dissolve.
2. It would show **very good biocompatibility, strong osteogenic potential and infect inhibiting effects.**

The challenge was to develop the right magnesium-based alloy suitable for osteosynthesis. The MAGNEZIX® alloy is based on the MgYREZr system and shows adequate values of strength properties (yield strength > 260 MPa, tensile strength > 290 MPa) and is free of known allergenic elements. Additionally, adapted casting, powdermetallurgical and extrusion processes significantly enhance the unique properties of the final product.

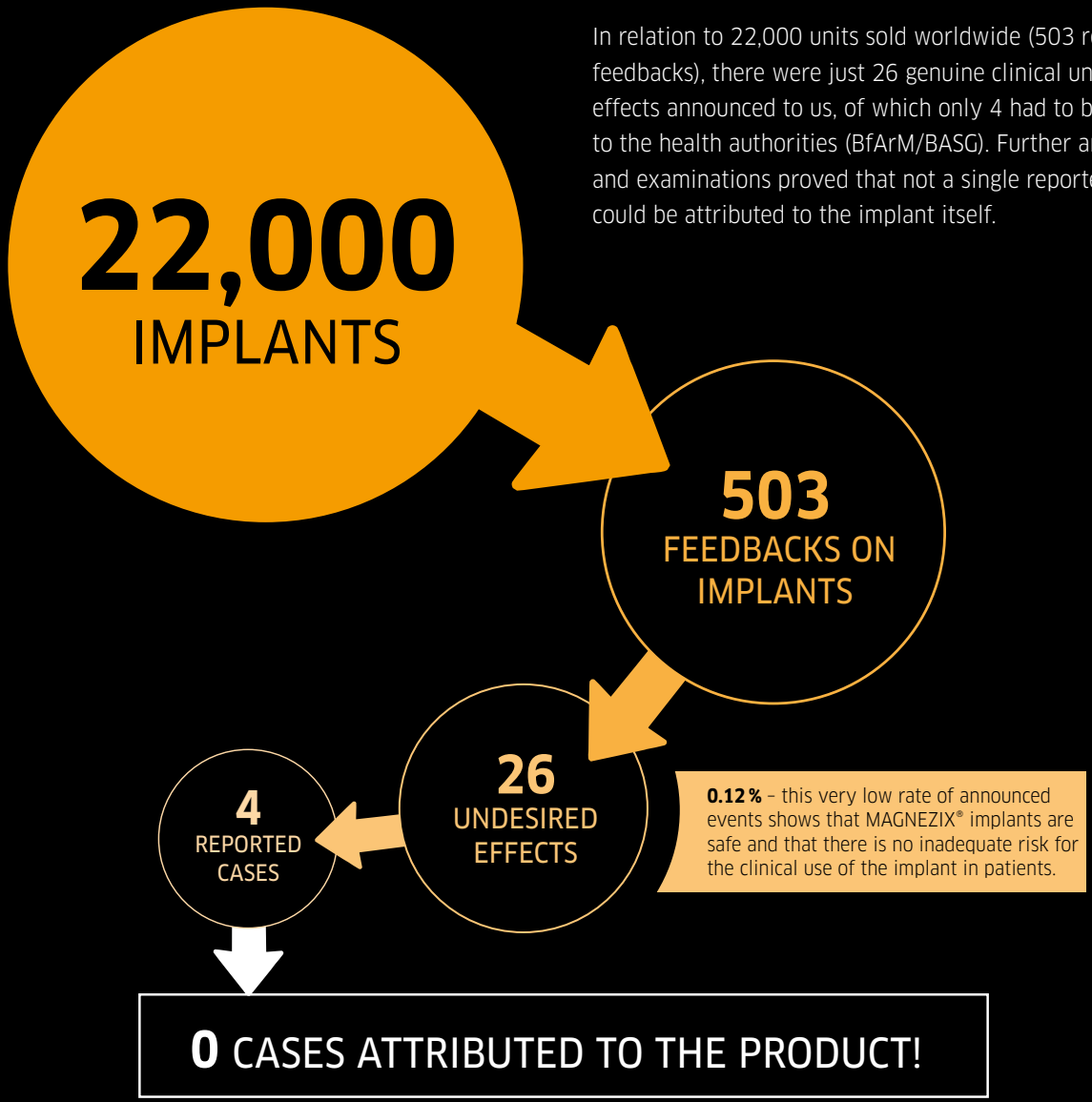
CE

CE approval for MAGNEZIX® compression screws (CS) was granted in 2013, for the first time enabling the clinical use of a degradable bio-metal in Europe. In 2015 and 2016, new screw sizes and the MAGNEZIX® Pin broadened the CE-approved portfolio

Progress requires change

The implementation of this innovation has not only led to a vast range of new possibilities, but also had and still has to deal with prejudices and reservation. In the end, every innovation requires reconsideration and every state-of-the-art product once was new and uncommon!

IN THOUSANDS OF SURGERIES NOT A SINGLE UNWANTED RESULT WAS ATTRIBUTED TO THE PRODUCT!*



In relation to 22,000 units sold worldwide (503 received feedbacks), there were just 26 genuine clinical undesirable effects announced to us, of which only 4 had to be reported to the health authorities (BfArM/BASG). Further analysis and examinations proved that not a single reported case could be attributed to the implant itself.

0.12 % – this very low rate of announced events shows that MAGNEZIX® implants are safe and that there is no inadequate risk for the clinical use of the implant in patients.

*All mentioned events seem to have been caused by the applicants' learning curve for the proper use and normal clinical course of the implant. Not a single case could be attributed to the product itself or its material.
Under no circumstances the product can be regarded more risky than comparable products which are already in wide spread use worldwide.

Source: Official vigilance data Syntellix AG, August 2016

MAGNEZIX® IS AN INNOVATION WITH PROVEN BENEFITS!

BEING A NATURAL MATERIAL, MAGNESIUM IS SUBJECT TO A BIOLOGICAL DEGRADATION PROCESS!

When using magnesium implants for the first time, surgeons may not be used to some **degradation-related appearances** they see in conventional X-rays. First, on postoperative radiographs, a MAGNEZIX® screw is not as dense as a titanium or steel implant. Second, during radiological control, the phenomenon of radiolucency may temporarily occur around the implant. This is a general phenomenon of the magnesium material and also associated with the degradation processes of MAGNEZIX®: While the material dissolves, there is a naturally loss of mass and weight. Also, magnesium releases small quantities of hydrogen gas which will be resorbed over time. Due to the osteoconductive capacity of MAGNEZIX®, osteoclasts and osteoblasts will appear, helping to enable the process of bone remodeling, and osteoid (non-mineralized bone matrix) is formed.
Although sometimes visually inconvenient, **the described phenomenon of radiolucent zones around the implant is only short-term, does not effect bone healing and disappears by itself.** Experiences from laboratory testing, animal studies and the clinical use so far prove that the screw disappears within around 12 months and is replaced after 3 years at the latest by endogenous tissue that corresponds most closely to bone tissue. The development of degradation byproducts in the dissolving process of magnesium seemed to be a critical factor for a long time. By optimizing the production process and the specific alloy composition of **MAGNEZIX®, this issue was consequently reduced to a minimum level.**

It is recommended to include the phenomenon of potential radiolucency in the operating room note/discharge note, pointing out that it does not have any clinically relevant influence on the healing process. This will inform the caregivers involved in the follow-up treatment about the special aspects of the implants' dissolving process.

Scaphoid fracture

post-op

follow-up after 6 weeks

follow-up after 18 weeks

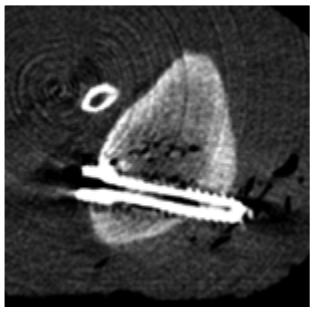
Post-op X-ray a.p.

6 months after surgery a. p.

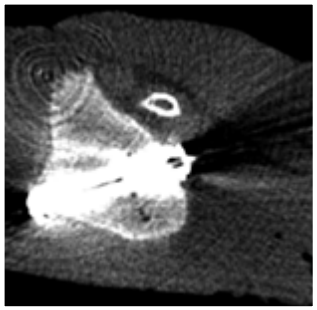
MAGNEZIX® IMPLANTS PROVIDE AN IDEAL STABILITY SINCE THEIR MECHANICAL PROPERTIES ARE VERY CLOSE TO THOSE OF CORTICAL BONE!

MAGNEZIX® implants are designed to be as stable as **steel or titanium screws and even 5x stronger than polymerbased pins.** Nevertheless, when the healing process is well advanced, deformed implants may be seen in diagnostic imaging. These implants did not break due to a lack of stability, but are degrading as intended while the bone continues to heal and gradually bears higher load capacity (see X-rays on the left side).

It should be noted that MAGNEZIX® CS implants follow a **magnesium-specific design** which should not be directly compared to titanium screws one to one (e.g. in terms of diameters). Thus, compared to titanium screws, it is recommended to use the next bigger MAGNEZIX® screw diameter in most cases.
The fact of using a self-cutting yet not a self-drilling screw should be considered as well. In some rare cases, the head of the screw had broken due to inadequate skipping of pre-drilling of either the cancellous or the cortical bone or both. For screws with **self-tapping tips, pre-drilling over the desired screw length is mandatory,** facilitating the subsequent tightening of the screw and reducing the rotation of small bone fragments.



MAGNEZIX® CS:
Minor interference signals in CT



Titanium:
Major interference signals in CT

MAGNEZIX® IMPLANTS ARE SUITABLE FOR MRI AND CT DIAGNOSIS!

The metallic MAGNEZIX® implants are **suitable for MRI and CT diagnostics.** Noise is greatly reduced and the implants only generate very few artefacts. In addition, unlike conventional screws made of steel and titanium, implants made of MAGNEZIX® do not generate any noticeable temperature increases during common MRI scanning. This helps to considerably improve the analysis of images by surgeons and radiologists.

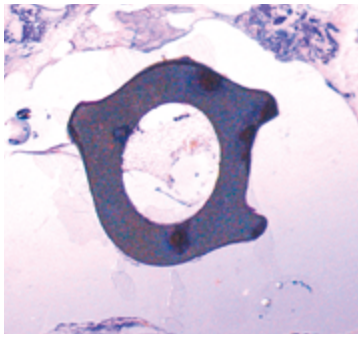
If X-rays are taken in order to intraoperatively evaluate implant positioning by means of fluoroscopy, the irradiated area should be **free of any other implants,** guide wires, instruments etc. Foreign materials in the irradiated field can raise the X-ray dosage, leading to inadequate exposure of MAGNEZIX® implants **(effect of „overexposure“)**.
The effect of overexposure can be reduced by **modification of the intensity of radiation.**

Source of CT images: Hannover Medical School, Institute for Diagnostics and Interventional Radiology

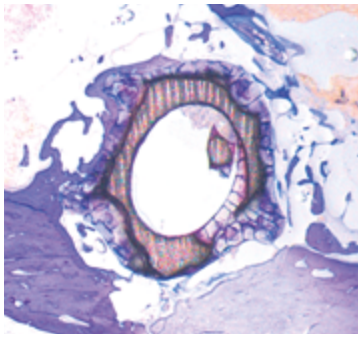
DEGRADING MAGNESIUM HAS OSTEOGENIC PROPERTIES AND REDUCES THE RISK OF INFECTIONS!

Magnesium is a biologically active material and can **support the healing process.** Both, *in vitro* and *in vivo* studies have shown excellent cell compatibility and distinct osteoconductive properties of magnesium alloys. *In vitro* trials with MAGNEZIX® have demonstrated a **high vitality of human osteoblasts** and their stimulation in proliferation tests.
Magnesium degrades via a corrosion process that creates a basic environment close to the implant, **inhibiting bacterial growth.** Furthermore, the presence of released hydrogen (or hydrogen ions) is described to be particularly advantageous in the human organism regarding cell and tissue protection. **Hydrogen, in this context, acts as an antioxidant** which selectively binds and defuses DNA-changing hydroxyl radicals or peroxi nitrides. These positive effects, proven for pure magnesium, can be strongly anticipated for MAGNEZIX®. Additionally, in order to minimize the risk of infection, all MAGNEZIX® implants are individually sterile packaged.

Supporting the healing process[1]



Histological preparation of an implanted MAGNEZIX® CS after a few days.



Transformation of MAGNEZIX® CS in progress after 3 months.

MAGNEZIX® CS conversion into calcium phosphate after 12 months with clear evidence of bone ingrowth.

MAGNEZIX® IMPLANTS ARE FREE OF NICKEL AND ALUMINIUM AND DO NOT PROVOKE ANY KNOWN ALLERGIES!

Magnesium itself has a **very good and proven biocompatibility,** which – amongst others – results from the high daily need of humans for the element magnesium. Within bone, it is easily available for resorption. This way, a magnesium implant that degrades within the bone can become a **source of essential magnesium ions.**
Since magnesium is a natural material essential for the body, generally it is very unlikely to provoke allergies. One advantage of MAGNEZIX® in this context is that it consists of more than 90 % magnesium. **It contains no nickel, cobalt, chromium or aluminium elements,** which are all under suspicion to cause severe diseases. In summary, there are absolutely **no allergies or foreign body reactions known for MAGNEZIX® implants!**

[1] Source: Waizy H, Diekmann J, Weizbauer A et al. (2014). In vivo study of a biodegradable orthopedic screw (MgYREZr-alloy) in a rabbit model for up to 12 months. J Biomater Appl 28 (5), 667-75.

THE EXPERIENCE OF OUR USERS IS THE BEST REFERENCE!

PATIENTS/IMPLANTS	INDICATIONS	PERIOD OF TIME	AUTHOR/SOURCE
17,000 implants in 20 countries	Multiple	Since market entry in 2013	Kirschner/Seitz Wehrmedizin und Wehrpharmazie 2/16, June 2016 (Article)
14 patients out of 26 for a final follow-up after 3 years	Hallux valgus	2011 to 2014	Reifenrath et al., 8th Symposium on biodegradable metals, May 2016 (Poster)
25 feet with hallux valgus deformity (15 left, 10 right)	Hallux valgus	March 2015 to April 2016	Thevendran, June 2016 (Presentation)
20 female patients	Hallux valgus	April 2015 to April 2016	Juutilainen, April 2016 (White paper)
100 MAGNEZIX® CS 3.2 implants	Hallux valgus	July 2014 to October 2015	Klauser/Wern, Orthopädische Nachrichten 4/16, April 2016 (Article)
4 patients	Scaphoid fractures	September 2015 to April 2016	Schächinger, 57th DAH Symposium, April 2016 (Presentation)

COUNTRY	DESCRIPTION/RESULTS
Over 20 different countries	By February 2016, 17,000 implants in 20 countries have been successfully placed on the market. **Clinically, positive results were achieved in almost every case of more than 7,000 implantations.**
Germany	For surgical treatment of hallux valgus deformities with distal metatarsal osteotomies, **magnesium compression screws showed comparable clinical results to titanium screws.** In detail, the clinical scores showed no statistical differences between the magnesium and titanium group as well as median MRI scores for edema, soft-tissue reaction, bone resorption and bone healing. The median MRI score for metal artifacts was significantly lower in the magnesium group (1 score-point). Additionally, a linear hypointensity could be seen in the magnesium group, outlining the former implant site without metal artifacts, whereas centrally, areas of intermediate signal intensity were found.
Singapore	MAGNEZIX® bioreabsorbable screws, when used in hallux valgus deformity correction, **are at least as good as conventional titanium alloy screws with regards to functional results and radiologic correction.** Bioreabsorbable implants, however, do not necessitate removal nor cause stress shielding. Socio-culturally, patients are much more receptive to having these implants.
Finland	The first 20 hallux valgus operations using MAGNEZIX® screws were uneventful. The preliminary results in this case are the same as compared to titanium or stainless steel screws. There were **no major problems during the healing period.** No deep infections were noticed and there was no need for a second operation. **There were no complications due to the used fixation material.** All patients were asked about subjective satisfaction of the operation, **all said that they would have the same operation if the other foot had to be operated in the future.** It is currently compulsory to countersink the proximal part of the screw and it is also recommended to drill the whole canal before inserting the screw. MAGNEZIX® screws should vanish in a few years. So there should be no need for hardware removal at any time. Altogether, MAGNEZIX® screws offer a good alternative for fixation of first metatarsal osteotomies.
Germany	Based on very positive results and experiences with the MAGNEZIX® CS according to the **uncomplicated intraoperative application and post-operative clinical development with good stability load-bearing capacity,** the use of MAGNEZIX® implants for Hallux valgus corrections has become standard in the Hand and Foot-Centres in Berlin, Potsdam and Frankfurt ("Hand- und Fußzentren"). The intraoperative handling of the screw is similar to implants made of steel or titanium. In general, the post-operative clinical development after implanting MAGNEZIX® CS is uncomplicated and works without problems. **The implant is a valuable alternative to polylactide implants as well as double threaded screws made of steel and titanium and is well-suited for stabilizing Chevron- and Youngswick-Osteotomies.** A removal of the implant is not necessary; security in MRI and CT diagnosis is given – just like the high bio-compatibility.
Germany	**Compared to compression screws made of titanium, when using the bio-degradable magnesium-based compression screw, there are no major differences concerning the operating technique or healing process and no clinical anomalies have been seen so far.** Temporary radiolucencies during radiological control seem to be clinically ineffectual and have to be clearly differentiated to known radiolucencies (like osteolysis because of an infection or loosening).

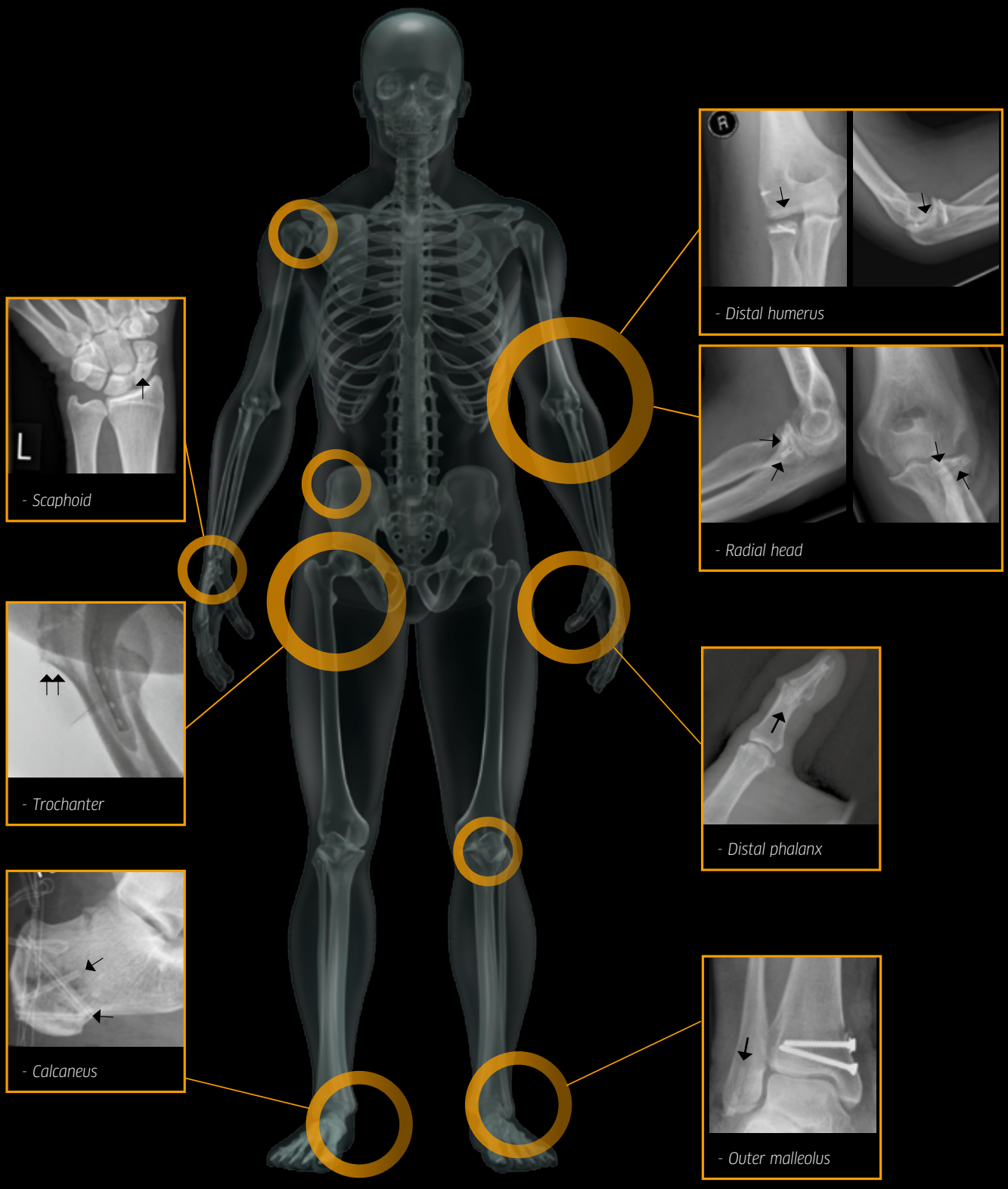
MAGNEZIX® MEETS ALL CRITERIA OF AN IDEAL IMPLANT!

	TITANIUM	STEEL	POLYMERS	MAGNEZIX©
Degradation	No	No	1-6 years, beginning immediately	1-2 years, beginning immediately
Loss of stability half-value period	Only fatigue	Only fatigue	10-50 % after 12 weeks	App. 50 % after 12 weeks
Young`s modulus (bone: 12-25 GPa)	105 GPa (5 times higher)	193 GPa (10 times higher)	4 GPa (lower)	47 GPa (2 times higher - ideal)
Tensile strength (bone: 150 MPa)	539 MPa	275-520 MPa	10-150 MPa	> 290 MPa
Biocompatibility	Gold standard	Foreign body reactions known	Foreign body reactions known	Good, proven with ISO 10993-1
Degradation products	No resorption	No resorption	Not finally checked	Biocompatible and bio-absorbable oxides and hydroxides, hydrogen gas
Radiology (CT, X-ray, MRI)	Well visible, partially with artefacts	Well visible, extensive arte-facts	No artefacts, partially not visible	Low artefacts, visible with X-ray

MAGNEZIX® has mechanical stability values which are far above the values of those bioresorbable materials previously available. The mechanical properties of the MAGNEZIX® alloy, determined after the final extrusion process, result in yield strength properties higher than 260 MPa, tensile strength properties higher than 290 MPa and elongation to failure properties higher than 8 %. With a Young's Modulus of 47 GPa, **the biomechanical properties of MAGNEZIX® are very close to those of human bone.** The good bone-like stress-strain ratio effectively counteracts stress shielding effects that can result in loss of bone density (osteopenia). Consequently, the significant higher elasticity compared to steel or titanium implants implies micro-movement in the fracture zone leading to better healing conditions.

MAGNEZIX

VARIOUS APPLICATIONS – ONE SIMILARITY: NO REMAIN OF FOREIGN MATERIAL!



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Implants are manufactured in Germany
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