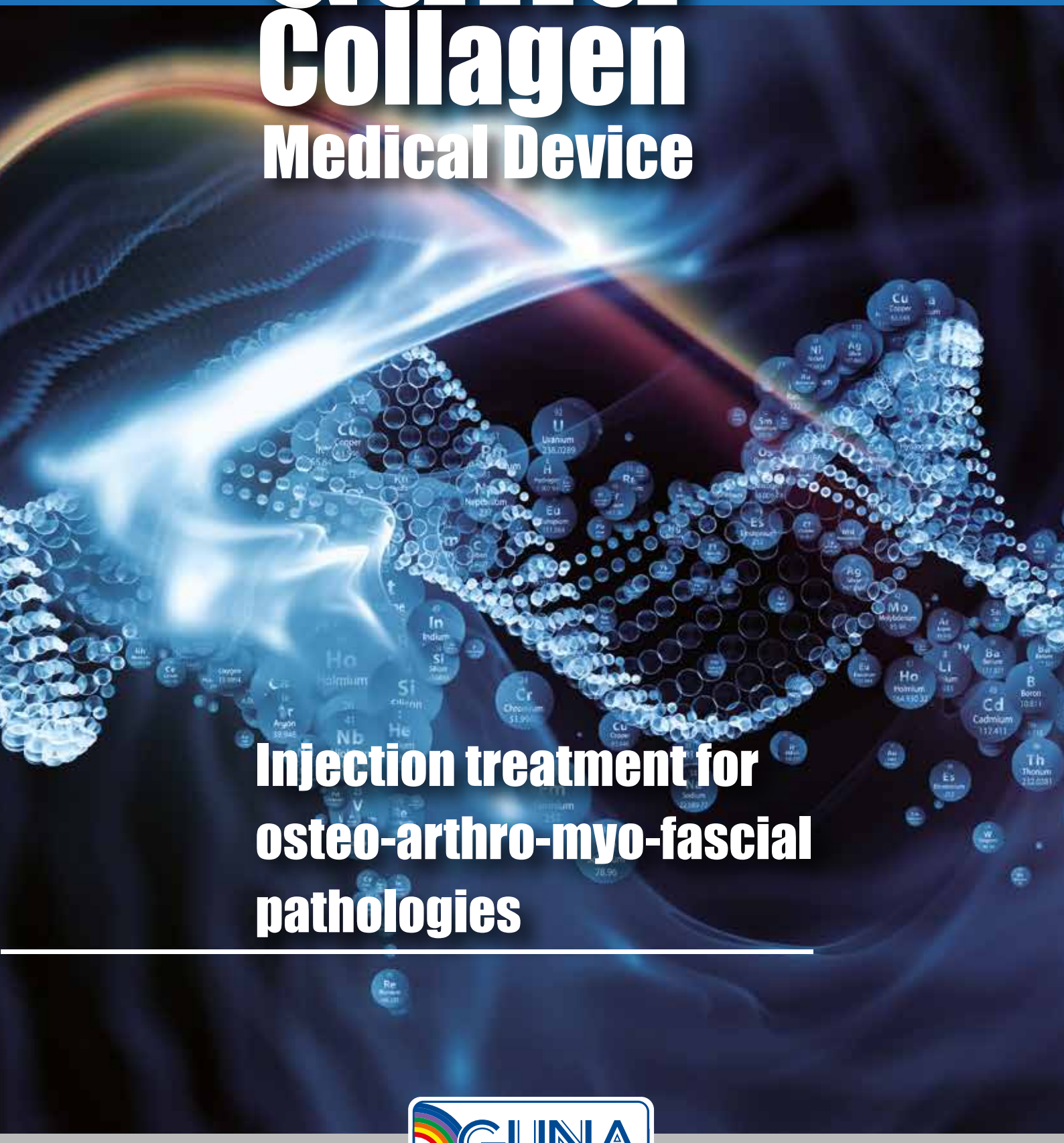
Guna Collagen

Medical Device



Injection treatment for osteo-arthro-myo-fascial pathologies

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Guna Collagen
Medical Devices

- Characteristics
- Mechanism of action
- Directions for use

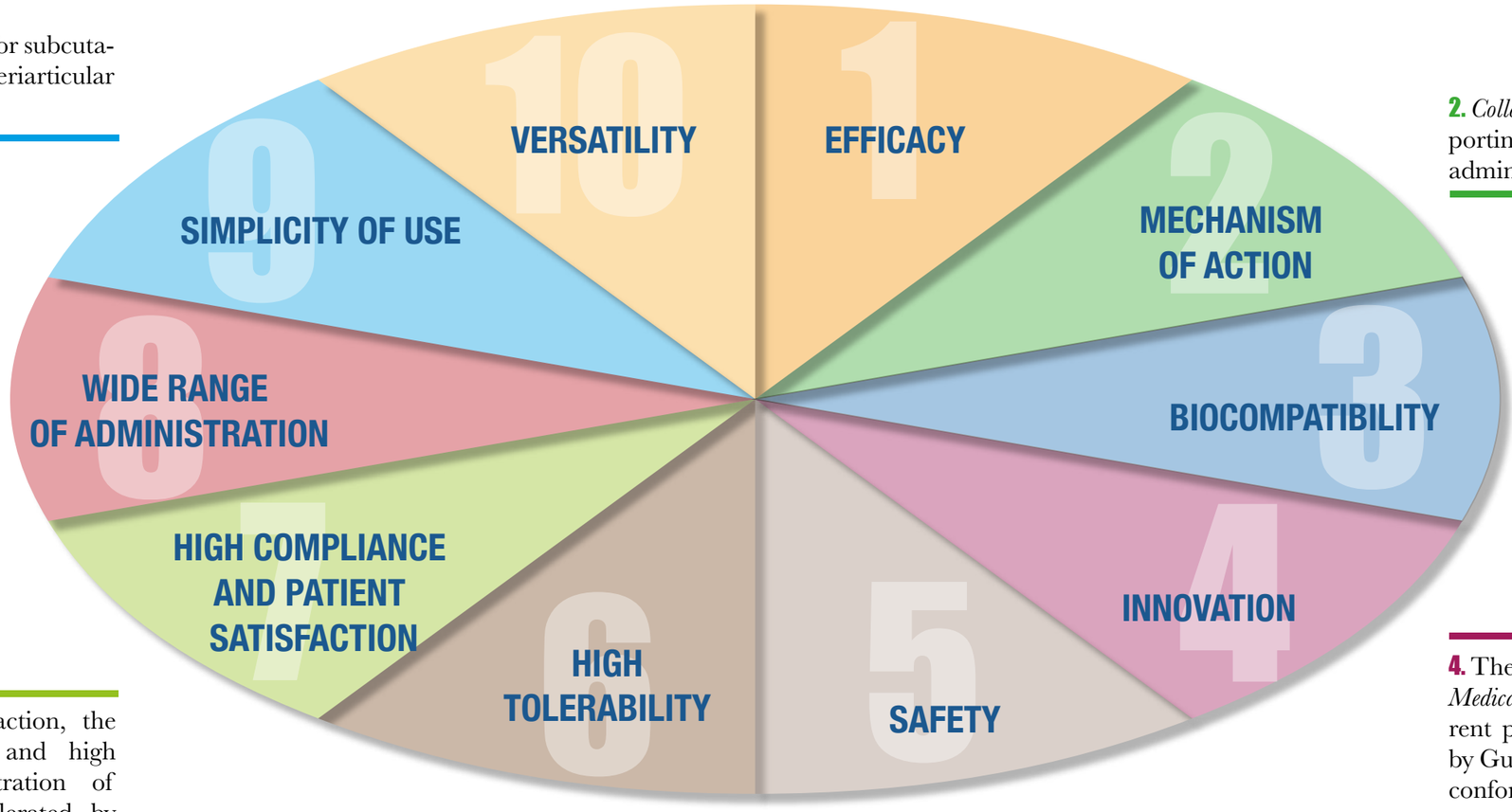
Why to administer Guna Collagen Medical Devices?

Ten "points of strength"
Guna Collagen Medical Devices

10. Guna *Collagen Medical Devices* can be administered singularly or in association with other MDs/medicines. There are no contraindications for patients undergoing a pharmacological or osteopathic therapy or in any other rehabilitation path. *Collagen Medical Devices* can be administered before or after surgery.

1. Restoring and reinforcing the damaged anatomical structures, *Collagen Medical Devices* improve mobility and functionality and act directly on the pain.

9. *Collagen Medical Devices* can be used for subcutaneous, intradermal, intramuscular, periarticular or intra-articular injections.



2. *Collagen Medical Devices* perform a supporting action in the specific routes of administration.

8. *Collagen Medical Devices* can be used to treat disorders with different origins (due to overuse, aging or injury) and in different medical fields (Rheumatology, Orthopedics, Rehabilitative Medicine, Traumatology, Sports Medicine, Anti Aging…) as well as in General Medicine.

3. Collagen (extract of porcine origin) and auxiliary substances are biocompatible.

7. Thanks to the mechanism of action, the absence of known side effects and high performance rates, the administration of *Collagen Medical Devices* is well tolerated by patients. The product meets both the patient's and the physician's expectations.

4. The collagen used to produce *Collagen Medical Devices* is the result of three different production processes implemented by Guna Laboratories (identification and conformity check of the porcine tissue, extraction phase, preparation and sterilization/viral inactivation of the collagen extract).

6. Up to now no side effects, allergic reactions nor drug interactions have been observed. A slight reddening in the injection area is due to the mechanical action of the needle.

5. Thanks to the implementation of cutting edge production processes, Guna Laboratories have obtained a safe product. *Collagen Medical Devices* have the chemical-physical characteristics to guarantee safety in clinical use.

Is it possible to slow down the degenerative processes and induce the repair processes of the Musculoskeletal System?

Tissues of the Musculoskeletal System can be damaged by:

a) **overuse**;
b) physiological **aging** processes;
c) **traumatic** events (implying an inflammatory component).

Guna Collagen Medical Devices represent a therapeutic tool ideal to manage repair and remodeling processes, which are essential in restoring damaged tissue *(Figure 1)*.

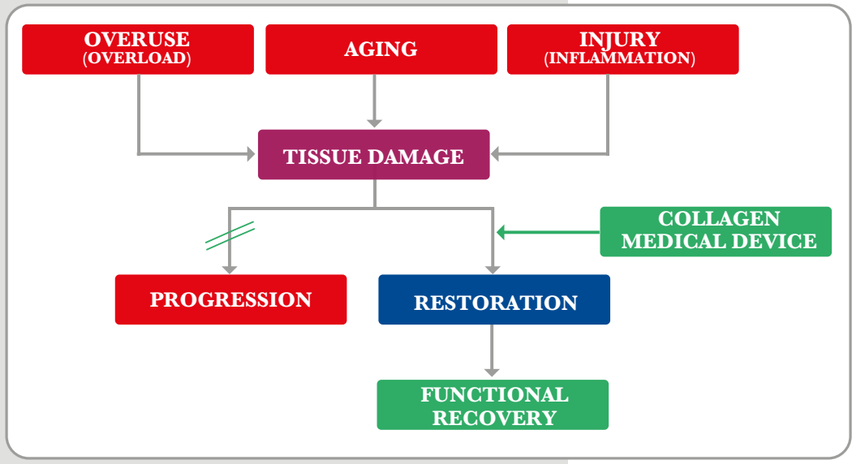


Figure 1
Flowchart of the events occurring after overuse, aging and injury which affect collagen fibers, and positioning of Guna Collagen Medical Devices.

In all cases (overuse, aging and injury), the most evident result is the loss of integrity of the collagen fibers which appear no longer organized in a linear way nor parallel to one another and may display lacerations. [1; 2]. *(Figure 2)*

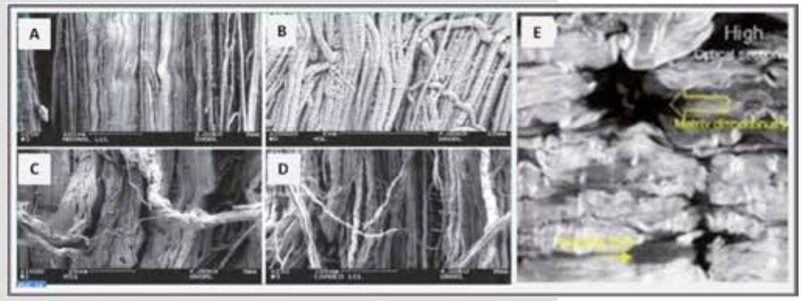


Figure 2
In the presence of overuse, aging and injury, typical microstructural alterations occur; among these, the progressive loss of the alignment of collagen fibers (**A-D**) and the so called "moth eaten" tissue (**E**).
- Microphotography in Provenzano P., Hurschler C., Vanderby R. Jr
- Connective Tissue Research, 42; 123-133; 2001.

The damaged tissue undergoes a long multiphase recovery process during which repair and *restitutio ad integrum* phenomena are linked to the deposition and reorganization of the extracellular matrix scaffold, primarily formed by collagen.

Anti-inflammatory drug therapies are only useful immediately after the traumatic damage occurs, obviously in the presence of inflammation. Prolonged use of inflammatory drugs during the repair and remodeling phases may have a detrimental result, because such drugs may interfere with the synthesis of new collagen[3]. *(Figure 3)*

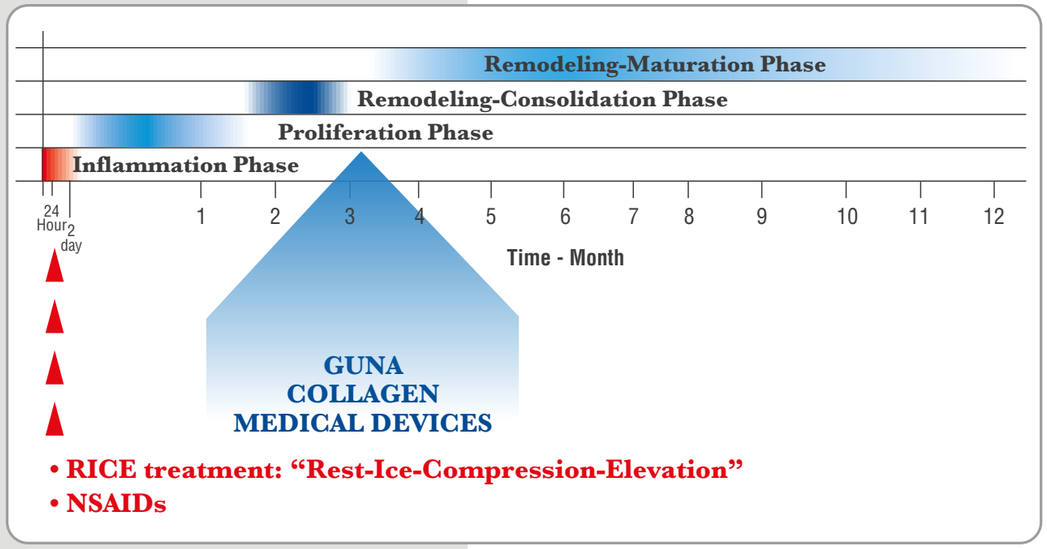


Figure 3
Chronobiology of tissue repair processes of the Musculoskeletal System. A short inflammatory phase is followed by a proliferative (repair) phase, after which occurs the remodeling phase. The tissue becomes more fibrous and the collagen fibers begin to re-organize in a linear way, increasing their tensile strength. The fibrous tissue is then transformed into an adhesive scar tissue. The tissue continues remodeling for up to a year following the pathological event.

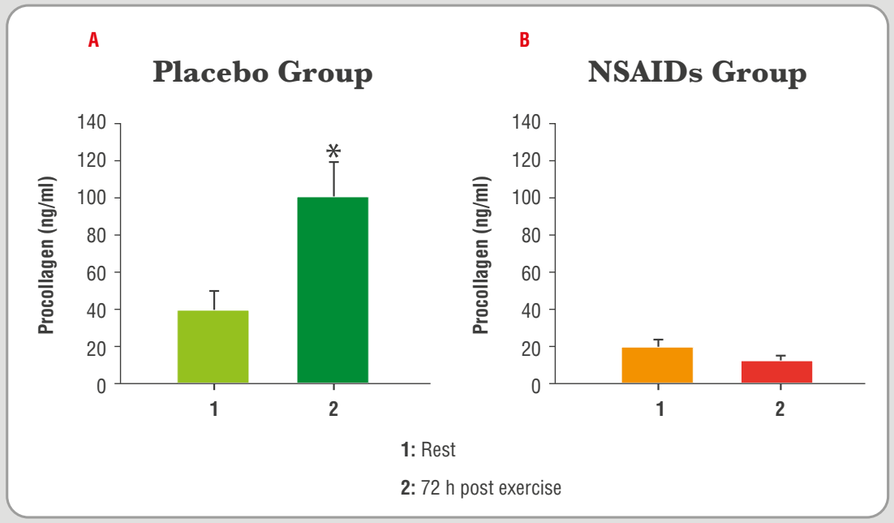


Figure 4
After approximately 48 hours following the appearance of the lesion, the "repair" phase, initiates, characterized by the active deposition of new collagen (**A**). Anti-inflammatory drug treatment (NSAIDs) by blocking prostaglandins (PGE2) reduces the synthesis of new collagen (PINP: procollagen) (**B**).
- Christensen B et al. J Appl Physiol 2011;110:137-141

The supplementation of collagen through the administration of *Guna Collagen Medical Devices* is valuable to protect tissues of the Musculoskeletal System from the results of overuse, from aging processes, and to support the physiological repair of the tissue damaged by injury. *(Figure 4)*

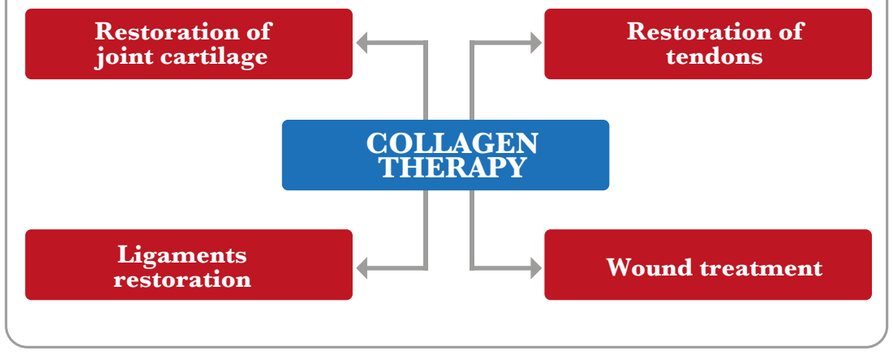


Figure 5
Effects of collagen administration in the main fields of application of Guna Collagen Medical Devices.

The therapeutic use of collagen is ideal to treat the pathologies which are due to damage or overuse of all tissues of the Musculoskeletal System and the Integumentary System [1]. *(Figure 5)*

Why is Collagen essential in the repair and remodeling processes?

Collagen represents 5-6 percent of body weight and is the most abundant protein in mammals. Collagen is the main component[4] of **ligaments**, **tendons**, **bones**, **cartilage**, **muscles**, **skin**, and the **extracellular matrix** (ECM).

The smallest subunit of collagen is **tropocollagen** formed by sequential glucose/galactose units and by 4 amino acids (proline, hydroxyproline, glycine and lysine). *(Figure 6)*

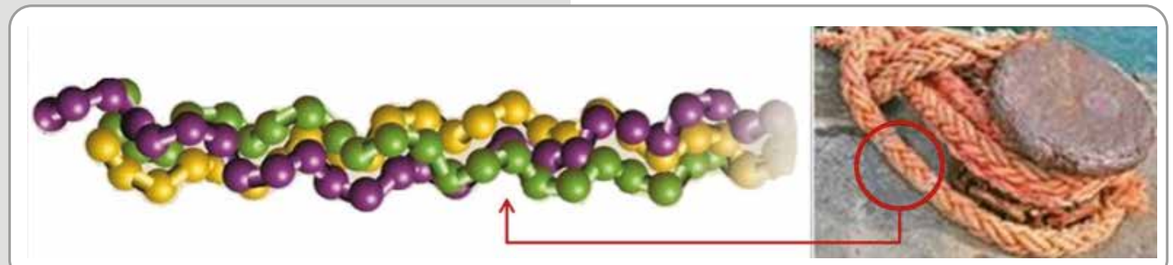
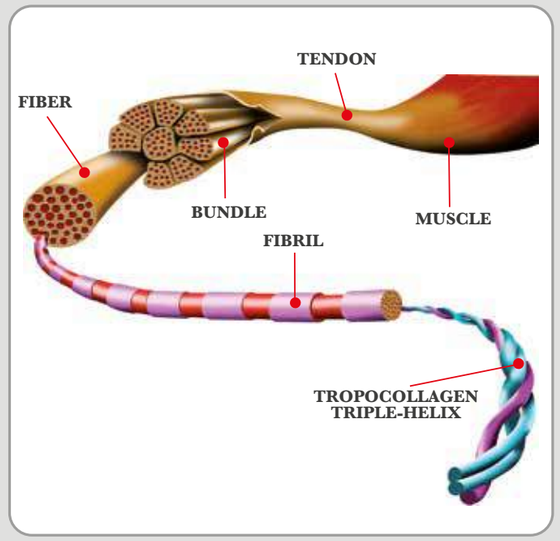


Figure 6
Tropocollagen triple helix is the basic functional unit of collagen.



Tropocollagen, organized in a triple helix, gives origin to mature collagen; collagen is then organized in fibers. These fibers are essential units that when thusly organized, participate in tissue and ECM formation. *(Figure 7)*

Figure 7
Schematic representation of the micro- and macro-organization of collagen fibers.

The mechanism of action of Guna Collagen Medical Devices

In detail, collagen synthesis can be described as a mechanism in 4 phases *(Figure 8)*:

1. Nuclear activation of **preprocollagen** synthesis;
2. **Procollagen** assembly and its exocytosis;
3. Conversion of **procollagen** into **tropocollagen** through the action of specific peptidases;
4. Assembly of **tropocollagen** in **collagen fibers** in the presence of **lysine-hydroxylase** in the extracellular matrix (**ECM**).

Guna Collagen Medical Devices provide only Collagen in the form of Tropocollagen *(Table 1)*, which is the substrate of the endogenous enzyme lysine-hydroxylase. Therefore, they do not exert any pharmacological action because the normal metabolism/catabolism of collagen remains unchanged.
The tropocollagen contained in *Guna Collagen Medical Devices* performs subsequently as a ***bio-scaffold*** [1].

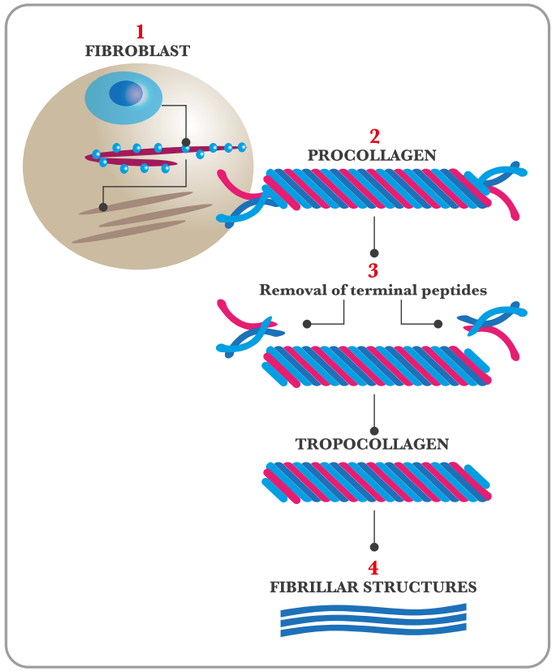


Figure 8
Schematic representation of the physiological synthesis of collagen performed by fibroblasts.

Characteristics of collagen in Guna Collagen Medical Devices

Type of collagen	Molecular weight of type I tropocollagen	Amount of tropocollagen in 1 vial/2ml	Molecules of tropocollagen in 100 µg of tropocollagen preparation
Type I Tropocollagen	**300 kDa**	**100 µg**	**$2X10^{14}$**

Table 1
Chemical-physical characteristics of collagen contained in *Guna Collagen Medical Devices*

The deposition of the neo-synthesized collagen fibrils in the damaged region, secondary to the injection of *Guna Collagen Medical Devices* in the affected area, produces a significant improvement of the mechanical properties of the injured tissue. In particular, the characteristics of the **ANISOTROPY** of the tissue are being restored.
Anisotropy is a mechanical property of collagen and it is the ability of its fibers to spread tensile forces, towards **one single preferred direction**.

This property, essential for many biological functions, is gradually lost when the collagen fibers are damaged by overuse, aging or injury [2; 5]. In particular, the hydrogen bonds between the collagen fibers, which are fundamental for the orientation of the fibers themselves, are altered.

The anisotropy of the collagen fibers is essential to insure that the "scaffolding" of the extra-cellular matrix, **thanks to the orientation of the collagen fibers towards a single direction** (hydrogen bonds are formed between one fiber and the other), is able to provide the mechanical support necessary for the proper functioning of, for example, the osteoarticular area.

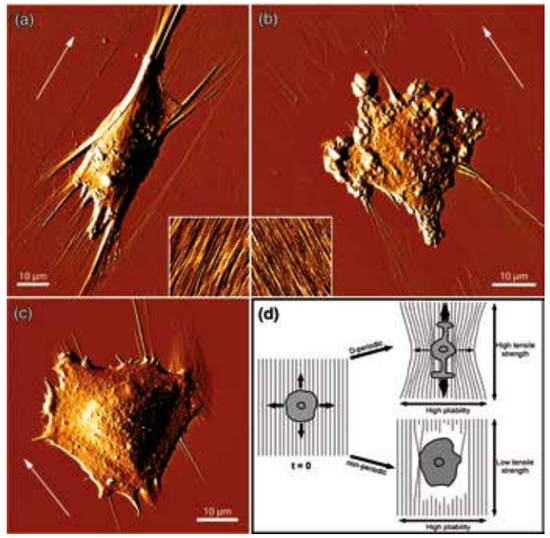


Figure 9
The rigidity of the matrix and its anisotropy [5] are necessary for cellular polarization (**A**). The loss of cellular polarization is owing to the loss of anisotropy (**B**; **C**).
- Friedrichs J. et al. Cellular Remodelling of Individual Collagen Fibrils Visualized by Time-lapse AFM. J. Mol. Biol. 2007

An optimal formation and distribution of collagen fibers is fundamental not only for the integrity and the structural function of the tissue, but it also plays a central role in the transmission of tensile forces to **FIBROBLASTS** dispersed in the matrix (through interaction with specific trans-membrane receptors called **INTEGRINS**) and is responsible for the deposition of collagen itself. *(Figure 9)*

Two aspects are essential for a proper function of fibroblasts:

- The ability to polarize inside the extra-cellular matrix;
- The ability to respond “biologically” to tensile forces.

INTEGRINS are special receptors present on the surface of fibroblasts and protrude into the extra-cellular matrix. These integrins are able to intercept a tensile strength and turn it into an intra-cellular signaling, i.e., they turn a mechanical force into a structural and biochemical response [6-8]. *(Figure 10)*

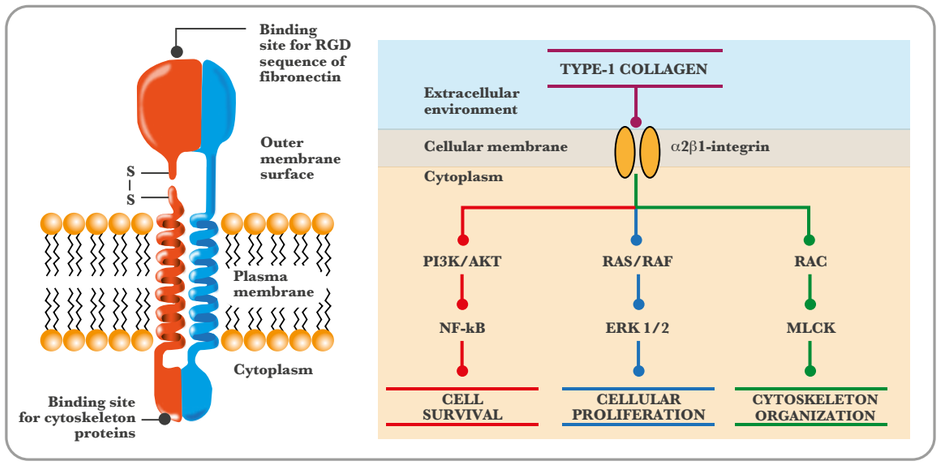


Figure 10
Structural model of Integrins and cellular pathways influenced by their activation.
- Modified from: Kjaer M. Role of extracellular matrix in adaptation of tendon and skeletal muscle to mechanical loading. Physiol Rev 2004; 84, 649-98.

A reduced anisotropy of the collagen fibers as a consequence of overuse, aging or injury results in a reduced ability to transmit tensile strength. *(Figure 11)*

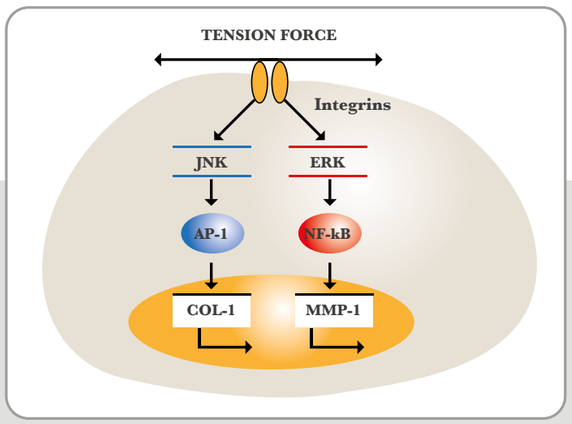


Figure 11
Expression of type I Collagen and MMP-1 by fibroblasts subjected to tensile strength (JNK-AP-1 signal / ERK-NF-KB mediated). Low tensile strength reduces the deposition of new collagen and the remodeling of the matrix due to damage.

Therefore, the **bidirectional communication** between fibroblasts and their surrounding microenvironment fails. From a biological viewpoint, this results in a reduced deposition of collagen, and therefore a reduced tissue repair [9-10].

Restoring the anisotropy of collagen fibers through local injections of *Guna Collagen Medical Devices* induces the same biological response that is obtained with **eccentric training** that is typical of the functional recovery phases after a tendon injury. Through the signaling induced by the stimulation of integrins, *Guna Collagen Medical Devices* are capable of inducing the cascade of growth factors [TGF-beta 1 (*Transforming Growth Factor beta 1*); CTGF (*Connective Tissue Growth Factor*); IGF-1 (*Insulin Growth Factor-1*)] necessary for the production of new collagen by the fibroblast [11]. *(Figure 12)*

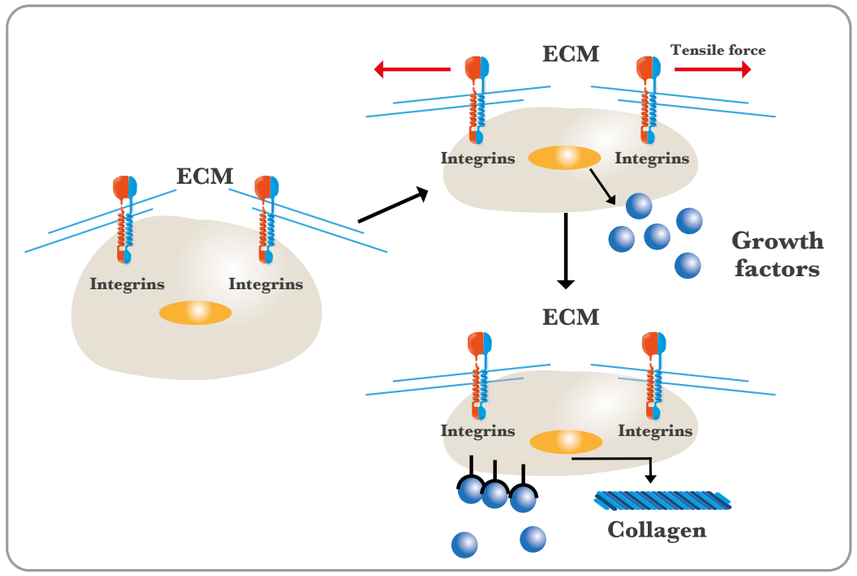


Figure 12
Biological response of fibroblasts to tensile strength. The activation of integrins by the tensile strength induces the production of growth factors (TGF-beta; CTGF; IGF-1) and consequent neo-synthesis of collagen

This is a sophisticated biological mechanism that, through local collagen injection, mechanically reactivates the ability of a fibroblast to synthesize new collagen, inducing autologous mechanisms of **repair** and **remodeling** of the injured connective tissue. Moreover, fibroblasts are capable of both generating and exerting tensile strength. These fibroblast contraction forces are essential to wound healing.

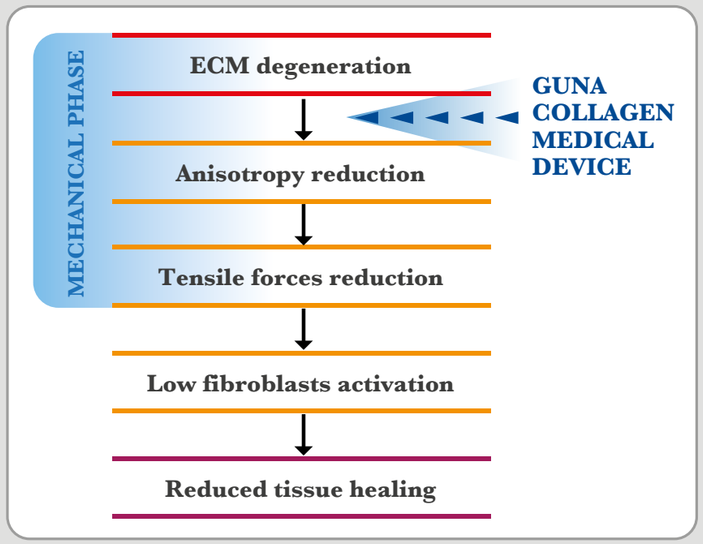


Figure 13
Guna Collagen Medical Devices act in the very early stages of tissue damage by stopping the degeneration of the tissues and promoting their physiological repair.

Why porcine collagen?

The collagen contained in *Guna Collagen Medical Devices* is **type I collagen of porcine origin**. It is better than bovine collagen because it is more similar to human collagen. Choosing porcine collagen guarantees a high level of safety thanks to its very low immunogenicity. This makes it a material of choice for many applications, for instance in the medical aesthetic field, including bio-scaffolds production and dermo-cosmetic fillers [12-16]. *(Figure 14)*

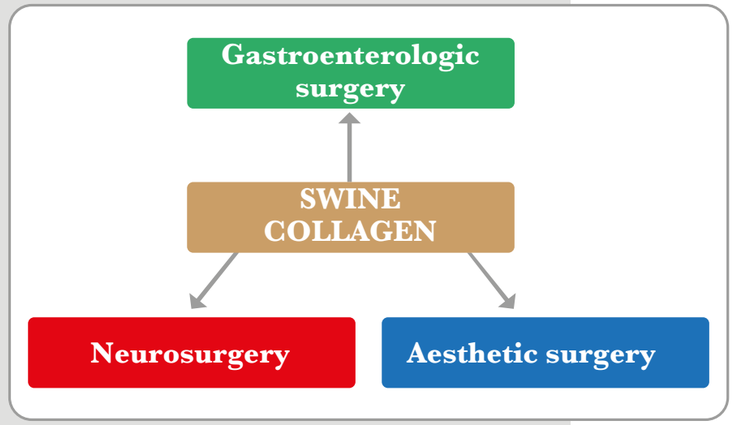


Figure 14
Main fields of medical application where porcine collagen gives good results and guarantees a high level of safety.

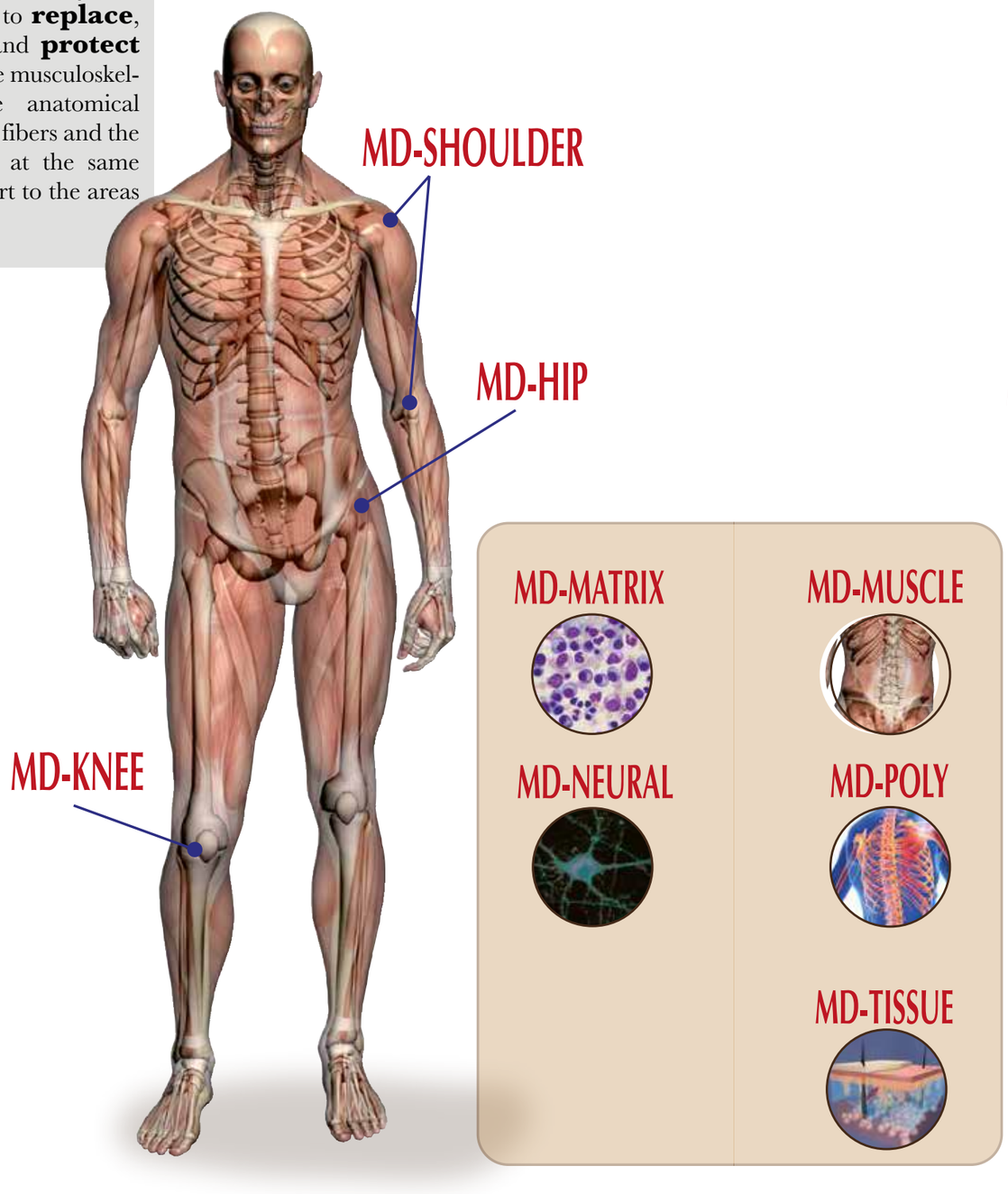
To obtain a safe product without contaminants, with standardized chemical-physical characteristics, the collagen of *Guna Collagen Medical Devices* undergoes three manufacturing processes:

- **identification and conformity check of the porcine tissue**
- **extraction phase**
- **preparation and sterilization/ viral inactivation of the collagen extract.**

GUNA's industrial production process, thanks to an exceptionally high standardization of the product allows the manufacture of a safe product, suitable for clinical applications.

What is the scope of the injectable collagen?

The collagen of *Guna Medical Devices* is injected locally where "needed", in order to **replace**, **strengthen**, **restructure** and **protect** (adherent barrier) the tissues of the musculoskeletal apparatus, improving the anatomical structure and function of collagen fibers and the structures containing them and, at the same time, providing mechanical support to the areas involved.



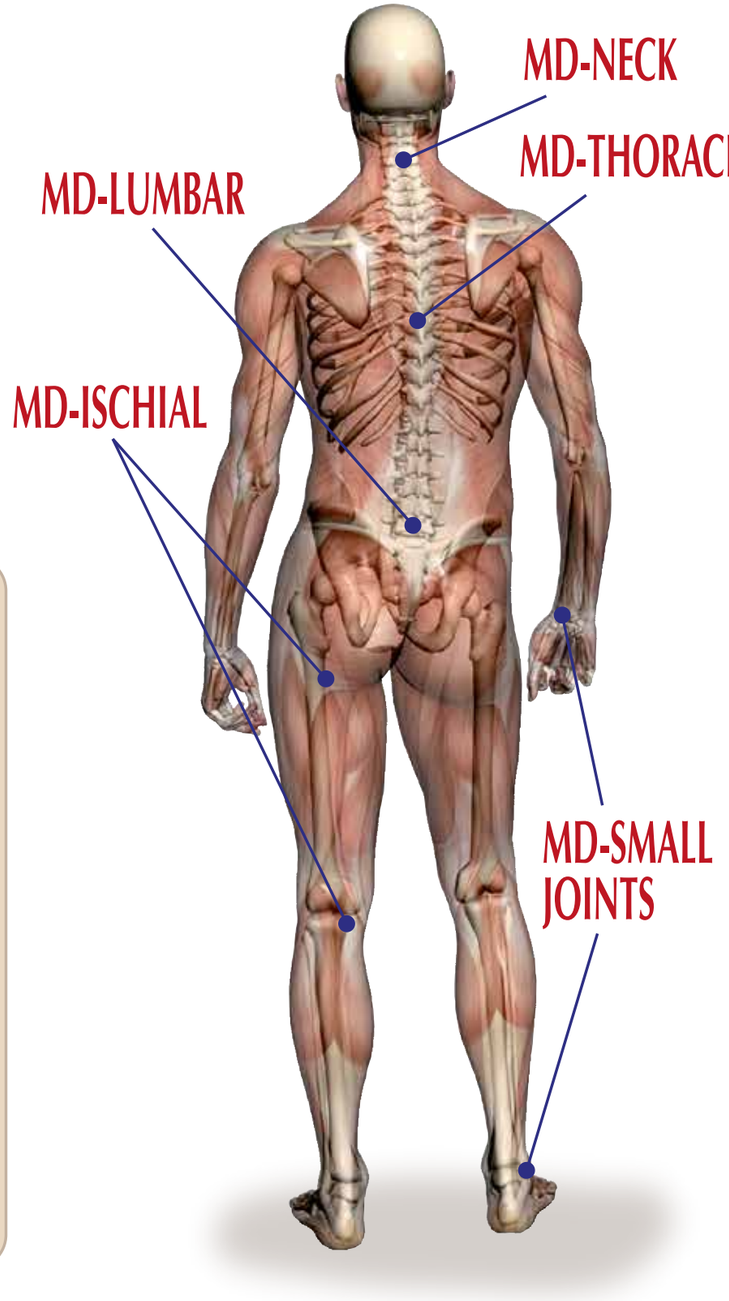


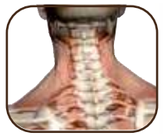
Figure 15
The whole range of the 13 *Guna Collagen Medical Devices* allows an effective injection of collagen in specific areas, thanks to the auxiliary substances that deliver and stabilize it.

- **7 Guna Collagen Medical Devices** are specific to each skeletal area and for the related diseases [MD-NECK (**Cervical region**); MD-THORACIC (**Thoracic region**); MD-LUMBAR (**Lower Back region**); MD-SHOULDER (**Shoulder region**); MD-HIP (**Hip**); MD-KNEE (**Knee**); MD-SMALL JOINTS (**Small Joints**)];

- **1 Guna Collagen Medical Device** is specific to the area of the **ischial nerve** [MD-ISCHIAL];

- **5 Guna Collagen Medical Devices** have been designed to treat somatic diseases that affect the tissues of mesodermal origin [MD-MUSCLE (**Muscles**); MD-NEURAL (**Nerves**); MD-POLY (**Joints**); MD-MATRIX (**Extra-Cellular Matrix**); MD-TISSUE (**Soft Tissues**).

Summary table of the 13 Guna Collagen Medical Devices and related fields of application

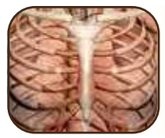


MD-NECK (neck)

Collagen

Silica

Improve mobility of the cervical region of the spine, promote cervical muscle stretching, help to support cervical muscle tissue, help to support cervical muscle tissue in bad posture disorders, soothe cervical column pain due to movement



MD-THORACIC (thorax)

Collagen

Cimicifuga

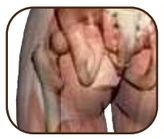
Improve mobility of the thoracic tract of the spine, help muscle stretching, help to support muscle tissue in bad posture disorders, soothe leg pain, pain due to movement and bad posture

MD-LUMBAR (lumbar)

Collagen

Hamamelis

Help lumbar region mobility, help muscle stretching of the lumbo-sacral area, help to support the lumbar muscle tissue, soothe local pain, pain at rest or caused by movement and bad posture



MD-ISCHIAL (sciatic nerve)

Collagen

Rhododendron

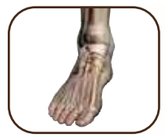
Improve leg mobility, leg muscle stretching, help to support leg muscle tissue, soothe leg pain while starting to move legs again after a long inactivity period

MD-SHOULDER (shoulder)

Collagen

Iris

Improve shoulder- and arm-joint mobility, help muscle stretching, help to support the muscle tissue, soothe local pain and pain due to movement



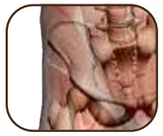
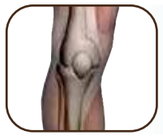
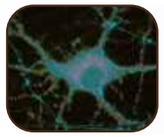
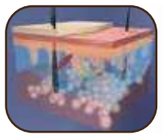
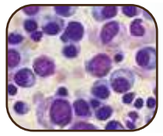
MD-SMALL JOINTS (small joints)

Collagen

Viola

Improve mobility of the small joints of hand, foot and ankle, help muscle stretching, help to support muscle tissue, soothe local pain and pain due to movement

Summary table of the 13 Guna Collagen Medical Devices and related fields of application

 **MD-HIP** (hip)	Collagen	Calcium phosphate	Improve mobility of the hip joint, help muscle stretching in the lumbo-sacral area, help to support peri-articular muscle tissue, soothe local pain and pain due to joint movement or bad posture
 **MD-KNEE** (knee)	Collagen	Arnica	Improve knee mobility, help muscle stretching, soothe knee pain while moving legs and knee
 **MD-MUSCLE** (muscles)	Collagen	Hypericum	Enhance muscle relaxation and functioning, help to support the muscle tissue in bad posture disorders, improve joint mobility, soothe local pain, pain at rest or caused by movement and bad posture
 **MD-NEURAL** (nerves)	Collagen	Colocynthis	Strengthen perineurium collagen structure, soothe neural local pain
 **MD-POLY** (joints)	Collagen	Drosera	Improve joint mobility, help muscle stretching, help to support the muscle tissue in bad posture disorders, soothe local pain and pain due to joint movement or bad posture
 **MD-TISSUE** (soft tissues)	Collagen	Ascorbic acid Magnesium gluconate Pyridoxine hydrochloride Riboflavin Thiamine hydrocloride	Act as a defensive barrier against free radicals, counterbalance the physiological aging of the connective tissue, soothe local pain caused by movement
 **MD-MATRIX** (extracellular matrix)	Collagen	Citric acid Nicotinamide	Strengthen extra-cellular matrix tissues where the collagen barrier is located, act as a defensive barrier against free radicals

Why auxiliary substances?

A **Medical Device** can be **supported in its primary action** by one or more auxiliary substances, through pharmacological, immunological or metabolic action which, by definition, must not be more predominant than the main constituent (collagen) [Directive 93/42 / EEC and subsequence modifications and integrations] . The word auxiliary comes from the Latin **ancilla = servant**, **helper**.
The function of the auxiliary substances (also known as accessory) is complementary: "**in the service of collagen**".

Each *Guna Collagen Medical Device* is highly specific for a certain region. Each specific tropism is favored by the presence of specific auxiliary substances associated to collagen. Indeed, any substance, for its intrinsic nature, develops a tropism for one or more specific tissues in accordance with the herbal medicine pharmacokinetics (for plant-derived auxiliary substances) or with metabolic mechanisms (for mineral substances, vitamins and trace elements).

Auxiliary substances and regional specificity of Guna Collagen Medical Devices

A minimal presence of specific auxiliary substances associated with the collagen in each *Guna Collagen Medical Device* improves the performance of each product. Specific local injections, which enhance the features of tissue tropism of various auxiliary substances, is required in order to have a Collagen Delivery System, i.e., an efficient system capable of delivering the collagen to the specific areas to be treated. Each auxiliary substance has been chosen to optimize the effect of the collagen and to obtain the best tropism toward the target.

SILICA (MD-NECK)

Silica, the auxiliary substance contained in MD-NECK, is an essential element present in small amounts in higher order animals and is fundamental for bone and cartilage formation and growth. Silica has been included in the formulation of MD-NECK because it acts synergistically with the porcine collagen in order to improve the stabilization of the intervertebral joints of the neck.
Moreover, *Silica* is significantly involved in the formation of glycosaminoglycan-protein [17] complexes on the level of the ground substance.

VIOLA (MD-SMALL JOINTS)

According to Traditional Medicine, *Viola* is used to treat carpal and metacarpal pain, and also rheumatism [18]. This is the rationale why low doses of this auxiliary substance have been used in MD-SMALL JOINTS with a synergistic action compared to the mechanical action of collagen.

RHODODENDRON (MD-ISCHIAL)

Traditional Medicine uses many *Rhododendron* species as an anti-inflammatory and anti-nociceptive [19]. In particular, its leaves are rich in flavones responsible for these biological activities. *Rhododendron* is described as a highly effective plant to treat rheumatic pain [20].
This is the reason why, according to Traditional Medicine, low doses of this plant are being used to treat rheumatism and nerve pain (especially low back pain and sciatica) and has been selected as an auxiliary substance for a medical device specific for sciatica pain.

HAMAMELIS (MD-LUMBAR)

Based on a histological affinity, *Hamamelis* seems to be capable of regulating and stabilizing the tone of striated muscles. This is particularly important in back pain, which is mainly caused by trauma or bad posture and is characterized by low back muscle contractures.

DROSERA (MD-POLY)

Drosera is the auxiliary substance contained in low doses in MD-POLY with a synergistic action compared to the mechanical action of collagen. It contains significant amounts of naphthoquinones (droserone), with an anti-inflammatory action [21].

COLOCYNTHIS (MD-NEURAL)

The Traditional Medicine of many countries (especially Middle East and Asian countries) considers *Colocynthis* as effective in order to relieve pain of nervous origin and joint pain [22; 23]. This is the rationale why low doses of *Colocynthis* have been included in the formulation of MD-NEURAL, acting synergistically compared to a mechanical action of collagen.

HYPERICUM (MD-MUSCLE)

Hypericum contains high amounts of hypericin (dianthraquinone), tannins and terpenes of the essential oil of hypericum. *Hypericum* acts as an antispasmodic in two ways: by inhibiting the uptake of calcium and inhibiting phosphodiesterase [24]. This improves muscle tone, which is one of the main targets of MD-MUSCLE.

CITRIC ACID and VITAMIN PP (MD-MATRIX)

Both elements are essential for cell metabolism: electrons transport, antioxidant activity and energy production [25; 26]. These features make MD-MATRIX particularly effective in strengthening the extracellular matrix and in creating a defensive barrier against free radicals.

VITAMINS C; B1; B2; B6.

MAGNESIUM GLUCONATE (MD-TISSUE)

Ascorbic acid (**vitamin C**) is one of the most important water-soluble biological antioxidants, capable of neutralizing many oxygen and nitrogen reactive species [27; 28]. *Magnesium gluconate* is one of the main forms for delivering magnesium, whose deficit in the human body can cause the onset of many diseases, including osteoporosis. *Pyridoxine hydrochloride* (**vitamin B6**) exerts an anti-neurotoxin action [29].
Riboflavin (**vitamin B2**) has an antioxidant action [30]. *Thiamine hydrochloride* (**Vitamin B1**) has an antioxidant, erythropoietic, anti-atherosclerotic and detoxifying action. This brief description of the properties of these substances explains the rationale why they have been chosen as auxiliary substances for this MD, which aims to create a defense barrier against free radicals and counteract connective tissue aging.

ARNICA (MD-KNEE)

The choice of using *Arnica* as an auxiliary substance in this MD is due to the need of counteracting acute inflammation [31; 32], especially of traumatic origin, which frequently affects the knee (its function is to stabilize the musculoskeletal system), and especially the inflammatory signs *dolor* (pain) and *tumor* (swelling). *Arnica* contains some active ingredients (arnidiol, faradiol, arnicolides and isoquercetin), which help it to exert its auxiliary action, thus creating the best conditions for the main action of collagen, i.e., the stabilization of the knee joint.

CIMICIFUGA (MD-THORACIC)

Cimicifuga is used to treat “neck and back stiffness and contractures” and "intercostal rheumatisms." For both these reasons, low doses of *Cimicifuga* have been used with a synergistic action compared to the mechanical action of collagen in the diseases that affect the thoracic region.

IRIS (MD-SHOULDER)

Iris is used to treat joint pain, especially stinging pain [33; 34] in the shoulder. Iris has been included within this formulation in low doses, which act synergistically with the mechanical action of collagen in shoulder arthropathy.

CALCIUM PHOSPHATE (MD-HIP)

Calcium phosphate is the main mineral constituent of bone tissue. Its role is fundamental in the formation of callus and bone metabolism [35]. *Calcium phosphate* has been selected as an auxiliary substance for this medical device because hip osteoarthritis is often accompanied (or caused) by osteochondrosis of the femoral head or osteoporosis.

When to intervene with Guna Collagen Medical Devices

Guna Collagen Medical Devices represent the ideal treatment tool in 3 types of clinical cases in orthopedics-traumatology:

- **overuse** pathologies;
- the **aging processes** that affect the tissues derived from the mesoderm, such as bones, tendons, ligaments, muscles and, in general, in the ailments of the extra-cellular matrix;
- degenerative phenomena secondary to chronic inflammatory processes of **traumatic origin**.

Even though *Guna Collagen Medical Devices* show effectiveness in the etiological treatment of acute and chronic benign pain affecting the musculoskeletal system (thanks to the auxiliary and secondary anti-inflammatory action of a number of the auxiliary substances contained in them) **they cannot and should not be considered pain-killers**.
In fact, the reduction of painful symptoms is only a secondary action due, for example, to the stabilization of the joint, resulting in decreased stimulation of the nociceptive endings.

Each protocol must be adapted to the patient's medical history and the specific clinical case. Their use in the **acute phase of disease** is:

- 1 treatment daily (every 24 hours) for 3 consecutive days; then 2 treatments weekly until complete remission of symptoms. Continue with 1 treatment weekly.
- When necessary, 3 applications (1 weekly) may be useful 3 months after the last session of the basic treatment.

As part of an *overlapping* treatment, in acute osteo-arthro-myofascial pain, *Guna Collagen Medical Devices* are the ideal support to any anti-inflammatory treatment.
They may be associated with either anti-inflammatory treatments with synthetic drugs [NSAIDs (mostly via periarticular mesotherapy) or corticosteroids (especially intra-articular route)] or homeopathic medicines.
It is a good practice not to mix drugs and *Guna Collagen Medical Devices* in the same syringe.

While respecting each individual case, in the **treatment of chronic diseases**, the standard protocol provides:

- 1 treatment 2 times weekly for the first 2 weeks; then 1 treatment weekly for 6 consecutive weeks.
- 1 application may be useful 3 months after the last session of basic treatment and then every 3 months.

During treatment with *Guna Collagen Medical Devices* any oral treatment can be administered at the same time.

Guna Collagen Medical Devices

Product information sheets

MD-Hip

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Calcium Phosphate, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-HIP is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-HIP is a medical device that helps hip movement. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-HIP is intended to be used by a qualified staff in private or public health Facilities to:
⇨ Improve the movement of the hip joint.
⇨ Help muscle stretching of the lumbosacral area.
⇨ Support the periarticular muscle tissue.
⇨ Soothe local pain, pain caused by joint movement or bad posture.

Directions for use
Therapeutic protocol:
1 treatment weekly for 10 consecutive weeks.

Periarticular injection technique (the site of application must be aseptic; insert the needle at 6-8 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Intraarticular injection technique
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.

The application of a topical anaesthetic on the skin area to be treated is recommended.
• Needles: sterile 22 G.
• Syringes: 2 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
Patients treated with anticoagulants or with recognized vessel fragility should be carefully monitored during the therapy.
There is no history of hypersensitivity to MD-HIP. Patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
Hip pain requires differential diagnosis for primary or metastatic cancer pain, referred nerve pain of lumbar origin, inguinal hernia.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

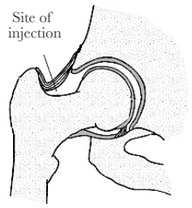
Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-HIP may be used as a single treatment or mixed with other medical devices of the same range in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for acute pain, MD-HIP can be associated with MD-NEURAL, MD-POLY and MD-MUSCLE (together with one or more than one of these).
Moreover, when a supportive treatment is needed for the connective tissue matrix or when the physiological aging process is needed to be slowed down, MD-HIP can be associated with MD-MATRIX and MD-TISSUE.
It may also be used as mechanical support while treating the following diseases:
• Hip joint osteoarthritis.
• Hip joint capsule inflammation.
• Hip joint osteoarthritis with rheumatoid arthritis (in association with MD-POLY).
• Hip joint pain of muscle origin (in association with MD-MUSCLE).
• Hip joint pain of nerve origin (*burning hip*, in association with MD-NEURAL).
• Hip joint pain due to prolonged bed rest.

Administration may vary according to individual needs.

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

The trochanteric bursa is located over the lateral prominence of the greater trochanter of the femur.
There can be an anterior or a lateral approach to the hip.
The patient is lying supine. The anatomic landmark is located 2 cm below the superior border of the greater trochanter in between its anterior and posterior borders. The skin overlying this location is marked and prepared in a sterile way. A 22 gauge needle is injected parallel to the floor and perpendicular to the femoral shaft.



Hip – Intraarticular injection

MD-Ischial

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Rhododendron, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-ISCHIAL is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-ISCHIAL is a medical device designed to help movement, specifically the low back area of the vertebral spine. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-ISCHIAL is intended to be used by a qualified staff in private or public health Facilities to:
⇨ Improve leg movement.
⇨ Help leg muscle stretching.
⇨ Help to support the leg muscle tissue.
⇨ Soothe leg pain while starting to move legs again, after a period of prolonged inactivity.

Directions for use
Therapeutic protocol:
1 treatment weekly for 10 consecutive weeks.

Periarticular injection technique (the site of application must be aseptic; insert the needle near the sacroiliac joint at 2-4 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-ISCHIAL. Patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
Sciatic pain requires differential diagnosis for secondary muscle pain, full-blown disc herniation, vertebral canal stenosis, Cauda equine syndrome.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.

Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-ISCHIAL may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for acute pain, MD-ISCHIAL can be associated with MD-NEURAL, MD-POLY and MD-MUSCLE (together with one or more than one of these).
Moreover, when a supportive treatment is needed for the connective tissue matrix or when the physiological aging process should be slowed down, MD-ISCHIAL can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
• Sciatic pain.
• Lumbar-sciatic pain (in association with MD-LUMBAR and MD-NEURAL).
• Nerve pain in the lower lumbar spine (in association with MD-MUSCLE).
• Leg nerve pain due to post-surgery treatment of disc herniation L4-L5, L5-S1.
• Morton neuroma (in association with MD-NEURAL).

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

MD-Lumbar

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Hamamelis, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-LUMBAR is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-LUMBAR is a medical device designed to help movement, specifically the lumbosacral area of the vertebral spine. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-LUMBAR is a medical device intended to be used by a qualified staff in private or public health Facilities to:
⇨ Help lumbar movement.
⇨ Help muscle stretching of the lumbosacral area of the spine.
⇨ Help to support the lumbar muscle tissue.
⇨ Soothe local pain, pain at rest or caused by movement and bad posture.

Directions for use
Periarticular therapeutic protocol:
2 treatments weekly for the first 2 weeks; 1 treatment until improvement of symptoms (average 8-10 sessions). Chronic pathologies: go on with 1 treatment weekly for one month until improvement of symptoms, then with 1 treatment monthly or – according to individual needs – every 45-50 days.
The site of application must be aseptic. Insert the needle near the lumbar and lumbosacral joints at 3-4 mm depth.

For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-LUMBAR. Patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
Spinal pain requires differential diagnosis for herniated disk, primary or secondary cancer pain; reflex or referred pain from internal organs.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-LUMBAR may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for acute pain, MD-LUMBAR can be associated with MD-NEURAL, MD-POLY and MD-MUSCLE (together with one or more than one of these).
Moreover, when a supportive treatment is needed for the connective tissue matrix or when the physiological aging process should be slowed down, MD-LUMBAR can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:

- Lumbar pain secondary to cartilage degenerative lumbar spine disorders (lumbar and lumbar-sacral arthrosis).
- Lumbar vertebral osteophytosis.
- Low-back pain secondary to musculo-tendinous trigger points (in association with MD-MUSCLE).
- Postural low-back aches (in association with MD-NEURAL and MD-MUSCLE).
- Lumbar and lumbar-sacral mechanical imbalance.
- Lumbar and lumbar-sacral spinal ligament syndrome.
- Sacro-iliac syndrome.
- Spinal lumbar and lumbar-sacral nerve root pain (in association with MD-NEURAL and MD-ISCHIAL).

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

MD-Knee

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Arnica, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-KNEE is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-KNEE is a medical device designed to help knee movement. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-KNEE is a medical device intended to be used by a qualified staff in private or public health Facilities to:
⇨ Improve the knee movement.
⇨ Help muscle stretching.
⇨ Soothe pain while moving legs and knee.

Directions for use
Therapeutic protocol:
1 treatment weekly for 10 consecutive weeks.

Periarticular injection technique (the site of application must be aseptic; insert the needle at 2-4 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Intraarticular injection technique
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
The application of a topical anaesthetic on the skin area to be treated is recommended.
• Needles: sterile 22 G.
• Syringes: 2 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-KNEE. Patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

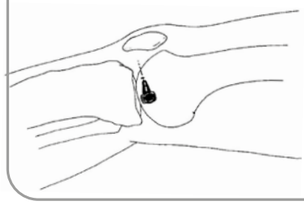
Warnings and precautions
Knee pain requires differential diagnosis for collateral or cruciate ligament injuries, prepatellar bursitis, hip joint pathologies, osteochondritis disseccans, inflammatory arthropathy, gout, pseudo gout, septic arthritis.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-KNEE may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for acute pain, MD-KNEE can be associated with MD-NEURAL, MD-POLY and MD-MUSCLE (together with one or more than one of these).
Moreover, when a supportive treatment is needed for the connective tissue matrix or when the physiological aging process should be slowed down, MD-KNEE can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
- Knee arthrosis (in association with MD-POLY).
- Patello-femoral arthrosis.
- Knee localization of rheumatoid arthritis or of other autoimmune diseases (in association with MD-POLY).
- Knee acute and chronic arthrosynovitis secondary to arthrosis or to rheumatoid arthritis (in association with MD-POLY).
- Post-traumatic or post-surgery acute and chronic arthrosynovitis.
- Traumatic lesions of cruciate or collateral ligaments of the knee.
- Meniscal lesions (in association with MD-MUSCLE).
- Knee joint preparation to meniscectomy (in association with MD-MUSCLE).
- Maintenance therapy after knee surgery (in association with MD-MUSCLE and MD-NEURAL).

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.



The patient should lay supine with the knee comfortably extended. A 22 G needle is inserted in a direction parallel to the plane of the posterior surface of the patella in a medial and lateral position.

Knee – Intraarticular injection technique (internal side)

MD-Matrix

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Citric acid, Nicotinamide, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-MATRIX is a medical device designed to help movement by limiting a physiological degeneration of joints and connective tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

Due to its special function, MD-MATRIX is also intended for firming the subcutaneous and microvascular connective tissue *layer* of localized adiposities and cellulite in the connective tissue, especially those at the root of the thighs and in the inner area of the knee.

MD-MATRIX is a medical device designed to help movement, by strengthening the supportive tissue of the joints, and of the skin and its subcutaneous tissue.
Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-MATRIX is a medical device intended to be used by a qualified staff in private or public health Facilities to:
⇨ Strengthen the extra-cellular matrix tissues where the collagen is applied.
⇨ Act as a defensive barrier against free radicals.

Directions for use
Therapeutic protocol:
2 treatments weekly for the first 2 weeks, 1 treatment weekly until improvement of symptoms (average 8-10 sessions). It is possible to go on with 1 treatment every other week for 10 weeks at most. For chronic pathologies: go on with 1 treatment weekly for 1 month until improvement of symptoms, then 1 treatment monthly.

- *Intradermal and subcutaneous injection technique:* the site of application must be aseptic; insert the needle at 1-3 mm depth and microinject 0.2-0.3 ml into the affected tissue.
- *Periarticular injection technique:* the site of application must be aseptic; insert the needle near the joint at different depths.

Preparation for injection
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G, 4 mm.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-MATRIX. However, patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-MATRIX may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
Concerning its use for the treatment of localized adiposity, and for firming the subcutaneous connective tissue *layer*, MD-MATRIX should preferably be associated with MD-TISSUE (e.g. MD-MATRIX 2 vials, MD-TISSUE 1 vial / treatment).
It may be used in patients who need a collagen supplementation or a topical antiaging treatment.

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

MD-Muscle

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Hypericum, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-MUSCLE is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-MUSCLE is a medical device designed to help muscle and joint movement. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-MUSCLE is a medical device intended to be used by a qualified staff in private or public health Facilities to:
⇨ Help muscle stretching and function.
⇨ Help to support the muscle tissue in bad posture disorders.
⇨ Improve joint movement.
⇨ Soothe local pain, or pain caused by movement and bad posture.

Directions for use
Therapeutic protocol:
1-2 treatments weekly for 10 consecutive weeks.

Intramuscular injection technique (the site of application must be aseptic; insert the needle into the muscle to be treated at 2-4 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Intramuscular injection technique
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
The application of a topical anaesthetic to the skin is recommended.
• Needles: sterile 22 G.
• Syringes: 2 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-MUSCLE. However, patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be carefully monitored for 1 hour.

Warnings and precautions
Muscle pain requires differential diagnosis for metameric nerve pain, tendonitis, and deep blood accumulation.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-MUSCLE may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for the connective tissue matrix or when an antiaging action is necessary, MD-MUSCLE can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
• Pain management: acute, subacute, and chronic.
• Referred somatic pain area management (in association with MD-NEURAL).
• Trigger points management (in association with MD-NEURAL).
• Fibromyalgia syndrome (in association with MD-NEURAL).
• Dermatomyositis.

Administration may vary according to individual needs.

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

MD-Neck

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Silica, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-NECK is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-NECK is a medical device designed to help neck movement, specifically the cervical area of the vertebral spine. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-NECK is a medical device intended to be used by a qualified staff in private or public health Facilities to:
⇨ Improve the movement of the cervical tract of the spine.
⇨ Help cervical muscle stretching.
⇨ Help to support cervical muscle tissue.
⇨ Help to support cervical muscle tissue in bad posture disorders.
⇨ Soothe pain in cervical column movements.

Directions for use
Therapeutic protocol:
1-2 treatments weekly for 10 consecutive weeks.

Periarticular injection technique (the site of application must be aseptic; insert the needle at 2-4 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
Patients treated with anticoagulants or with recognized vessel fragility or affected by coagulation diseases should be carefully monitored during the therapy.
There is no history of hypersensitivity to MD-NECK. However, patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
Cervical spine pain requires differential diagnosis for cervical discopathies, primary or secondary cancer pain, spondylolisthesis.

A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-NECK may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for acute pain, MD-NECK can be associated with MD-NEURAL, MD-POLY and MD-MUSCLE (together with one or more than one of these). Moreover, when a supportive treatment is needed for the connective tissue matrix or when the physiological aging process should be slowed down, MD-NECK can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
• Neck pain due to cartilage degenerative cervical spine disorders (cervical osteoarthritis, in association with MD-POLY).
• Neck pain due to cervical muscular trigger points (in association with MD-MUSCLE).
• Stiff neck syndrome (in association with MD-NEURAL).
• Simple neck pain (in association with MD-NEURAL and MD-MUSCLE).
• Whiplash (in association with MD-NEURAL and MD-MUSCLE).
• Postural neck ache (in association with MD-NEURAL and MD-MUSCLE).
• Mechanical imbalance (facet joint syndrome) (in association with MD-NEURAL).
• Cervical spinal ligament syndrome (in association with MD-NEURAL).
• Cervical spinal nerve root pain (in association with MD-NEURAL).

Administration may vary according to individual needs.

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

MD-Neural

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Colocynthis, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-NEURAL is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-NEURAL is a medical device designed to help joint movement, specifically in bad posture disorders. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-NEURAL is a medical device intended to be used by a qualified staff in private or public health Facilities.

Directions for use
Therapeutic protocol:
1-2 treatments weekly for 10 consecutive weeks.

Periarticular injection technique (the site of application must be aseptic; insert the needle at 2-4 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Intraarticular injection technique
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
The application of a topical anaesthetic on the skin area to be treated is recommended.
• Needles: sterile 22 G.
• Syringes: 2 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-NEURAL. However, patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
Nerve pain requires differential diagnosis for visceral pain, primary or metastatic cancer pain.

A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-NEURAL may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for the connective tissue matrix or when an antiaging action is necessary, MD-NEURAL can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
• Brachial pain (in association with MD-NECK).
• Brachial nerve pain due to cervical entrapment (in association with MD-NECK).
• Persistent intercostal neuralgia (in association with MD-THORACIC).
• Postherpetic neuralgia (in association with MD-THORACIC or MD-LUMBAR).
• Atypical facial neuritis (in association with MD-NECK).
• Trigeminal neuralgia (in association with MD-NECK).
• Temporomandibular joint pain (in association with MD-NECK).
• Cervical, thoracic, lumbar and sacrolumbar nerve root pain (respectively in association with MD-NECK, MD-THORACIC, MD-LUMBAR and MD-ISCHIAL).

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

MD-Poly

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Drosera, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-POLY is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-POLY is a medical device designed to help movement, specifically the vertebral spine. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-POLY is a medical device intended to be used by a qualified staff in private or public health Facilities to:
➩ Improve movement of the joints.
➩ Help muscle stretching.
➩ Help to support the muscle tissue in bad posture disorders.
➩ Soothe local pain, or pain caused by movement and bad posture.

Directions for use
Therapeutic protocol:
1-2 treatments weekly for 10 consecutive weeks.

Periarticular injection technique (the site of application must be aseptic; insert the needle at a 3-6 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Intraarticular injection technique
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
The application of a topical anaesthetic on the skin area to be treated is recommended.
• Needles: sterile 22 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-POLY. However, patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
Joint pain requires differential diagnosis for acute or subacute joint viral diseases, pain due to overweight (leg joints), hyperuricemia, gout.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-POLY may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for the connective tissue matrix or when an antiaging action is necessary, MD-POLY can be used together with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
• Small joints rheumatoid arthritis of hand and foot (in association with MD-SMALL JOINTS).
• Non-specific diffuse pain (in association with MD-NECK and MD-NEURAL).
• Costo-sternal syndrome (in association with MD-NEURAL).
• Chronic polyarthritis due to auto-immune diseases (e.g. Lupus erithematosus sistemicus) (in association with MD-NEURAL when nerve pain is dominant; in association with MD-MUSCLE when muscle pain is dominant).
• Breakbone fever (when nerve pain is dominant in association with MD-NEURAL; when muscle pain is dominant in association with MD-MUSCLE).
• Joint pain due to viral or protozoic disease (in association with another Guna medical device containing the same type of collagen contained in the joint to be treated).
• Joint pain due to cancer (chronic leukaemia, multiple myeloma) (in association with another Guna medical device containing the same type of collagen contained in the joint to be treated).

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

MD-Shoulder

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Iris, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-SHOULDER is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-SHOULDER is a medical device designed to help joint movement of the shoulder and the arm. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-SHOULDER is a medical device intended to be used by a qualified staff in private or public health Facilities to:
➩ Improve movement of the shoulder joint and the arm.
➩ Help muscle stretching.
➩ Help to support the muscle tissue.
➩ Soothe local pain and pain caused by movement.

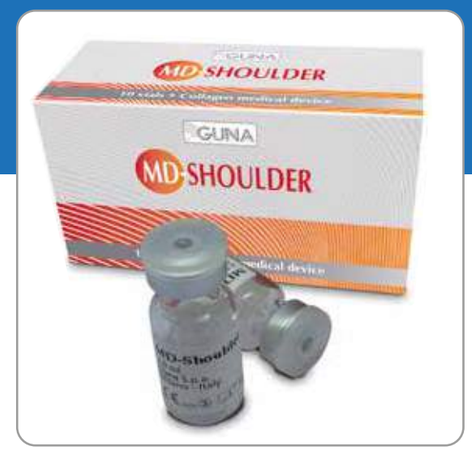
Directions for use
Therapeutic protocol:
1-2 treatments weekly for 10 consecutive weeks.

Periarticular injection technique (the site of application must be aseptic; insert the needle at a 2-4 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Intraarticular injection technique
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
The application of a topical anaesthetic on the skin area to be treated is recommended.
• Needles: sterile 22 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-SHOULDER. However, patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
Shoulder pain requires differential diagnosis for chronic cervical syndrome, ischemic heart disease (acute/chronic, only on the left side), gallbladder disease (only on the right side), cervical-brachial nerve pain, muscle trigger in the trapezium muscle.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction.



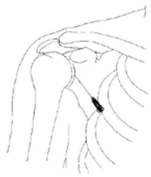
The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-SHOULDER may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for acute pain, MD-SHOULDER can be associated with MD-NEURAL, MD-POLY and MD-MUSCLE (together with one or more than one of these).
Moreover, when a supportive treatment is needed for the connective tissue matrix or when the physiological aging process should be slowed down, MD-SHOULDER can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
• Shoulder-arm polyarthritis (in association with MD-POLY).
• Rotator cuff syndrome (in association with MD-MUSCLE).
• Shoulder-arm syndrome (in association with MD-NEURAL and MD-MUSCLE).
• Frozen shoulder (in association with MD-MUSCLE).
• Shoulder pain due to dislocation (therapeutic rest, in association with MD-NEURAL).
• Epicondylitis (in association with MD-NEURAL and MD-POLY).

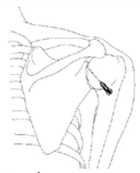
Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.



Anterior approach. With the patient's hand on the thigh and the shoulder muscles relaxed, the glenohumeral joint can be palpated by placing the fingers between the coracoid process and the humeral head. As the shoulder is internally rotated, the humeral head can be felt turning inward and the joint space can be felt as a groove just lateral to the coracoid process. A 22 G needle can be inserted lateral to the coracoid. Insert the needle into the joint space.

Shoulder – Intra-articular injection, anterior approach

Posterior approach. The posterior aspect of the shoulder joint can be identified by making the patient's arm rotate. This position is achieved by placing the patient's ipsilateral hand on the opposite shoulder. The humeral head can be palpated by placing a finger posteriorly along the acromion while the shoulder is rotated. A 22 G needle is inserted about 1 cm inferior to the posterior tip of the acromion and directed anteriorly and medially.



Shoulder – Intra-articular injection, posterior approach

MD-SMALL JOINTS

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Viola, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-SMALL JOINTS is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-SMALL JOINTS is a medical device designed to help movement of small joints (such as those of foot, hand and ankle). Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-SMALL JOINTS is a medical device intended to be used by a qualified staff in private or public health Facilities to:
⇨ Improve movement of the small joints of hand, foot and ankle.
⇨ Help muscle stretching.
⇨ Help to support the muscle tissue.
⇨ Soothe local pain and pain caused by joint movement.

Directions for use
Therapeutic protocol:
1 treatment weekly for 10 consecutive weeks.

Periarticular injection technique (the site of application must be aseptic; insert the needle at a 2-4 mm depth)
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Intraarticular injection technique
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
The application of a topical anaesthetic on the skin area to be treated is recommended.
• Needles: sterile 22 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Ankle intraarticular application
Foot joints can be treated with intraarticular injections in the ankle. This treatment can be also applied to the ankle joint.
For medial and lateral approach, the foot is first placed at about a 45-degree angle of plantar flexion.

Contraindications / Side effects
There is no history of hypersensitivity to MD-SMALL JOINTS. However, patients with known hypersensitivity to any ingredient or excipi- ent should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
Hand/foot and small joints pain requires differential diagnosis for primary nerve pain, post-traumatic pain, secondary pain due to recent or past bone fractures.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-SMALL JOINTS may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for acute pain, MD-SMALL JOINTS can be associated with MD-NEURAL, MD-POLY and MD-MUSCLE (together with one or more than one of these).
Moreover, when a supportive treatment is needed for the connective tissue matrix or when the physiological aging process should be slowed down, MD-SMALL JOINTS can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
• Osteoarthritis of the fingers.
• Rhizoarthrosis of the thumb (Forestier disease).
• Arthrosis pain due to hammer toe.
• Carpal-tunnel syndrome (in association with MD-NEURAL).
• De Quervain disease (in association with MD-NEURAL).
• Metatarsal pain.
• Metatarsal pain accompanied by Morton's neuroma (in association with MD-NEURAL).
• Rheumatoid arthritis of the hand/foot (in association with MD-POLY).
• Hand/foot tendon pain due to prolonged immobilization.

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

Medial approach. A 22 G needle is placed about 4 cm proximal and lateral to the distal end of the medial malleolus. The flexor hallucis longus tendon is just lateral to this point. The needle is directed 45 degrees posteriorly, slightly upward, and laterally.

Lateral approach. A 22 G needle is placed about 1 cm proximal and medial to the distal end of the lateral malleolus. The needle should be inserted 45 degrees posteriorly, slightly upward.

Ankle –Intra-articular approach

MD-Thoracic

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Cimicifuga, NaCl, Water for injection.

For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-THORACIC is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

MD-THORACIC is a medical device designed to help movement, specifically the thoracic area of the vertebral spine. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-THORACIC is a medical device intended to be used by a qualified staff in private or public health Facilities to:
⇨ Improve movement of the thoracic tract of the spine.
⇨ Help muscle stretching.
⇨ Help to support the muscle tissue in bad posture disorders.
⇨ Soothe local pain, pain caused by movement and bad posture.

Directions for use
Periarticular injection technique:
2 treatments weekly for the first 2 weeks, 1 treatment weekly until improvement of symptoms (average 8-10 sessions). For chronic pathologies: go on with 1 treatment weekly for 1 month until improvement of symptoms, then 1 treatment monthly.

The site of application must be aseptic; insert the needle at a 2-4 mm depth.

For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles: sterile 27 G.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-THORACIC. However, patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injec-tion into one arm and be monitored for 1 hour.

Warnings and precautions
Spinal pain requires differential diagnosis for primary or secondary cancer pain, reflex and referred pain from internal organs.
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-THORACIC may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
When a supportive treatment is needed for acute pain, MD-THORACIC can be associated with MD-NEURAL, MD-POLY and MD-MUSCLE (together with one or more than one of these).
Moreover, when a supportive treatment is needed for the connective tissue matrix or when the physiological aging process should be slowed down, MD-THORACIC can be associated with MD-MATRIX and MD-TISSUE.

It may also be used as mechanical support while treating the following diseases:
• Thoracic pain due to cartilage degenerative thoracic spine disorders (thoracic osteoarthrosis) (in association with MD-POLY).
• Thoracic pain due to scoliosis (in association with MD-MUSCLE and MD-NEURAL).
• Thoracic pain due to thoracic long muscle trigger points (in associati-on with MD-MUSCLE).
• Pain due to thoracic spine osteophytosis (in association with MD-NEURAL).
• Pain from spinal osteoporosis (in association with MD-NEURAL and MD-MUSCLE).
• Mechanical imbalance (costo-vertebral facet joint syndrome) (in association with MD-NEURAL).
• Thoracic spinal ligament syndrome (in association with MD-NEURAL).
• Thoracic spinal nerve root pain (in association with MD-NEURAL.

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

MD-Tissue

Manufacturer: GUNA S.p.a., Via Palmanova 71, 20132 Milano, Italy

Composition: Collagen.

Excipients: Ascorbic acid, Magnesium gluconate, Pyridoxine hydrochloride, Riboflavin, Thiamine hydrochloride, NaCl, Water for injection.
For this medical device the following packages are available:
• Box: 5 vials (single vial 2 ml – extraction volume)
• Box: 10 vials (single vial 2 ml – extraction volume)
• Box: 50 vials (single vial 2 ml – extraction volume)

Intended use
MD-TISSUE is a medical device designed to help movement by limiting a physiological degeneration of joints and tissues as well as by counterbalancing any damage caused by:
• aging
• bad posture
• concomitant chronic diseases
• blows and injuries
• pollutants.

Due to its special function, MD-TISSUE is also intended to limit the physiological deterioration of the skin and subcutaneous connective tissue, and counterbalance the effects of chrono-ageing and photo-ageing, such as:
• local anti-ageing treatment
• face and neck wrinkles
• firming of the subcutaneous and perivascular connective layer of the face and neck
• alteration of the trophicity of the connective tissue of face and neck induced by airborne pollutants / metabolic disorders.

MD-TISSUE is a medical device designed to help movement by counteracting the physiological aging of the connective tissue. Its main therapeutic functions include:
1. A barrier effect.
2. A lubricating action.
3. Mechanical support while administering other pharmacological treatments.

MD-TISSUE is a medical device intended to be used by a qualified staff in private or public health Facilities to:
➪ Act as a defensive barrier against free radicals.
➪ Counteract the physiological aging of the connective tissue.
➪ Soothe local pain caused by movement.

Directions for use
Therapeutic protocol:
2 treatments weekly for the first 2 weeks, 1 treatment weekly until improvement of symptoms (average 8-10 sessions). It is possible to go on with 1 treatment every other week for 10 weeks at most.
For chronic pathologies: go on with 1 treatment weekly for 1 month until improvement of symptoms, then 1 treatment monthly.

• *Intradermal injection technique:* the site of application must be aseptic; Microinjections: insert the needle at 1-3 mm depth, and inject 0.2-0.3 ml into the affected tissue.
Tunnelling injection technique: inject 0.3 ml per wrinkle. Insert the needle beneath the skin the full length of the needle, cannulate the wrinkle by moving the needle gently to left and right, while injecting the content of the syringe as the needle is withdrawn.
• *Periarticular injection technique:* the site of application must be aseptic; insert the needle perpendicular to the skin surface at 2-4 mm depth, and perform microinjections of 0.3-0.5 ml.

Preparation for injection
For this purpose the use of the following materials and accessories is recommended:
• Materials for aseptic skin preparation: single-use gloves, iodine solution, alcohol solution, sterile gauze pads, ethyl chloride spray for the skin.
• Needles for microinjections: sterile 27 G, 4 mm.
• Needles for tunnelling injection technique: sterile 30 G, 13 mm.
• Syringes: 5 or 10 cc size, according to the volume of the solution to inject.

Contraindications / Side effects
There is no history of hypersensitivity to MD-TISSUE. However, patients with known hypersensitivity to any ingredient or excipient should be tested before use, making a spot injection into one arm and be monitored for 1 hour.

Warnings and precautions
A slight reddening at the injection site may be due to a mechanical effect of the needle or to a skin reaction. The application might cause symptoms of burning/pain at the injection site, that usually solve spontaneously within 5-10 minutes after the treatment.
Skin cleansing/disinfection is required before and after application. Pyogenic bacteria may produce injection site abscesses.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Do not use after the expiration date. The expiration date refers to a product properly stored in its original and undamaged package. Use the product immediately after opening.

Instructions on use
MD-TISSUE may be used as a single treatment or mixed with other medical devices of the same range, in order to make a customised treatment according to clinical evolution.
Concerning its use for the treatment of face and neck wrinkles, and for firming the subcutaneous connective tissue layer, MD-TISSUE should preferably be associated with MD-MATRIX (e.g. MD-TISSUE 2 vials, MD-MATRIX 1 vial / treatment).
It may be used in patients who need a collagen supplementation or a topical antiaging treatment.

Instructions in case of damage to the sterile vials
Do not use if the seal is broken or if the vial is not perfectly sealed. Once open, the content of the vial must be immediately injected. Do not use if the package is damaged.

Guna Collagen Medical Devices

Therapeutic ATLAS

Cervical region

MD-NECK

SECONDARY POINTS

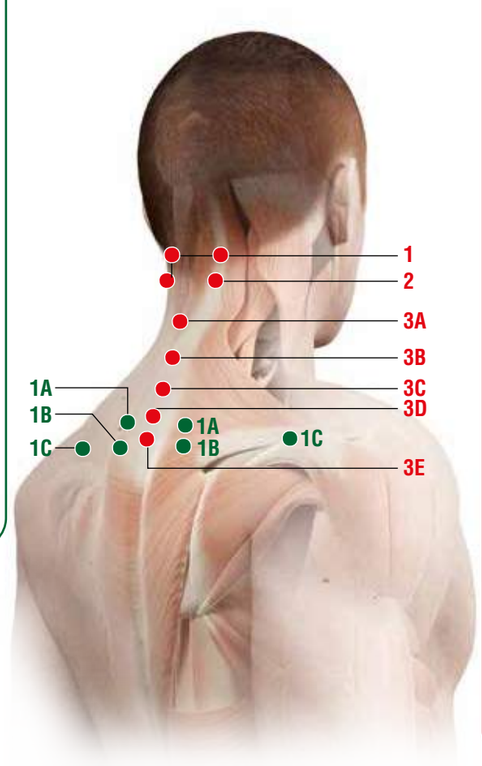
1

Anatomical landmarks:

A) 3-4 cm lateral to the space between the spinous processes of C6 and C7 (bilateral)
B) 3-4 cm lateral to the space between the spinous processes of C7 and T1 (bilateral)
C) midway along the line joining the spinous process of C7 and the acromion.

MDs:
MD-Muscle
MD-Neural + MD-Muscle if neck pain radiates to the trapezius muscle unilaterally or bilaterally

How to inject:
i.m. at a depth of 5-6 mm.



MAIN POINTS

1

Anatomical landmark:

Below the external occipital protuberance, in the muscle insertion, just below the transverse process of the atlas.

How to inject: s.c.

2

Anatomical landmarks:

3-4 cm lateral to the space between the spinous processes of C2 and C3.

How to inject: s.c.

3

Anatomical landmark:

- From the top:
A) below the spinous process of C2
B) below the spinous process of C4
C) below the spinous process of C5
D) below the spinous process of C6
E) below the spinous process of C7.

How to inject i.d.

Remarks:
*All the subcutaneous (**s.c.**) and intradermal (**i-d.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
*All the intramuscular (**i.m.**) injections must be made with a needle of 40 mm length, 21 G (Gauge) diameter.*

- When making subcutaneous injections, insert the needle at approximately a 45° degree angle (45°);
- When making intradermal injections, insert the needle at approximately a 30° degree angle (30°) ;
- When making intramuscular injections, insert the needle at approximately a 90° degree angle (90°) .

Cervical Region – MD-NECK

CORE INSTRUCTIONS ON USE AND COMBINATIONS WITH OTHER MDs
- Inject in the main points

- Neck pain due to cartilage degenerative cervical spine disorders (cervical osteoarthritis): **MD-Neck + MD-Poly**
- Neck pain due to cervical muscular trigger points: **MD-Neck + MD-Muscle**
- Stiff neck syndrome: **MD-Neck + MD-Muscle + MD-Neural**
- Neck pain due to muscle tension: **MD-Neck + MD-Neural + MD-Muscle**
- Whiplash: **MD-Neck + MD-Neural + MD-Muscle**
- Postural neck ache: **MD-Neck + MD-Neural + MD-Muscle + MD-Tissue**
- Mechanical imbalance (facet joint syndrome): **MD-Neck + MD-Neural**
- Cervical spinal ligament syndrome: **MD-Neck + MD-Neural + MD-Matrix**
- Cervical spinal nerve root pain: **MD-Neck + MD-Neural**.

Thoracic Region

MD-THORACIC

SECONDARY POINTS

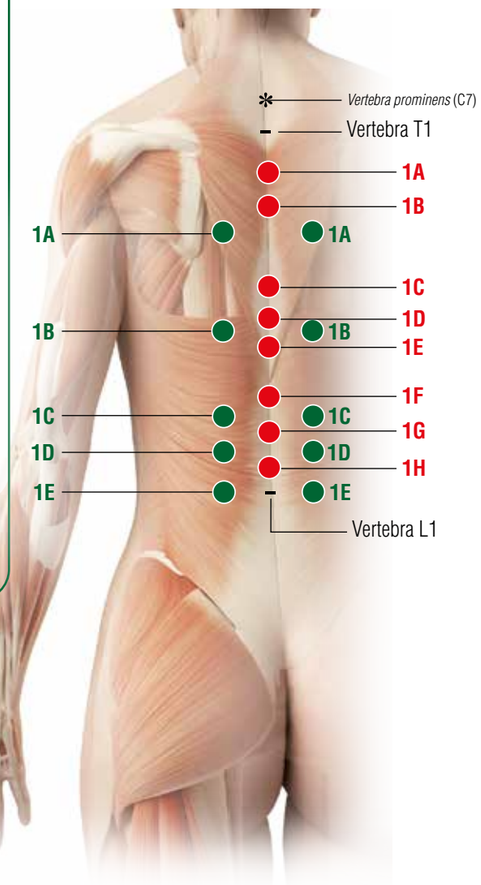
1

Anatomical landmarks:

- From the top:
A) 3-4 cm lateral to the space between the spinous processes of T3 and T4
B) 3-4 cm lateral to the space between the spinous processes of T7 and T8
C) 3-4 cm lateral to the space between the spinous processes of T10 and T11
D) 3-4 cm lateral to the space between the spinous processes of T11 and T12
E) 3-4 cm lateral to the space between the spinous processes of T12 and L1.

MDs:
MD-Muscle + MD-Neural.

How to inject:
s.c.



MAIN POINTS

1

Anatomical landmarks:

- From the top:
A) below the spinous process of T2
B) below the spinous process of T3
C) below the spinous process of T6
D) below the spinous process of T7
E) below the spinous process of T8
F) below the spinous process of T10
G) below the spinous process of T11
H) below the spinous process of T12.

How to inject:
i.d.

Remarks:
1) For the numbering of the spinous processes of the vertebrae indicated in Main Points and Secondary Points, you can start from the vertebra prominens: spinous process of C7; in full anterior cervical flexion this is the main and most prominent landmark.*
It's the most important landmark of the whole spine.

*2) All the subcutaneous (**s.c.**) and intradermal (**i.d.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
- When making subcutaneous injections, insert the needle at approximately a 45 degree angle (45°);
- When making intradermal injections, insert the needle at approximately a 30 degree angle (30°).

Thoracic Region – MD-THORACIC

CORE INSTRUCTIONS ON USE AND COMBINATIONS WITH OTHER MDs
- Inject in the main points

- Thoracic pain due to cartilage degenerative thoracic spine disorders (thoracic osteoarthritis and arthritis): **MD-Thoracic + MD-Poly**
- Thoracic pain due to scoliosis: **MD-Thoracic + MD-Muscle + MD-Neural**
- Thoracic pain due to thoracic long muscle trigger points: **MD-Thoracic + MD-Muscle**
- Pain due to thoracic spine osteophytosis: **MD-Thoracic + MD-Neural + MD-Matrix**
- Thoracic pain due to spinal osteoporosis: **MD-Thoracic + MD-Neural + MD-Muscle + MD-Tissue**
- Mechanical imbalance (costo-vertebral facet joint syndrome): **MD-Thoracic + MD-Neural + MD-Matrix**
- Thoracic spinal ligament syndrome: **MD-Thoracic + MD-Neural**
- Thoracic spinal nerve root pain: **MD-Thoracic + MD-Neural**.

Lumbar Region

MD-LUMBAR

SECONDARY POINTS

1

Anatomical landmarks:

A) On the iliac crest, approximately 8-10 cm from the posterior midline.

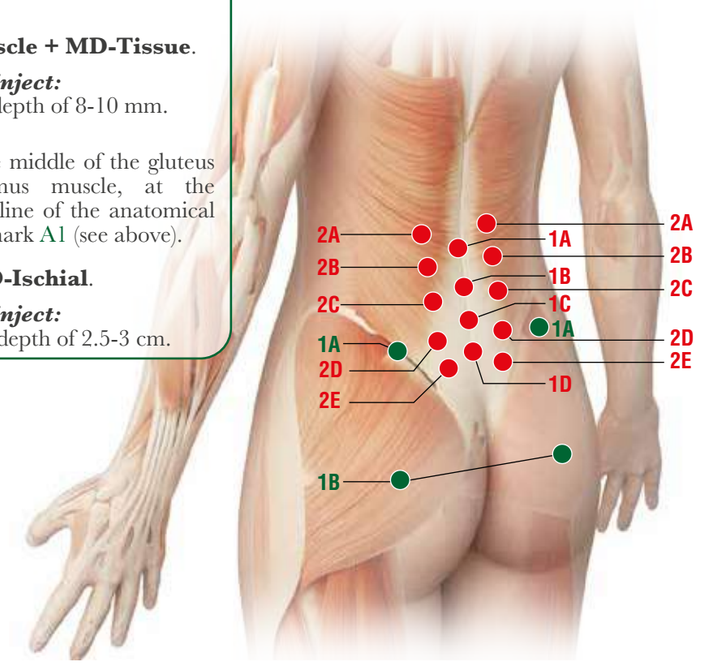
MDs:
MD-Muscle + MD-Tissue.

How to inject:
i.m. at a depth of 8-10 mm.

B) In the middle of the gluteus maximus muscle, at the same line of the anatomical landmark A1 (see above).

MD: **MD-Ischial**.

How to inject:
i.m., at a depth of 2.5-3 cm.



MAIN POINTS

1

Anatomical landmarks:

- From the top:
A) below the spinous process of L2
B) below the spinous process of L3
C) below the spinous process of L4
D) below the spinous process of L5.

How to inject:
i.d. or s.c.

2

Anatomical landmarks:

- From the top:
A) 5-6 cm lateral to the space between the spinous processes of L1 and L2
B) 5-6 cm lateral to the space between the spinous processes of L2 and L3
C) 5-6 cm lateral to the space between the spinous processes of L3 and L4
D) 5-6 lateral to the space between the spinous processes of L4 and L5
E) 3-4 cm lateral to the space between the spinous processes of L5 and S1.

How to inject:
i.m. at a depth of 10-12 mm.

Remarks:
*All the subcutaneous (**s.c.**) or intradermal (**i.d.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
*All the intramuscular (**i.m.**) must be made with a needle of 40 mm length, 21 G (Gauge) diameter.*
- When making subcutaneous injections, insert the needle at approximately a 45° angle (45°);
- When making intradermal injections, insert the needle at approximately a 30° angle (30°);
- When making intramuscular injections, insert the needle at a 90° angle (90°).

Lumbar Region – MD-LUMBAR

CORE INSTRUCTIONS ON USE AND COMBINATIONS WITH OTHER MDs
- Inject in the main points

- Lumbar pain secondary to cartilage degenerative lumbar spine disorders (lumbar and lumbar-sacral arthrosis): **MD-Lumbar** + **MD-Muscle** + **MD-Neural**
- Lumbar vertebral osteophytosis: **MD-Lumbar** + **MD-Neural** + **MD-Matrix**
- Low-back pain secondary to musculo-tendinous trigger points: **MD-Lumbar** + **MD-Muscle**
- Postural low-back aches: **MD-Lumbar** + **MD-Neural** + **MD-Muscle** + **MD-Tissue**
- Lumbar and lumbar-sacral mechanical imbalance: **MD-Lumbar** + **MD-Neural**
- Lumbar and lumbar-sacral spinal ligament syndrome: **MD-Lumbar** + **MD-Matrix**
- Sacro-iliac syndrome: **MD-Lumbar** + **MD-Neural** + **MD-Matrix**
- Spinal lumbar and lumbar-sacral nerve root pain: **MD-Lumbar** + **MD-Neural** + **MD- Ischial**.

Ischial Nerve

MD-ISCHIAL

SECONDARY POINTS

Anatomical landmarks:

A) Midway of the anterior thigh, about 20 cm above the upper edge of the patella
B) Midway of the anterior thigh, about 15 cm above the upper edge of the patella.

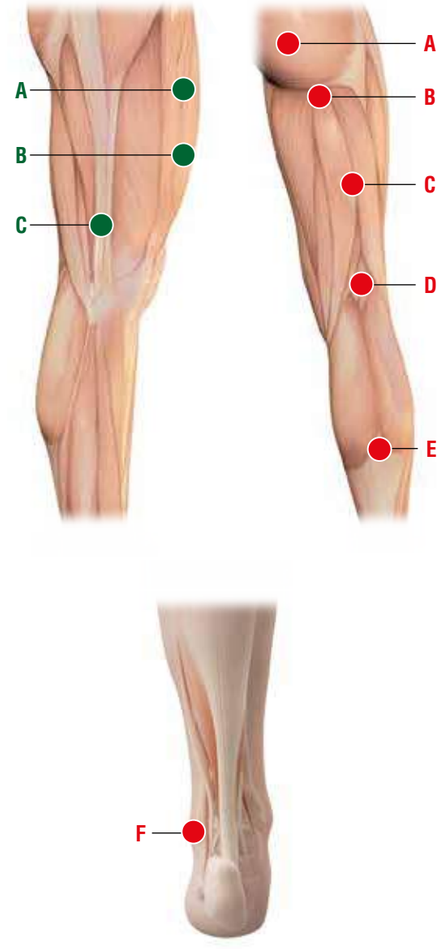
MDs:
MD-Neural + MD-Matrix.

How to inject:
i.m. o s.c.

C) Patient standing straight, on the lateral surface of the thigh, at the point where the patient's middle finger touches the thigh.

MDs:
MD-Neural + MD-Matrix.

How to inject:
s.c.



MAIN POINTS

Anatomical landmarks:

A) Midway of the gluteus maximus muscle, 5-6 cm lateral from the posterior midline
B) Midway of the gluteal-femoral fold
C) Midway of the posterior surface of the thigh, midway between the anatomical landmark B (see above) and the anatomical landmark D (see below)
D) Midway of the popliteal crease
E) Point of intersection between the two muscles of the gastrocnemius and the tendon of the soleus muscle
F) 3-4 cm from the tip of the lower and posterior external malleolus.

How to inject:
A, B and C : i.m.
D: i.d.
E, F: s.c.

Remarks:
*All the subcutaneous (**s.c.**) or intradermal (**i.d.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
*All the intramuscular (**i.m.**) injections must be made with a needle of 40 mm length, 21 G (Gauge) diameter.*

- When making subcutaneous injections, insert the needle at approximately a 45 degree angle(45°);
- When making intradermal injections, insert the needle at approximately a 30 degree angle(30°);
- When making intramuscular injections, insert the needle at approximately a 90 degree angle(90°).

Ischial Nerve – MD-ISCHIAL

CORE INSTRUCTIONS ON USE AND COMBINATIONS WITH OTHER MDs
- Inject in the main points

- Sciatic pain: **MD-Ischial**
- Lumbar-sciatic pain: **MD-Ischial** + **MD-Lumbar** + **MD-Neural**
- Nerve pain in the lower lumbar spine: **MD-Ischial** + **MD-Muscle**
- Persistent sciatic pain due to post-surgery treatment of disc herniation L4-L5, L5-S1: **MD-Ischial** + **MD-Neural**
- Morton's neuroma: **MD-Ischial** + **MD-Neural** + **MD-Tissue**.

Shoulder

MD-SHOULDER

SECONDARY POINTS

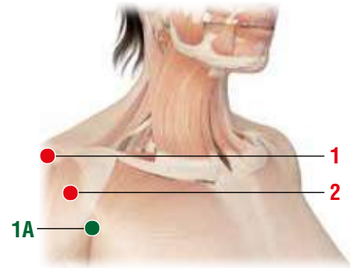
1

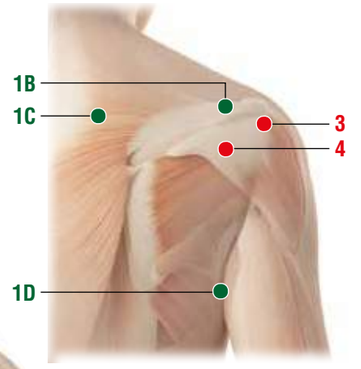
Anatomical landmarks:

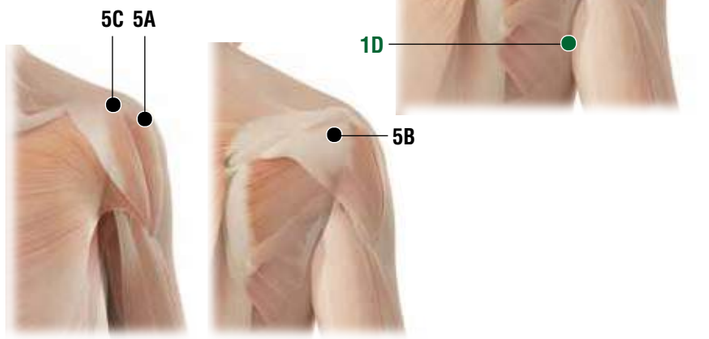
A) The highest point of the anterior axillary fold
B) Point of intersection between the supraspinatus muscle and the posterior aspect of the acromion
C) 7 cm lateral to the spinous process of C7
D) Highest point of the posterior axillary fold.

MDs: **MD-Muscle + MD-Neural**.

How to inject:
i.m. at a the depth of 0.8 - 1 cm.







Remarks:
*All the subcutaneous (**s.c.**) or intradermal (**i.d.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
*All the intramuscular (**i.m.**) injections must be made with a needle of 40 mm length, 21 G (Gauge) diameter.*
*The intra-articular injections (**i.a.**) must be made with dedicated needle.*
- When making subcutaneous injections, insert the needle at approximately a 45 degree angle (∠45°);
- When making intradermal injections, insert the needle at approximately a 30 degree angle (∠30°);
- When making intramuscular injections, insert the needle at approximately a 90 degree angle (∠90°).

Shoulder – MD-SHOULDER

CORE INSTRUCTIONS ON USE AND COMBINATIONS WITH OTHER MDs - Inject in the main points

- Shoulder-arm polyarthritis: **MD-Shoulder** + **MD-Poly**
- Rotator cuff syndrome: **MD-Shoulder** + **MD-Muscle** + **MD-Tissue**
- Shoulder-arm syndrome: **MD-Shoulder** + **MD-Neural** + **MD-Muscle**
- Frozen shoulder: **MD-Shoulder** + **MD-Muscle**
- Shoulder pain due to dislocation (pre and post relocation): **MD-Shoulder** + **MD-Neural**.

MAIN POINTS

1

Anatomical landmark:

Lateral-external surface of the shoulder, in the acromioclavicular joint, the dimple that is formed by lifting the arm.

How to inject:
s.c., i.d., i.a.

2

Anatomical landmark:
Midway of the segment joining the acromio-clavicular joint to the highest point of the anterior axillary fold (Secondary point1A).

How to inject:
Peri-articular injection at a 90 degree angle to the skin surface, very close to the joint capsule.
- Alternatively: s.c.

3

Anatomical landmark:
Upper limb in horizontal position; postero-external surface, in the dimple that is formed between the acromion and the greater tubercle of the humerus.

How to inject:
Peri-articular injection at a 90 degree angle to the skin surface, very close to the joint capsule.
- Alternatively: s.c.

4

Anatomical landmark:

On the vertical line drawn through the posterior axillary fold (Secondary point 1D), in the dimple of the posterior aspect of the shoulder joint.

How to inject:
i.m., s.c.

5

Anatomical landmarks:

1) The shoulder joint (glenohumeral joint) can be injected in the anterior, lateral and upper aspect. It is generally easier to access in these locations.
   - The lateral approach **5A** and posterior approach **5B** are the most used in ambulatory care
2) The acromioclavicular joint is easy to access.
   - The approach can be posterosuperior (**5C**).

How to inject:
Intra-articular.
A common standard needle for i.m. injection can be easily used.

Elbow

MD-SHOULDER

SECONDARY POINT

Epicondylitis

1

Anatomical landmark:

2-3 cm more distal from the anatomical landmark 2 of the main Points.

MD: **MD-Muscle**.

How to inject:
s.c. or i.m.
(at a depth of 5-6 mm).

Epicondylitis

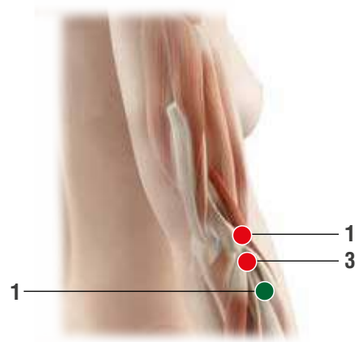
2

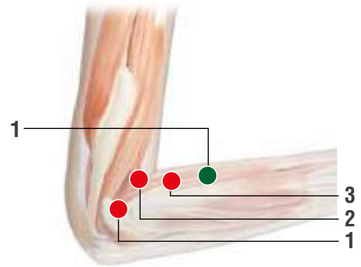
Anatomical landmark:

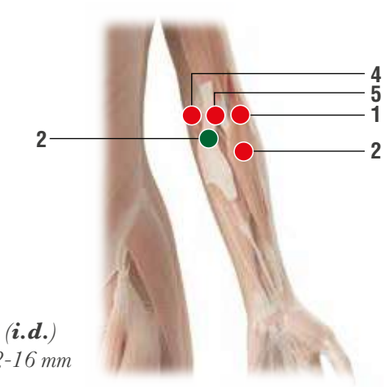
The midway point of the elbow crease, on the internal side of the biceps tendon.

MDs:
MD-Matrix + MD-Tissue.

How to inject:
s.c. or i.d.







Remarks:
*All the subcutaneous (**s.c.**) or intradermal (**i.d.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
*All the intramuscular (**i.m.**) injections must be made with a needle of 40 mm length, 2 1 G (Gauge) diameter.*
- When making subcutaneous injections, insert the needle at approximately a 45 degree angle(∠45°);
- When making intradermal injections, insert the needle at approximately a 30 degree angle(∠30°);
- When making intramuscular injections, insert the needle at approximately a 90 degree angle(∠90°).

Elbow – MD-SHOULDER

CORE DIRECTIONS ON USE AND COMBINATIONS WITH OTHER MDs

- Epicondylitis
- Epitrochleitis
  As for the MDs to be injected, please see main and secondary points
- De Quervain syndrome (stenosing tenosynovitis): **MD-Shoulder** + **MD-Neural**.

MAIN POINTS

Epicondylitis

1

Anatomical landmark:

Elbow flexed at a 90 degree angle, just in front of the epicondyle.

MDs:
MD-Shoulder + MD-Matrix.

How to inject:
s.c. at a 90 degree angle to the bone surface.

2

Anatomical landmark:

At the external tip of the folded elbow flexed at a 90 angle.

MD: **MD-Muscle**.

How to inject
s.c. or i.m. (at a depth of 5-6 mm).

3

Anatomical landmark:

Elbow flexed at a 90 degree angle approximately 4 cm in front of the anatomical landmark 2.

MD: **MD-Muscle**.

How to inject
s.c. or i.m. (at a depth of 5-6 mm).

Epicondylitis

4

Anatomical landmark:

On the posteroanterior aspect of the elbow, between the medial condyle of the humerus (trochlea) and the olecranon.

MDs:
MD-Shoulder + MD-Matrix.

How to inject:
s.c. at a 90 degree angle to the bone surface.

5

Anatomical landmark:

At the tip of the internal crease of the elbow flexed at a 90 degree angle.

MD: **MD-Muscle**.

How to inject:
s.c. or i.m. (at a depth of 4-5 mm).

Wrist

MD-POLY, MD-SMALL JOINTS

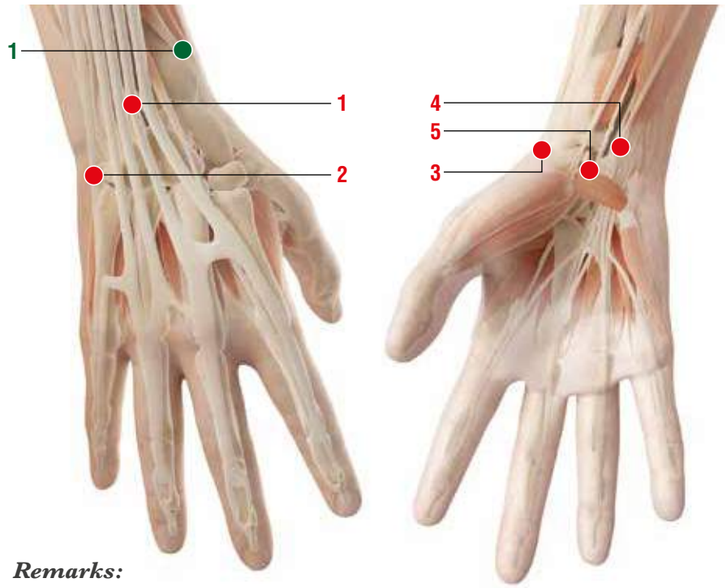
SECONDARY POINT

1

On the external edge of the radius (proximal to the dorsal surface of the forearm), approximately 6-7 cm from the flexion crease of the wrist.

MDs:
MD-Poly + MD-Neural.

How to inject: s.c.



Remarks:
*All the subcutaneous (**s.c.**) or intradermal (**i.d.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
- When making subcutaneous injections, insert the needle at approximately a 45 degree angle (45°);
- When making intradermal injections, insert the needle at approximately a 30 degree angle (30°);

MAIN POINTS

1

Anatomical landmark:

On the dorsal surface of the forearm, approximately 2 cm above the dorsal crease of the wrist, on the internal side of the radius (hand in a supinated position).

How to inject: s.c. or i.d.

2

Anatomical landmark:

On the internal border of the hand, in a dimple between the 5th metacarpal and the hamate bone.

How to inject: s.c.

3

Anatomical landmark:

In the radial depression, on the flexion crease of the wrist.
On the external border of the hand in a dimple, above the head of the 1st metacarpal bone.

How to inject: i.d.

4

Anatomical landmark:

2 cm above the flexion crease of the wrist, between the pisiform bone and styloid process of the ulna.

How to inject: s.c.

5

Anatomical landmark:

Midway of the flexion crease of the wrist.

How to inject: s.c.

Wrist – MD-POLY, MD-SMALL JOINTS

CORE INSTRUCTIONS ON USE AND COMBINATIONS WITH OTHER MDs - Inject in the main points

- Arthritis of the fingers (local painful points): **MD-Small Joints**
- Rhizoarthrosis of the thumb (Forestier disease): **MD-Small Joints** + **MD-Poly** + **MD-Neural**
- Carpal-tunnel syndrome: **MD-Small Joints** + **MD-Neural**
- De Quervain disease (see also Elbow core directions on use and combinations with other MDs): **MD-Small Joints** + **MD-Neural**
- Rheumatoid arthritis of the hand: **MD-Small Joints** + **MD-Matrix**
- Hand tendon pain due to prolonged immobilization: **MD-Small Joints** + **MD-Matrix** + **MD-Tissue**.

Hip

MD-HIP

SECONDARY POINT

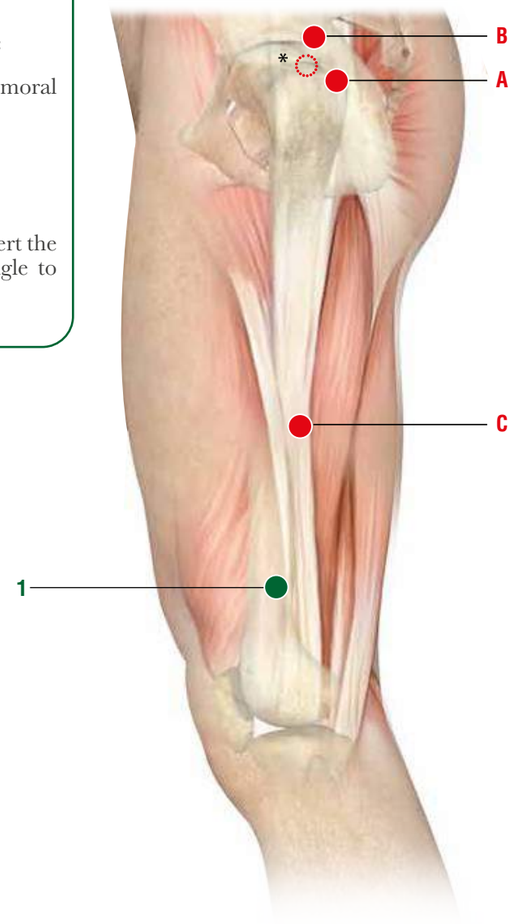
1

Anatomical landmark:

8 cm above the external femoral condyle.

MD:
MD-Muscle.

How to inject:
i.m. at a depth of 1 cm, insert the needle at a 90 degree angle to the skin surface
- Alternatively: s.c.



MAIN POINTS

Anatomical landmarks:

A) Patient in orthostatic position with feet together, posterior margin of the greater trochanter. With patient lying on the healthy side, the anatomical landmark is localized on the apex of the greater trochanter*.
B) 2 cm above and in front of the highest margin of the greater trochanter (anatomical landmark A).
C) Patient in orthostatic position: upper limb along the trunk, point on the thigh touched by the top joint of the middle finger.

How to inject:
For A) and B): i.a.
- Alternatively:
For A) and B): i.m. at a depth of 2 cm; needle inclination towards the hip joint
For C): i.m. at a depth of 1 cm; insert the needle at a 90° degree angle from to the skin surface.

Remarks:
*All the subcutaneous (**s.c.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
*All the intramuscular (**i.m.**) injections must be made with a needle of 40 mm length, 21 G (Gauge) diameter.*
*The intra-articular injections (**i.a.**) must be made with dedicated needle.*
- When making subcutaneous injections, insert the needle at approximately a 45 degree angle(45°);
- When making intramuscular injections, insert the needle at approximately a 90 degree angle(90°).

Hip – MD-HIP

CORE INSTRUCTIONS ON USE AND COMBINATIONS WITH OTHER MDs - Inject in the main points

- Hip joint osteoarthritis: **MD-Hip**
- Hip joint capsule inflammation: **MD-Hip** + **MD-Matrix**
- Hip joint osteoarthritis with rheumatoid arthritis: **MD-Hip** + **MD-Poly**
- Hip joint pain of muscle origin: **MD-Hip** + **MD-Muscle** + **MD-Neural**
- Hip joint pain of nerve origin (*burning hip*): **MD-Hip** +**MD-Neural**
- Hip joint pain due to prolonged bed rest: **MD-Hip** + **MD-Matrix** + **MD-Tissue**.

Knee

MD-KNEE

SECONDARY POINTS

Anatomical landmarks:

A) 4-5 cm above the maximum convexity of the patella
B) midpoint of the popliteal fossa.

MDs:
For A): **MD-Muscle**.
B): **MD-Matrix**.

How to inject:
For A): i.m., depth of 6-8-10 mm, at a 90 degree angle to the skin surface.
B): s.c.

MAIN POINTS

1

Anterior anatomical landmarks:

A) Top margin of the patella and 2 cm (right and left) from this area follow the curved edge of the patella.
B) inferior-lateral margin of the patella, at the height of the interspace of the knee joint.

How to inject:
s.c. or i.a. only for lateral A.

2

Posterior anatomical landmarks:

C) On the inner surface of the knee, at the height of the interspace of the knee joint
D) On the inner surface of the knee, on the upper edge of the upper end of the tibia, proximal to the joint interspace.

How to inject:
s.c., 5-6 mm deep, at a 90 degree angle to the skin surface.

Remarks:
*All the subcutaneous (**s.c.**) injections must be made with a needle of 12-16 mm length, 25-28 G (Gauge) diameter.*
*All the intramuscular (**i.m.**) injections must be made with a needle of 40 mm length, 21 G (Gauge) diameter.*
- While making subcutaneous injections, insert the needle at approximately a 45 degree angle (45°);
- While making intramuscular injections, insert the needle at approximately a 90 degree angle (90°).
The three most common sites of i.a. injections of the knee are: anterolateral, anteromedial (patient positioned with the knee flexed at 90 degrees) and lateral midway of the patella (extended knee).
Needle: 5 cm length, 21 G (Gauge) diameter.

Knee – MD-KNEE

CORE INSTRUCTIONS ON USE AND COMBINATIONS WITH OTHER MDs
- Inject in the main points

- Knee arthrosis: **MD-Knee + MD-Poly**
- Painful knee due to rheumatoid arthritis or other autoimmune diseases: **MD-Knee + MD-Poly**
- Knee acute and chronic arthrosynovitis secondary to injury, osteoarthritits or rheumatoid arthritis: **MD-Knee + MD-Poly**
- Arthrosynovitis, acute and chronic post-traumatic or post-surgery arthrosynovitis: **MD-Knee + MD-Matrix**
- Traumatic lesions of cruciate or collateral ligaments of the knee: **MD-Knee + MD-Tissue**
- Meniscal lesions: **MD-Knee + MD-Poly**
- Knee joint preparation to meniscectomy: **MD-Knee + MD-Muscle**
- Maintenance therapy after knee surgery: **MD-Knee + MD-Muscle + MD-Neural**.

Ankle

MD-SMALL JOINTS, MD-POLY

SECONDARY POINTS

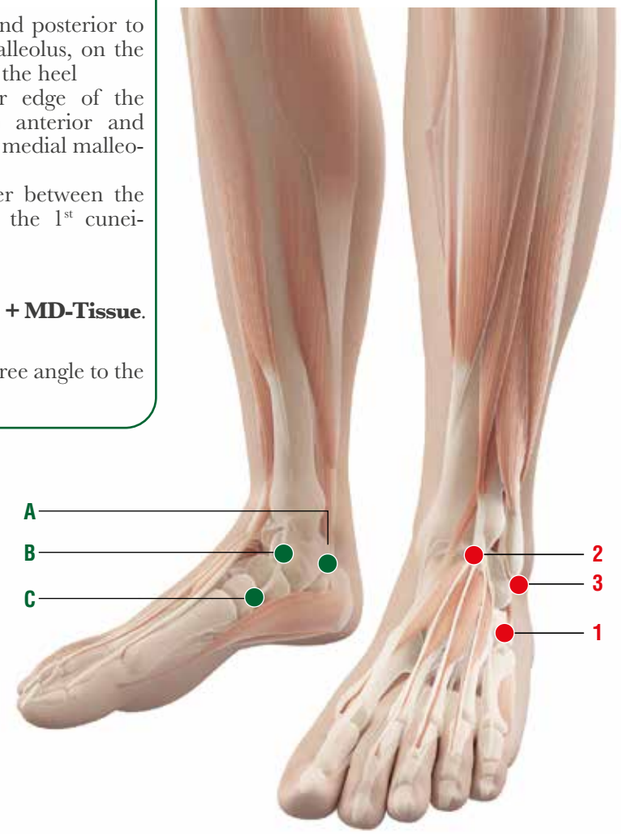
1

Anatomical landmarks:

A) 2 cm below and posterior to the medial malleolus, on the upper edge of the heel
B) On the inner edge of the instep, 2 cm anterior and inferior to the medial malleolus
C) On the border between the scaphoid and the 1st cuneiform bone.

MDs:
MD-Small Joints + MD-Tissue.

How to inject:
5 mm, at a 90 degree angle to the skin surface.



MAIN POINTS

1

Anatomical landmark:

2 cm anterior and inferior to the external malleolus on the calcaneal-cuboid joint.

How to inject:
5 mm, at a 90 degree angle to the skin surface.

2

Anatomical landmark:

On the central fold of extension of the foot (instep), immediately below the tibia.

How to inject:
5 mm, at a 90 degree angle to the skin surface.

3

Anatomical landmark:

1 cm below and slightly behind the external malleolus, just above the heel.

How to inject:
5 mm, at a 90 degree angle to the skin surface.

Remarks:
The injections of 5 mm depth, at a 90 degree angle to the skin surface (perpendicular), must be made with needle of 12-16 mm length, 25-28 G (Gauge) diameter (90°).

Ankle – MD-SMALL JOINTS, MD-POLY

CORE DIRECTIONS ON USE AND COMBINATIONS WITH OTHER MDs
- Inject in the main points

- Arthrosis pain due to hammer toe: **MD-Small Joints + MD-Poly**
- Metatarsal pain: **MD-Small Joints**
- Metatarsal pain accompanied by Morton's neuroma: **MD-Small Joints + MD-Poly + MD-Neural**
- Rheumatoid arthritis of the foot: **MD-Small Joints + MD-Poly + MD-Matrix**
- Foot tendon pain due to prolonged immobilization: **MD-Small Joints + MD-Poly + MD-Matrix**.

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