technical information

update

Rationale and Benefits of Spryng™ for Management of Canine Lameness Issues, Joint Pain, and Osteoarthritis

spryng™ with OsteoCushion™ Technology

Most every small-animal practitioner routinely encounters cases of lameness, joint pain, and osteoarthritis (OA) across their patient population. OA (also termed degenerative joint disease or osteoarthrosis) is the most common form of arthritis in dogs, affecting approximately a quarter of the population. A chronic joint disease, OA is characterized by loss of joint cartilage, thickening of the joint capsule, and new bone formation around the joint (osteophytosis). If left unmanaged, OA often leads to debilitating, painful lameness, and in geriatric dogs, OA incapacity may be the major contributing factor in decisions for euthanasia.[1-4]

Unfortunately, available treatment options for lameness issues, joint pain, and OA are limited and typically focus on pain and inflammation control, and attempts to slow disease progression (e.g., steroid and/or hyaluronic acid injections). Non-steroidal anti-inflammatory drugs (NSAIDs) remain the treatment option most preferred by veterinarians, but this approach offers little success in halting or slowing degeneration and can impose serious side effects (e.g., gastric problems, deleterious impacts on kidney and liver function). Thus, much interest exists for additional therapeutic tools that could help moderate the devastating impacts of lameness issues, joint pain, and OA in companion animals.

KEY POINTS

- Spryng™ with OsteoCushion™ Technology is an intra-articular, injectable, veterinary medical device that provides a relieving cushion of *naturally derived* particulate matrix to help manage lameness issues, joint pain, and osteoarthritis (OA).
- Spryng delivers a natural, inert, protein-carbohydrate aggregate of shock-absorbing matrix material that mimics natural cartilage in protecting and cushioning the joint, and augments the complimentary function of synovial fluid with cartilage.
- By securely remaining in the synovial space, Spryng provides relatively long-term benefit after a single application.
- The excellent safety profile of Spryng has been demonstrated in humans, laboratory animals, horses, and dogs.
- Dogs of any age are likely to benefit from Spryng, evidenced by improved articulation and reduced lameness.

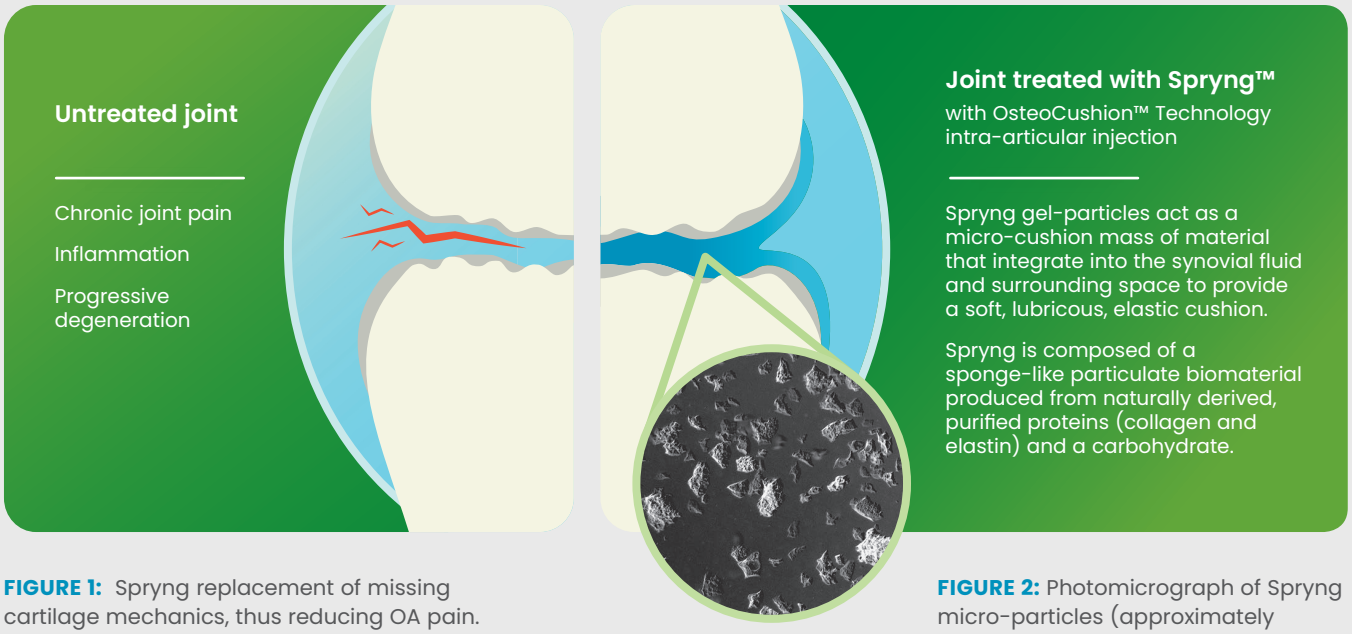

FIGURE 1: Spryng replacement of missing cartilage mechanics, thus reducing OA pain.

FIGURE 2: Photomicrograph of Spryng micro-particles (approximately 100 µm in diameter, or 0.1 mm).

INTRODUCING SPRYNG™ WITH OSTEOCUSHION™ TECHNOLOGY

Spryng,™ from PetVivo, represents a novel technological advance that can help practitioners achieve optimal therapeutic outcomes for patients with lameness issues, joint pain, and OA. Spryng is an injected 'veterinary medical device,' a gelatinous particulate biomaterial (Figure 2) produced from *naturally derived* components (animal protein and carbohydrate) that offers a novel state-of-the-art advancement for long-term management of lameness issues, joint pain, and OA. Unlike pharmaceuticals (NSAIDs, corticosteroids) or monoclonal antibodies that just mask pain and/or joint damage symptoms, Spryng provides a bio-mechanical support substrate that directly addresses the root cause of lameness and pain associated with OA. Thus, Spryng is categorized as a veterinary medical device by the FDA (not a drug) since it does not rely on chemical or metabolic action in the animal body to achieve intended effects.

Spryng is indicated to aid in the management of joint pain from the loss of cartilage or tissue-bone mechanical malfunction caused by joint dysfunction not associated with infection (e.g., lameness, osteoarthritis, degenerative joint disease).

MODE OF ACTION

Spryng with OsteoCushion™ Technology works by replacing missing and damaged cartilage mechanics, which defines the cause of lameness issues, joint pain, and OA (Figure 1). Upon intra-articular injection, Spryng provides long-term joint reinforcement and protection from regular stress and strain endured by the animal.

Spryng delivers millions of micronized hydrogel matrices derived from natural components into the joint space. OsteoCushion Technology provides both reinforcing natural joint support and natural scaffolding.

Each Spryng intra-articular injection supplies a shock-absorbing matrix with natural fluid biomechanics that work together with synovial fluid to mimic joint cartilage in both form and function. Spryng absorbs and releases synovial fluid in response to joint force, with elastic stiffness that complements natural synovial fluid and cartilage dynamics. The components also provide a natural scaffold, thus managing the affliction of lost or damaged cartilage and not simply masking symptoms. Further, Spryng components are sized to remain in the synovial space, for relatively long-term benefits after a single application.

CONSTITUENTS/FORMULATION

Spryng is composed of microscopic particles embedded in a gelatinous material for easy intra-articular injection (Figure 2). The Spryng micro-particles are made from a complex of 2 proteins (elastin, collagen) and a carbohydrate (heparin) via proprietary/patented processes. The particulate matrix of Spryng forms using the natural self-assembly characteristics of proteins that also occur in nature, generating strong hydrated materials from these natural tissue matrix scaffolding components. The sterilized, hydrogel micro-particles (~1 million/cc) are precisely sized to form an insoluble and pliable matrix that allows easy injection and correct articular spacing for painless joint motion. The inert micro-particles do not readily dissolve, are resistant to interstitial proteases, and are too large to pass through the pores of the synovium, thus providing long-duration joint protection after a single application.

History

The materials comprising Spryng were originally developed as a human dermatologic filler by Gel-Del, a US-based company focusing on protein-based biomaterials that mimic bodily tissues and allow augmentation, integration, and tissue reinforcement for long-term implantation. The safety and efficacy of human use was supported by a 145-patient dermal-filler clinical trial for FDA evaluation.[5] As a result of this record of success, PetVivo first licensed and later acquired these patented biomaterials with the intent of developing their use in veterinary medicine for treatment of animals with orthopedic joint afflictions. This technology provided the basis for development of the Spryng veterinary medical device, designed to help reinforce articulating cartilage tissue for the management of lameness issues, joint pain, and OA in companion animals and equines.

TABLE 1 – Spryng rheological characteristics.[a]

Material	Tensile strength (kPa)	Maximum load (N)	Young's Modulus (kPa)
Spryng	**6.05**	**4.27**	**23.93**
20.1% gelatin	4.11	2.90	13.76
13.4% gelatin	2.00	1.41	7.28
6.7% gelatin	1.04	0.74	6.54

[a] Average results, n=10/material; kPa = kilopascal; Young's Modulus is a measure of elasticity

FIGURE 3: Packaged syringe containing 2 cc Spryng, and an example of intra-articular administration to a dog

Rheological characteristics

Spryng particulate-matrix technology provides enhanced shock absorbing and rheological characteristics compared to conventional gelatinous materials, including typical collagen gels (rheology is the study of the flow of matter, typically in response to an applied force). At approximately 18% solids, Spryng exhibited far greater tensile strength, maximum load capacity, and Young's Modulus (elasticity) outcomes than even 20% gelatin in a laboratory evaluation of material-science parameters (Table 1; n=10 samples/group).[6]

USE AND ADMINISTRATION

Spryng is supplied in sterilized, aseptically filled syringes containing 2 cc of material. It is intended for single-dose intra-articular injection (Figure 3), using a quantity sufficient to fill approximately 65% to 85% of the synovial space.

Dogs of any age, particularly those with only early to moderate cartilage damage, will likely benefit from Spryng, demonstrating improved articulation and reduced lameness. Pets are typically able to return to normal daily activities, as well as high-impact sports, competitive events, and training. Veterinarians have used Spryng in dogs as old as 13 years, and report that the comforting effects of Spryng typically last about a year (duration affected by body weight and the frequency/intensity of impacts on the treated joint). The Spryng particles are known to gradually resorb into the surrounding synovial tissue.

For patients with severe or advanced lameness issues, joint pain, or OA disease, Spryng should be used concomitantly with anti-inflammatory therapy to provide the best and most immediate outcomes. Spryng represents an excellent additional therapy that can work well with other established or preferred protocols for management of lameness issues, joint pain, and OA.

SAFETY

Spryng is composed of materials that approximately meet the 'generally regarded as safe' (GRAS) requirements of the FDA. Spryng components derive from certified bovine and porcine tissue sources that do not harbor prion disease or bovine spongiform encephalopathy. Additionally, steps in the manufacturing process have been validated for deactivating all viruses. Case studies collected over 5 years have provided positive testimonials from many veterinarians, and no adverse effects or interactions have been observed other than some mild, short-term injection-site swelling.

Joint safety study

The company that initially developed Spryng conducted a pilot study to evaluate product safety when used as a replacement for joint synovial fluid.[7] The study involved 6 white rabbits (New Zealand) that were injected in both stifle joints (knees) with a quantity of Spryng to fill but not extend the synovial space (~0.5 cc/site). Animals were evaluated daily for abnormal clinical signs and tested every other day for range of motion and joint observations. Three rabbits were euthanized after 1 week on test, with the other 3 sacrificed after 4 weeks. Joints were subjected to extensive histopathological examination, with 2 additional non-injected animals used as negative controls for these evaluations.

Evaluations of animals treated with Spryng revealed no abnormal scores for range of motion, withdrawal response, or joint observations (all animals 100% normal). Further, Spryng was retained and present in all treated joints, and cartilage surfaces of the femoral and tibia condyles and the menisci were grossly and histologically 100% normal for all animals at 1 or 4 weeks post-administration. The product did not stick to or adversely affect articular cartilage, but attached in a mono-layer to fibrocartilage and periosteum tissues within the synovial fluid-contained space.

Investigators concluded that Spryng did not cause inflammation or damage to knee joints, did not cause changes in the articular cartilage of the femur or tibia, and was completely compatible with synovial fluid and all contacted tissues. Spryng particles were deemed very safe and appropriate for testing in clinical joint-treatment studies (university research currently underway).

Human safety

The predecessor of Spryng was developed for use in humans as a dermal filler (cosmetological applications). The sponsoring company conducted several biocompatibility animal studies, including skin studies in rabbits and guinea pigs, all with no adverse safety responses. In addition, a randomized double-blind clinical trial also yielded positive efficacy and safety outcomes in humans.[5] Patients injected with the Spryng predecessor product had no serious inflammatory, irritation, or immunogenic responses, indicating the product was biocompatible with human tissues. The absence of antibody responses during the clinical trial further supported the apparent wide margin of product safety.

CONCLUSIONS

Spryng represents a novel technological advance that can help practitioners achieve optimal therapeutic outcomes for patients with lameness issues, joint pain, and OA. Upon injection into the intra-articular space of a dog, the naturally derived particulate matrix of Spryng helps restore missing cartilage biomechanics and thereby moderate symptoms of lameness issues, joint pain, and OA. The resulting long-term reinforcement also may help protect the joint from further injury, unlike other interventions that only treat symptoms. Further, Spryng offers excellent safety, with no reported adverse events or interactions. As a result, pet owners may enjoy a dog with a revitalized quality of life, realized with less overall client cost and devoid of safety concerns typically associated with previous treatment approaches.

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spryng™ with OsteoCushion™ Technology

To learn more, visit SpryngHealth.com

To order, contact info1@petvivo.com or 844-PET-VIVO (844-738-8486)

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