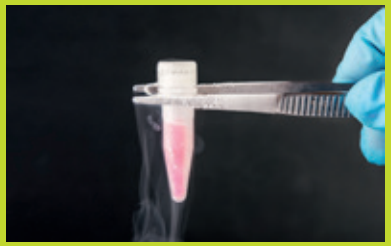

greenside
Regenerative therapies
& rehabilitation

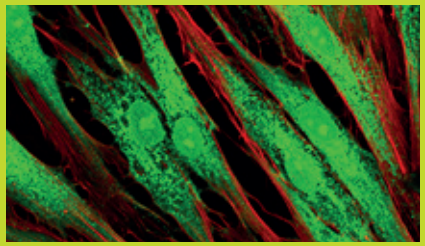
Regenerative medicine at Greenside Veterinary Practice

Regenerative medicine utilises the body's own cells to heal and regenerate damaged tissues in acute and chronic conditions, including arthritis and soft tissue injuries. Regenerative therapies include platelet rich plasma (PRP), stem cell therapy and laser therapy. The use of regenerative medicine is becoming increasingly popular in both human and veterinary medicine for multiple disease processes. Mounting evidence and proper clinical trials have aided in the acceptance of regenerative medicine therapies.

Greenside Veterinary Practice was the first practice in the UK to use culture expanded mesenchymal stem cells to treat osteoarthritis in dogs and cats. Since the initial trials done in June 2014, we have treated hundreds of dogs and cats with stem cell therapy. We have currently treated more animals with regenerative medicine therapies than anyone else in the UK and have collected data on every patient that we have treated. We therefore hold the most extensive data base of treatment responses in this country. We have a greater than 90% success rate in reducing pain and debility with our combination therapies, which is greater than that reported by other centres.

We accept referrals for regenerative therapies from all over the UK and have recently received our first case from the European mainland. We have extensive experience in this new technology and are actively involved in collecting data and publishing our work to promote the use of these therapies in animals. Andy Armitage BSc BVM&S MRCVS heads up the regenerative medicine team at Greenside veterinary practice and has pioneered new treatment options for lumbo-sacral disease and spinal osteoarthritis and has developed protocols for combination therapies to give the best chance of treatment success.



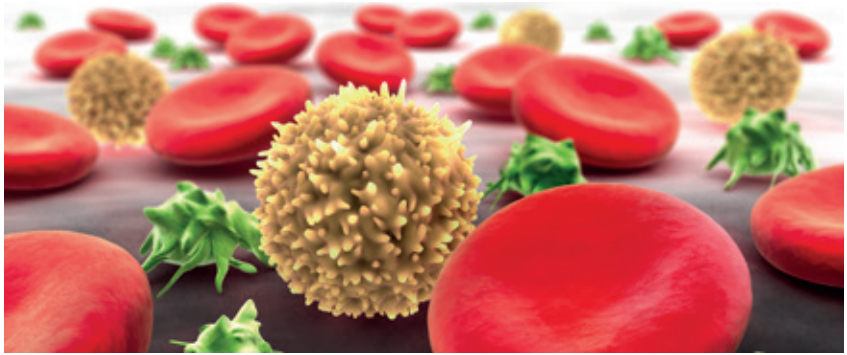


Platelet rich plasma or PRP

The world of veterinary medicine continues to evolve and with it comes new treatment modalities. Platelet rich plasma (PRP) is a prime example of this evolution. For years it has been used in human medicine to help with bone grafts, healing tendons and ligament lesions and to promote wound healing. It was not until recently that PRP therapy and its benefits has made its way over to veterinary medicine.

What exactly is PRP and why is it beneficial?

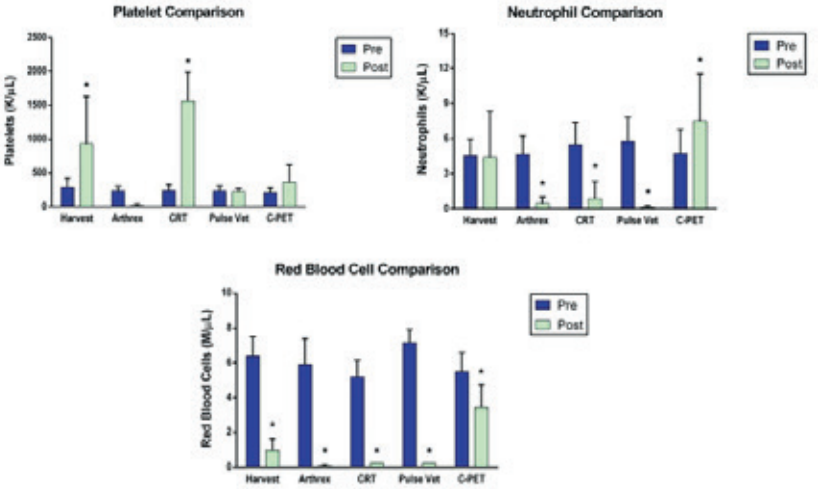
Platelet rich plasma is an autologous (self-derived) conditioned plasma that contains a high concentration of platelets. Platelets contain numerous growth factors that facilitate tissue repair and healing. These growth factors are contained in the alpha granule portion of the cell and are released from the platelet when it is activated (usually at an area of injury). A few examples of these growth factors are: Transforming Growth Factor β (TGF-β), Platelet Derived Growth Factor (PDGF), Insulin-like Growth Factor (IGF-1), Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGF) and Fibroblast Growth Factor (FGF). Roles of these growth factors range from vessel development and repair to cellular recruitment and activation. Many of these growth factors have been shown in recent studies to promote cartilage health and reverse the cartilage breakdown seen with osteoarthritis. Platelets have been shown to recruit and activate stem cells and PRP is increasingly being used in combination with stem cell therapy to augment the effects.



What can PRP be used for?

In veterinary medicine, PRP has been used for a wide range of indications, including acute and chronic soft tissue injuries, osteoarthritis and even certain spinal conditions. Because PRP is obtained from the patient's own blood, there is minimal risk and the positive effects of treatment can last for up to a year. In addition to these benefits, PRP is relatively inexpensive and can be done at patient-side in less than 30 minutes.

We use the Companion CRT system to produce high quality PRP in house without the need to send samples to external laboratories for processing. The Companion Regenerative Therapies PurePRP® kit is the best performing platelet concentrating system in the veterinary market. This system is specifically validated for use in canine patients, and provides the optimal concentration of platelets while effectively removing more than 95% of red blood cells and 85% of neutrophils*. Greenside Veterinary Practice was the first practice in the UK to use this system as all other PRP systems available in the UK were either not validated for canine patients or failed to meet all the criteria for medical PRP properties. The Companion Regenerative Therapies (CRT) system has been specifically validated for use in canine patients. In a multicenter study*, the CRT Pure PRP system was the only system that increased platelet concentration while significantly reducing the red blood cell and neutrophil concentrations.



References:
*Carr, B, Canapp, S. *et al.* "Canine Platelet Rich Plasma Systems: A Multicenter, Prospective Analysis." (2015) Front Vet Sci. 2015; 2: 73

Why is it important to reduce neutrophils and red blood cells (RBCs)?

The goal is to obtain the highest concentration of platelets and growth factors, whilst removing the other blood components such as the red and white blood cells, which can cause pain and inflammation.

White blood cells: neutrophils

- Multiple studies show that neutrophils increase concentrations of unwanted inflammatory mediators (IL-1β, TNF-α, IL-6, IL-8).
- Increased concentrations of neutrophils in PRP positively correlate with an increased MMP-9 concentration, which leads to degradation of collagen and other extracellular matrix molecules.

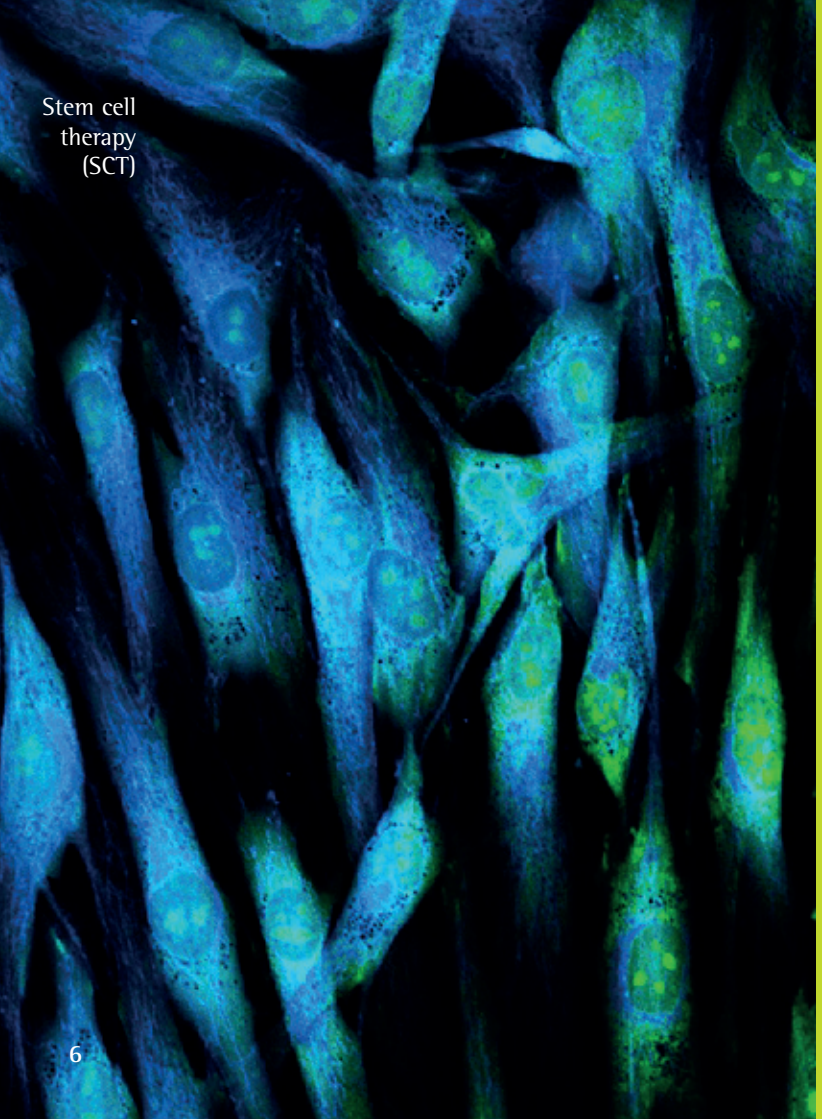
Red blood cells

- RBCs damage cartilage and synovium directly via iron-catalyzed formation of Reactive Oxygen Species (ROS).
- RBCs increase concentration of unwanted inflammatory mediators (IL-1 and TGF-α).
- PRP with high concentration of RBCs caused significantly more synoviocyte death when compared to PRP preparations with lower RBC count.

What should I expect if my pet has a PRP injection?

PRP is commonly given as a single injection but sometimes repeat injections are required two weeks apart. For certain conditions or advanced osteoarthritis, PRP is combined with stem cells and injected into the joint. Approximately 50% of dogs require more than one injection for a significant improvement, however this is dramatically reduced if it is combined with stem cell therapy. PRP therapy is a minimally invasive procedure that is performed in house under sedation. Approximately 30 to 60 ml of blood is collected from the jugular vein, which is then processed and prepared for injection. The patient is sedated and the treatment site clipped and aseptically prepared. For joint injections, a needle is placed into the joint and arthritic joint fluid removed and replaced with PRP. For soft tissue injuries, ultrasound guidance is used to ensure accuracy of administration directly into the lesion. PRP can also be used to speed the healing of wounds and burns and we commonly use it combined with Manuka honey in wound dressings.

In people, mild discomfort has been reported following the injection for the first 24-72 hours and this can be managed with cold compresses and pain medication prescribed by us if required. Following treatment your pet will be rested for two weeks and then an appropriate rehabilitation program started to help with the regenerative process.



Stem cell therapy (SCT)

Stem cell therapy has gained much attention over the years through media and medical reporting. Whether it is ground breaking science in the generation of complete functional organs or the healing of spinal cord injuries, stem cells have remained at the forefront of the medical fields. The knowledge of these cells and their properties continues to grow and with that, new therapies and applications are becoming more readily available.

What are stem cells?

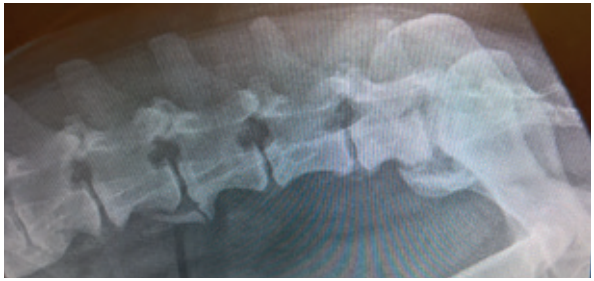
Stem cells may be classified into two groups based on their origin: embryonic and adult stem cells. For current veterinary use, we will focus on adult stem cells only. Adult stem cells are found in every tissue of the body including bone marrow, adipose tissue (fat), skin and the liver. These cells have the ability to differentiate into many types of tissue (pluripotent) under the appropriate circumstances and can additionally activate surrounding cells to aid in wound healing and tissue repair. Additionally, stem cells can also go through several cycles of cell division/replication without differentiating into a specific tissue type (i.e. they are self-replicating).

What is stem cell therapy?

Stem cell therapy is the process by which a tissue sample is obtained from the patient (either by fat or bone marrow extraction) and is then processed to isolate the stem cells, followed by administration back into the patient at the site of injury or disease by injection.

When stem cells are injected in a concentrated form, they act as a conductor for tissue repair by performing a number of tasks including:

- Differentiation into surrounding tissue type (e.g. chondrocytes to form new cartilage)
- Activation of surrounding resident stem cells
- Recruitment of other cell types, release of cytokines and growth factors to accelerate healing and tissue repair
- Regulation of inflammatory cytokines to reduce inflammation
- Stimulation of new blood supply
- Protection of cells from death
- Creation of a biological scaffold for healing tissues by forming extracellular matrix
- Reduction and/or elimination of scar tissue/fibrosis.
- Immune modulation



What has stem cell therapy been used for?

In veterinary medicine, stem cell therapy has been used for a wide range of indications including:

- Degenerative diseases
  - Tendon injuries or tendinopathies
  - Ligament Injuries
  - Hip and elbow dysplasia
  - Osteoarthritis
  - Certain spinal conditions such as spondylosis, lumbosacral disease and intervertebral disc disease.
- Fracture repair
- Osteochondral defects
- Organ dysfunction or failure (e.g. renal failure)
- Auto-immune disease

Where are the cells obtained?

Adult-derived mesenchymal stem cells (ADMSCs) used in veterinary regenerative therapies are harvested from adipose tissue (fat) or bone marrow. Both types of mesenchymal stem cell are able to differentiate into cartilage, bone, tendons, ligaments for repair and regeneration. There is currently no evidence to suggest that one type is superior to the other for regenerative therapies.

At Greenside Veterinary Practice, we can offer treatment with either culture expanded adipose derived mesenchymal stem cells (ADMSCs) or bone marrow aspirate concentrate (BMAC). The majority of cases are treated with ADMSCs due to the ease of harvest, ability to culture expand and store cells for future use if required.

BMAC

BMAC is obtained under general anaesthesia from the femur via a sterile surgical procedure. A small incision is made in the skin, a long needle is inserted into the centre of the bone (medullary cavity) and the cells are aspirated with a syringe preloaded with an anticoagulant. The sample is then processed in house by filtration and centrifugation using specialist equipment to yield a cell fraction containing concentrated mesenchymal stem cells, platelets, and haematopoetic stem cells. This can then be injected into the affected area either alone or in combination with PRP and biological scaffolds during the same procedure/anaesthetic. BMAC is only suitable to treat two to three joints in total but we can culture expand these cells so that they can be stored for future use or used in more than three joints. A disadvantage of this method of collection is that patients can be painful following bone marrow harvest but this can be minimised with an epidural anaesthetic prior to harvest and post-operative pain medications. Bone marrow harvest is considered more invasive than fat harvest.

ADMSCs

ADMSCs are harvested from fat taken from the inguinal fat pad in the groin or falciform ligament in the abdomen under general anaesthesia. Both sites require a small (2 cm) incision in the skin and there are no external sutures placed in the skin following harvest. A blood sample is also taken to provide serum, which is used to culture the cells and provide a medium in which the stem cells are suspended when they are returned for injection. This ensures that only cells and fluids from the same animal are implanted and therefore there is no risk of rejection or reaction. The fat is processed and sent by overnight courier to an external laboratory that extracts the stem cells from the fat. These cells are then culture expanded in medium containing autologous serum. The culture process takes two to three weeks depending on the total number of cells required. Any number of stem cells can be cultured which is ideal if multiple joints are requiring treatment or large numbers of cells are required for intravenous or spinal injections. ADMSCs are sterility tested and cryogenically frozen prior to shipping back to the practice. Implantation can then be arranged at any point, as the frozen cells can be stored for an extended period of time (many years in fact!). A sample of the patient's stem cells will be stored at the lab in case more cells are required in the future. These can then be used to culture more cells as required without having to undergo repeat fat harvest.

How are stem cells administered?

One of the most important aspects of SCT is the ability to get the cells to the target location. Treatment failures may result if the cells are not delivered correctly and it is imperative that the injections are therefore performed by a suitably qualified vet trained in using advanced modalities.

At Greenside Veterinary Practice, injections are performed under sedation using ultrasound guidance for soft tissue injuries. Joint injections are performed by experienced vets and correct placement of the needle into the joint is ensured by aspirating joint fluid prior to injection. Spinal injections are assisted using radiography to determine correct placement of the needle into the target tissue, if required. We have performed thousands of joint and spinal injections and you can rest assured that we are able to deliver regenerative therapies to their target location in every case.

For all intra-articular joint injections, joint fluid is removed prior to implantation. Arthritic joint fluid has been shown to be toxic to stem cells so removal ensures the best survivability of the implanted cells. Removal of joint fluid also makes room for the administered treatment without causing excessive joint capsule distension following injection, which can be associated with post implantation discomfort. We are currently exploring treatment protocols where the joint is pre-treated with PRP prior to SCT to change the environment within the joint to one that is more likely to ensure the survival of the implanted stem cells.

What conditions can be treated?

Tendon and ligament injuries

Tendon and ligament injuries are very common in active dogs and can take a long time to heal due to poor blood supply. Conservative treatment allows for scar tissue formation, which predisposes to re-injury or further degeneration resulting from decreased strength and flexibility. SCT heals the tendon or ligament injury through regeneration and elimination of fibrosis and scar tissue. Ultrasound guidance is used to target the stem cells directly into the site of injury and will also be used to monitor the repair process. Regenerative medicine is able to completely heal a tendon or ligament and, with integrity uncompromised by scar tissue, patients are able to return to full activity and function.

Examples of commonly treated tendons and ligaments:

Supraspinatous tendon

Biceps tendon

Iliopsoas tendon

Achilles tendon

Carpal, tarsal and stifle collateral ligament

Cranial cruciate ligament (partial tear)

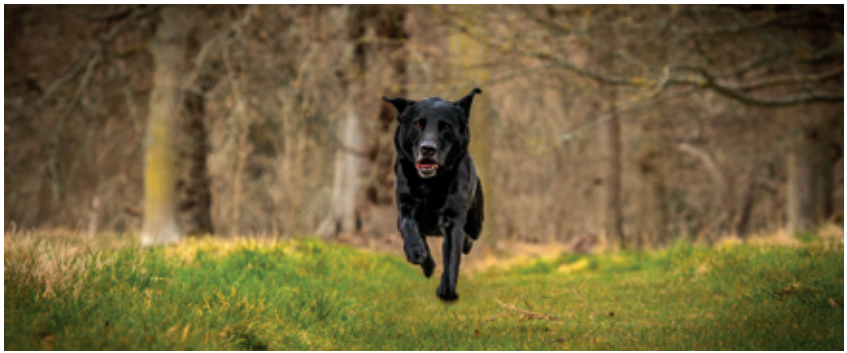
For severe tendon and ligament injuries that have resulted in ruptures or complete tears, surgical intervention is required. However, injecting stem cells around the damage will result in regeneration of fibres rather than scar tissue formation, which strengthens the repair.

Treatment of osteoarthritis (OA)

OA is a very common cause of pain and lameness in dogs and cats. OA is not just limited to older patients and we commonly see this condition in young animals and also as a result of hip or elbow dysplasia or trauma to the joint. OA is usually managed with painkillers (non-steroidal anti-inflammatories), joint supplements (such as Dasuquin and Synoquin), weight management and exercise modification. Physiotherapy and hydrotherapy are also important in maintaining muscle strength and fitness. Conservative management of OA often fails to provide a long term response and, once OA is present in a joint, it continues to progress with time. Stem cell therapy provides another treatment option in the management of OA. Stem cell therapy has the potential to reverse or stop the inevitable degeneration that occurs once OA occurs in a joint and can be used at any stage in the disease process. Stem cells have a very potent anti-inflammatory effect when placed in an arthritic joint and they also have the potential to form new cartilage. We have seen SCT remodel joints and remove arthritic bone resulting in increased range of motion and better functionality. In the majority of patients treated with SCT, they are able to stop their pain killers and return to normal exercise for an extended period of time.

Neurological conditions

Spinal conditions such as lumbosacral (LS) disease, intervertebral disc disease and spondylosis, can cause chronic pain and dysfunction in dogs. Treatment options vary depending on the severity of the condition but include medical management, surgical intervention, physiotherapy and laser therapy. The use of stem cell therapy has recently been reported as a positive treatment option for spinal disease in dogs. At Greenside Veterinary Practice, we have pioneered a regenerative treatment option for lumbosacral disease. We have treated over 50 cases now with intravenous and epidural implantation of stem cells with a very high success rate. LS disease is a chronically painful condition and can result in nerve dysfunction to the hind limbs, the bowels and the bladder. Greenside Vets have recently published a small case series on LS disease and the abstract can be seen here: www.greensidevetpractice.co.uk



Other conditions that have been treated with stem cell therapy at Greenside Vets include:

Renal failure

Chronic nephritis

Haematuria

Liver failure

Liver cancer

Auto-immune disease

Lupoid onychodystrophy

Skin defects

Allergic skin disease

Feline diabetes

Feline gingivitis stomatitis complex

Nerve damage

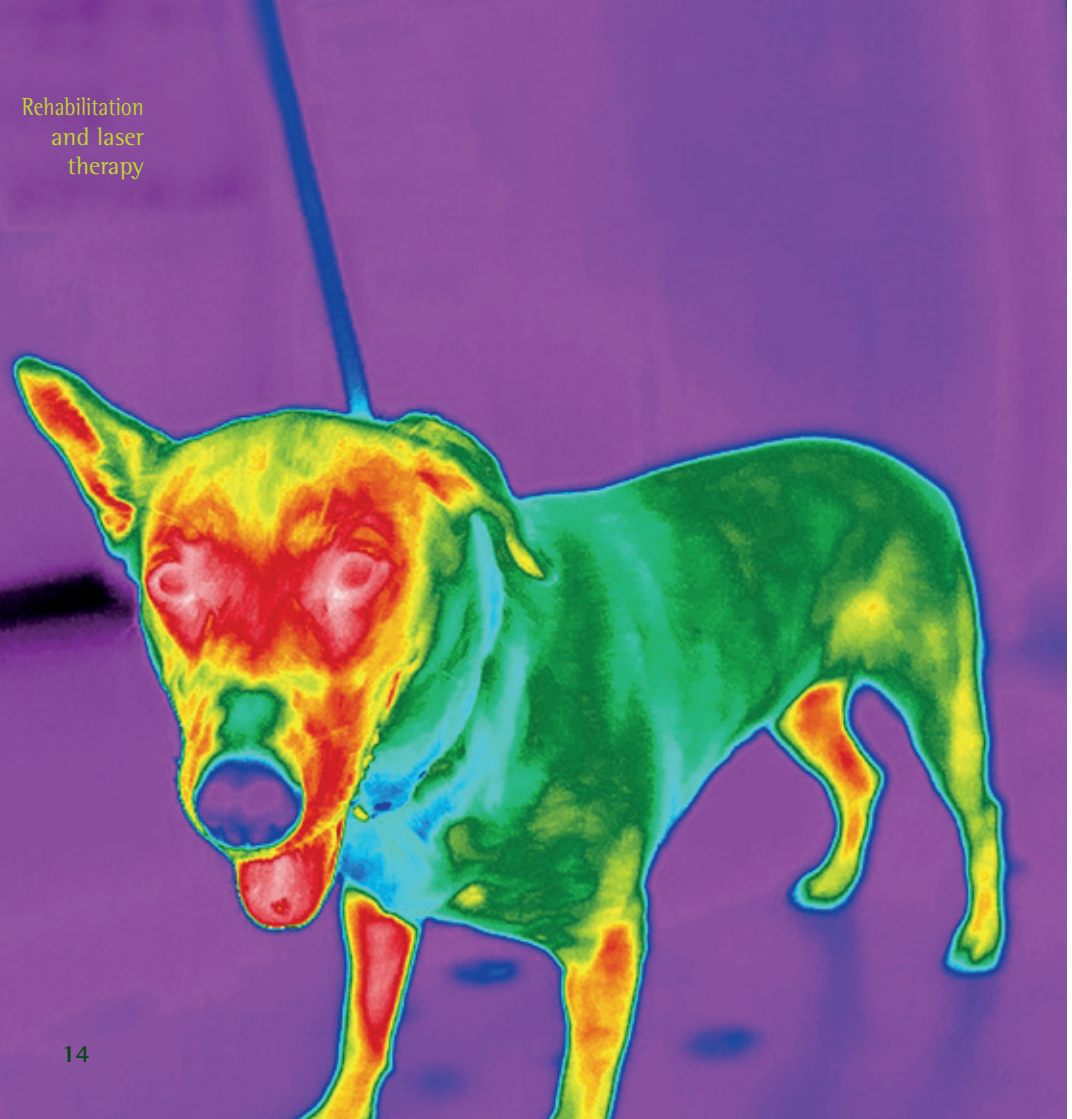
Feline infectious peritonitis

Pulmonary fibrosis

Following stem cell therapy, we recommend a course of laser therapy to commence immediately post implantation. Laser therapy energises the cells and stimulates the regenerative response through a process called photobiomodulation. Laser therapy also helps to reduce pain and inflammation associated with the joint injection until the stem cells can exert their anti-inflammatory and pain killing effects. We also recommend physiotherapy and hydrotherapy if appropriate to help the body adapt to the changes in function of the treated area and rebuild strength following periods of reduced use or compensation.

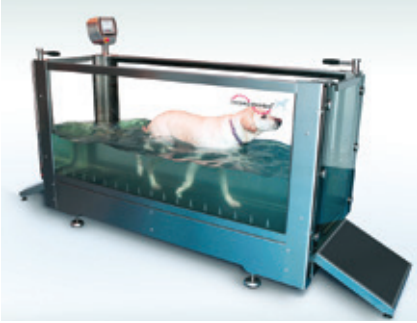
Stem cells can be stored for the lifetime of the animal in case a second treatment is required in the future. At Greenside Vets, we have a greater than 90% improvement rate with stem cell therapy but in a few cases a second injection maybe required to complete the healing process. For the treatment of OA it is not uncommon for a patient to require a booster stem cell treatment 18 months to two years following the first treatment. This can easily be done by culturing more cells from cryopreserved samples without the need for repeat fat or bone marrow harvest.

SCT is a treatment option for any age or breed of dog or cat. The conditions listed above are just a few examples of the commonly performed treatments at Greenside Veterinary Practice. Many other conditions can potentially benefit from SCT and these can be discussed during consultation with Andy Armitage, our head of regenerative therapies. Before this type of treatment can be performed, it is important to obtain a definitive diagnosis in order to target the treatment appropriately. We have a number of diagnostic aids that enable us to find the cause of the problem and then treat it with the most appropriate forms of regenerative medicine. Diagnostic aids include skilled veterinary physical examination, radiography, stance analysis, digital thermal imaging, gait analysis and musculo-skeletal ultrasound. Once a definitive diagnosis has been made, a detailed treatment protocol and an estimate of treatment costs will be provided by your regenerative medicine specialist. Response to treatment will be objectively assessed using appropriate tools to ensure your pet is progressing as expected following treatment. We are trialling a pet activity monitor to record your pet's vital signs and activity levels following stem cell therapy. This will allow us to collect data on how your pet is responding to treatment at home. If successful, this will give us valuable indicators on how your pet is doing at home, allowing us to complete the picture when monitoring treatment outcomes, as well as ensuring early intervention if things are not going as expected.



Rehabilitation and laser therapy

Just as people receive physical therapy after an injury, physical rehabilitation has become an option for your pet as well. After surgery for problems such as torn ligaments, broken bones or ruptured disks in the spine and after regenerative medicine therapies, our vets may deem it appropriate that your pet can be placed on a specific therapeutic program to help him or her recover faster. Rehabilitation modalities including walking in the water of an underwater treadmill or receiving light therapy from a therapeutic laser to decrease pain and increase a pet's range of motion when walking. These types of rehabilitative therapies, along with others, aid in the success of the surgery and your pet's overall well-being. It is also a great option to consider rehabilitation for issues that do not necessarily warrant surgery. Pets that suffer from chronic arthritis, nerve injury or sprains and strains can be excellent



candidates for receiving rehab. The exercise will help keep your pet from losing muscle mass while working on balance to maintain proper posture during all sorts of activities.

Whether it is an acute injury or a chronic ailment, hydrotherapy and laser therapy gives you another alternative to consider when exploring options for your pet. Our pets are living longer, so allowing your pet access to this aspect of veterinary medicine helps to maintain a better quality of life.

Post-surgical rehabilitation

Underwater treadmill

The underwater treadmill is a fantastic option for exercising your pet after surgery. The depth of the water can be changed to control the amount of weight that is being placed on the limbs while varying the speed of the treadmill to get your pet up and moving as quickly as possible for a better recovery.

Stance analyser

Utilising the stance analyser can visibly show you how your pet is progressing through his or her clinical and rehab visits when surgery has been completed. The data collected will keep track of how your pet is shifting weight from the surgical area to other limbs and give you insight into how well he or she is healing.

Non-surgical rehabilitation

Underwater treadmill

For those instances when surgery is not an option, your veterinary surgeon may determine that allowing a pet to walk in an underwater treadmill can still be extremely beneficial. Benefits include minimising how much muscle is lost due to inactivity, controlling a pet's exercise while he or she is recovering from injury and helping a pet's mental well-being by allowing those with degenerative diseases the opportunity to walk with the support of the water.

Stance analyser

The stance analyser will help evaluate injuries, degenerative changes and a prescribed treatment over a period of time. Subtle changes can be seen as a pet is standing on the device that can alert us as to a potential issue or disease process needing to be treated.

Weight loss

Underwater treadmill

If your pet is overweight, the underwater treadmill can be a great way to help your pet comfortably shed those unwanted pounds. Your rehabilitation therapist will start your pet slowly and gradually increase his or her time and pace as their weight decreases and he or she gets into better shape to improve his or her overall health.

Conditioning

Underwater treadmill

For those canine athletes that need an additional challenge, the underwater treadmill can really push your pet to his or her limits. Cardiovascular fitness, endurance, and muscle mass can all be increased when your pet exercises in water. And, for those times of the year when exercising outside is not ideal, this provides you with an option for keeping him or her in shape for the next competition.

Stance analyser

Allowing your pet's stance to be analysed can help you potentially see if your pet is experiencing any lameness or compensations from intense exercise. The data collected will give you information on what limb, or limbs, has/have an issue so you can be pro-active in preventing injuries.

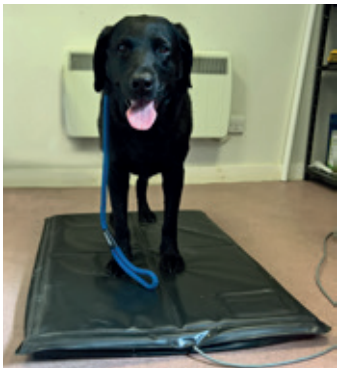
Diagnosis

Underwater treadmill

When pets walk in water, they tend to exaggerate how they step more than they do when they walk on land. This can allow us to observe if there is a problem with how they are walking and determine a course of action to treat the issue.

Stance analyser

The stance analyser is a great instrument for showing you which limb is affecting your pet. By narrowing down where the problem exists, you can focus your money and energy on the appropriate area for other diagnostics (if needed) and therapeutic interventions for the maximum outcome.



Laser therapy

Greenside Veterinary Practice is excited to offer our clients companion laser therapy. Laser therapy provides a non-invasive, pain-free, surgery-free, drug-free treatment that is used to treat a variety of conditions and can be performed in conjunction with existing treatment protocols. Relief and/or improvement is often noticed within hours depending on the condition and your pet's response. Whether your pet is rehabilitating from trauma or injury, healing from wounds, or simply aging, your companion can benefit from this innovative approach to treating pain. Laser therapy is often combined with regenerative therapies such as stem cell therapy to augment and speed the response.

Applications for laser therapy include:

- Treatment of arthritis, degenerative joint disease or hip dysplasia, alone or in combination with stem cell therapy
- General pain management (sprains, strains, and stiffness)
- Post-surgery pain (spays, neuters, and other surgeries)
- Skin problems (hot spots, lick granulomas, infections)
- Dental procedures
- Fractures and wounds (bites, abrasions, and lesions)
- Ear infections

How does it work?

Laser therapy stimulates the body to heal from within. Non-thermal photons of light are administered to the body for about three to eight minutes and absorbed by the injured cells. The cells are then stimulated and respond with a higher rate of metabolism. This results in relief from pain, increased circulation, reduced inflammation and an acceleration of the healing process.

What can my pet expect during a laser therapy treatment session?

Simply put, it provides relief. As the laser is administered, your pet should relax and enjoy the treatment. The almost immediate relief of pain will allow your pet to be comfortable and any anxiety that your pet initially experiences will dissipate.

Occasionally, angry cats will start to purr and canine companions will actually fall asleep during their therapy session. Frequently, after therapy, we hear: *"He's acting like a puppy again"* or *"She can actually jump onto the chair again."* Pain relief is provided in just a few minutes of therapy and that alone improves the quality of life for your companion.

What are the signs that my pet can benefit from companion laser therapy?

Many of our laser therapy patients are older animals with musculoskeletal ailments. Some signs that your senior companion is experiencing pain or discomfort are:

- Abnormal sitting or lying posture
- Circling multiple times before lying down
- Restlessness
- Whining, groaning or other vocalisations
- Limping, unable to get up or lie down
- Difficulty getting into car or down stairs
- Lack of grooming
- Won't wag tail
- Licking or biting area
- Lack of appetite
- Trembling

Therapy lasers have been scientifically proven and successful in treating post-surgical pain and many acute and chronic conditions such as:

Acute conditions

- Wounds
- Allergies
- Infections
- Cuts/bites
- Inflammations
- Tooth extraction pain relief
- Sprains, strains and fractures
- Post-surgical healing/pain relief

Chronic conditions

- Degenerative joint disease
- Inflammatory bowel disease
- Periodontal disease
- Lick granulomas
- Geriatric care
- Hip dysplasia
- Feline acne
- Tendonitis
- Arthritis

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Contact us

Contact our practice today to schedule an appointment or obtain additional information.

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To arrange a referral appointment, please get your veterinary surgeon to complete a referral form, which can be downloaded from our website and send it to us by email along with relevant clinical records and radiographs.