



Clinical Research Project Client Consent Form

Study Title: Investigation of the immunostimulatory response of high intensity focused ultrasound on naturally-occurring solid tumors.

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One of the missions of the Virginia-Maryland Regional College of Veterinary Medicine is to create, disseminate and apply medical knowledge through discovery, learning, and engagement. You are invited to participate in this mission by enrolling your animal in a clinical research study. Your participation is entirely voluntary, and you may withdraw your animal from the study at any time by notifying the Principal Investigator. There is no penalty if you choose not to participate.

Study Purpose:

Solid tumors (including soft tissue sarcomas, carcinomas and mast cell tumors) are a common form of cancer in dogs. They can invade tissues that are vital to normal function and surgical removal can be impossible without amputation or radiation therapy. In some cases, a tumor may be surgically resectable, but it could still recur at the surgical site or in a distant site like lymph node or lung.

One attractive option for such cases is immunotherapy. We propose using high-intensity focused ultrasound (HIFU) to kill tumor cells and release antigens from tumors, stimulating the patient's anti-tumor immune response. We hope to find out if HIFU application will result in both tumor cell death and immunologic activation in dogs. To determine if the treatment is effective, we are recruiting dogs with solid tumors who will undergo HIFU treatment prior to surgical removal of the tumor.

The application of this experimental therapy has the potential to directly enhance the quality of life of dogs diagnosed with the disease and defray the cost of treatment. At the same time, the results of our efforts may lead to improved treatment options for human cancer patients.

Study Design/Procedures:

If you agree to participate in this study we will perform the following procedures:

Pretreatment evaluation

Before beginning treatment your dog will undergo the following:

- 1. Complete physical exam**
- 2. Lab work:** We will obtain blood samples from your pet, if no recent bloodwork is not available, for a complete blood count and chemistry profile. Six mls (about 1 teaspoon) of blood will be collected from a vein in your pet's neck, which is the easiest access point. We will also collect 5 mls of urine via free catch. These are the standard methods for obtaining blood at the Veterinary teaching Hospital. This will be performed before your pet's treatment.
- 3. Fine needle aspirate of the tumor:** A tumor fine needle aspirate and cytology will be obtained for diagnostic purposes.

Treatment

The treatment will require a CT scan and two (2) surgical procedures. If your dog meets the study criteria (a neoplastic tumor or scar that is amenable to surgery and expected survival over 4 weeks without treatment), your dog will be scheduled for a CT scan and a surgical biopsy under general anesthesia. This includes removing a small sample of the tumor to determine its specific type. Subsequently, your dog will be scheduled for the HIFU treatment.

HIFU treatment will be performed on Day 0 (Monday). HIFU will be applied to the tumor under general anesthesia. During the procedure, blood samples (6 mls). Your dog will be recovered from the procedure and hospitalized in ICU under 24 hour monitoring, until Friday of the same week. Blood samples will be collected daily (6 mls) to assess your pet's immune response and definitive surgery to remove the tumor will take place on Friday. Your dog will recover in ICU and will be discharged as is standard for patients.

For the HIFU treatment, hair will be clipped over the tumor as is standard for any ultrasound in dogs. The actual treatment will be tailored to the individual tumor of each dog, and be delivered under general anesthesia in a series of bursts of sound will be focused on the tumor to raise its temperature (approximately 56 degrees celsius or 132 degrees Fahrenheit) with the goal of killing the cells deep in the tumor through unbroken skin surface. The HIFU treatment is expected to take 30 minutes to an hour.

Tumor and biologic material sampling

Your dog is going to be hospitalized for 4 nights and the following samples will be obtained:

1. **Biopsy of the tumor:** A tumor biopsy will be obtained under general anesthesia, at the time of the CT scan, for research purposes. Similarly, once removed, the tumor will be analyzed for research purposes.
2. **Lab work:** We will obtain blood samples from your pet for a complete blood count, flow cytometry and blood cytokine levels. Six mls (about 1 teaspoon) of blood will be collected from a vein in your pet's neck once per day for the four days of hospitalization for research purposes. The neck is the easiest access point in dogs.

Follow-up

Your pet will need to return to the Veterinary Teaching Hospital at 2 weeks after the definitive surgery, as part of the follow up after tumor resection for recheck and suture removal. At the recheck visit, your pet will have a physical exam, and additional diagnostics if indicated. We ask that you keep the clinical oncology service and investigators informed on the status of your pet's health.

Risks and Benefits:

We are trying to develop a new, more effective and safe therapy against cancer. In addition, the study will cover completely the cost of the CTs, biopsies, bloodwork, the cost of the HIFU treatment, the cost of the hospital stay, the cost of definitive surgery, and the cost the recheck visit.

Some of the procedures performed in this study are routine clinical procedures. **The HIFU therapy is experimental and not part of the standard treatment.** Side effects that may be seen in your pet during this study may include but are not limited to fever, tumor inflammation, tumor-site discomfort, systemic inflammation, risk for severe infection, and death.

Although unexpected, there could be problems with the diagnostic procedures (lab-work, staging, biopsy). These problems can be due to inflammation or infection and may result in bruising at the collection site. Additionally, all animals going under general anesthesia are in risk of adverse effects that may result even in death. We will try to minimize all these risks by taking extensive steps to prevent contamination of the biopsy site, and monitor continuously the vital functions of your pet when under general anesthesia and during the recovery period.

Study Costs and Compensation:

Once the pretreatment evaluation is performed at your cost, informed consent will be obtained and the study will cover the expenses for the subsequent lab-work, CTs, tumor biopsy and histopathology, the HIFU treatment, the cost of the hospital stay and associated costs, the cost of surgery and the cost of the scheduled recheck visit.

We have secured funding to cover all of the expenses for the aforementioned procedures. The typical average cost of surgical resection of a tumor in our hospital is **about \$3,000 to \$5,000**. You are responsible for any other clinical fees associated with medical complications of the HIFU therapy or other medical problems.

Confidentiality:

The data collected in the course of this study is confidential. In any publication or presentation of the study data, we will not include information that would make it possible to identify a research participant. Research records will be kept in a locked file; only researchers will have access to the records.

In giving my consent by signing this form, I acknowledge that I have been informed of the purpose and nature of this study and its associated procedures, as well as any possible side effects.

Statement of Consent:

I have read and understood the above information. I have been given the opportunity to ask questions and receive answers, and I consent to participate in the study. I further certify that I am the owner (or duly authorized agent of the owner) of _____ .

Owner or Agent Signature: _____ Date: _____

Attending Clinician Signature: _____ Date: _____

Please don't hesitate to contact us if you have any questions or concerns about this study.

The research and procedures have been reviewed and approved by the Virginia Tech Institutional Animal Care and Use Committee and the Virginia-Maryland Regional College of Veterinary Medicine Veterinary Teaching Hospital Board.

If you have any questions or concerns regarding the study and would like to talk to someone other than the researchers, please contact:

You will be given a copy of this form to keep for your records.