Detect and monitor vascularity, vascular leak, and changes in permeability in cancer and inflammatory states.

Do you need the ability to detect indicators of anti-angiogenic drug efficacy sooner?

Anti-angiogenic agents have emerged as viable anti-cancer therapies, either alone or in combination with standard chemotherapy. In preclinical cancer research models, assessing tumor size by caliper measurements is still the most commonly used noninvasive metric of drug efficacy. Though relatively simple and immediate, this method becomes less useful when assessing the effects of anti-angiogenic agents, because tumor volume measurement is a late indicator of efficacy. Early indicators, such as a decrease in tumor vascularity or an increase in tumor vascular permeability, can occur and be detectable days before a change in tumor size becomes evident. Using more invasive approaches, such as histology, will typically yield a deeper understanding of the underlying biology and the early changes associated. However, it can also cause delays due to processing needs, or it can miss critical time points, potentially underestimating the effects of the treatment and curtailing a drug candidate. The ability to noninvasively detect treatment efficacy sooner by measuring early indicators, prior to overt changes in tumor size, can speed up decision time, reduce costs, and provide more conclusive results.

What is angiogenesis?

Angiogenesis describes the formation of new blood vessels from pre-existing vessels. It is the process by which blood capillaries grow to supply nutrients and metabolites to metabolically active tissue. In both healthy and diseased tissues, the occurrence of angiogenesis is not static, but is known to change in response to metabolic demand, increasing or decreasing in proportion to changes in metabolic activity.

The ability to control angiogenesis and normalize abnormal vasculature, by stimulating new capillary growth or by destroying vasculature and/or inhibiting neovascularization, can be beneficial in a variety of different cancers as well as inflammatory states, such as:

Stimulate angiogenesis

- Ischemic heart disease
- Peripheral arterial disease
- Wound healing

Decrease/Inhibit angiogenesis:

- Rheumatoid arthritis
- Diabetic retinopathy
- Tumor growth

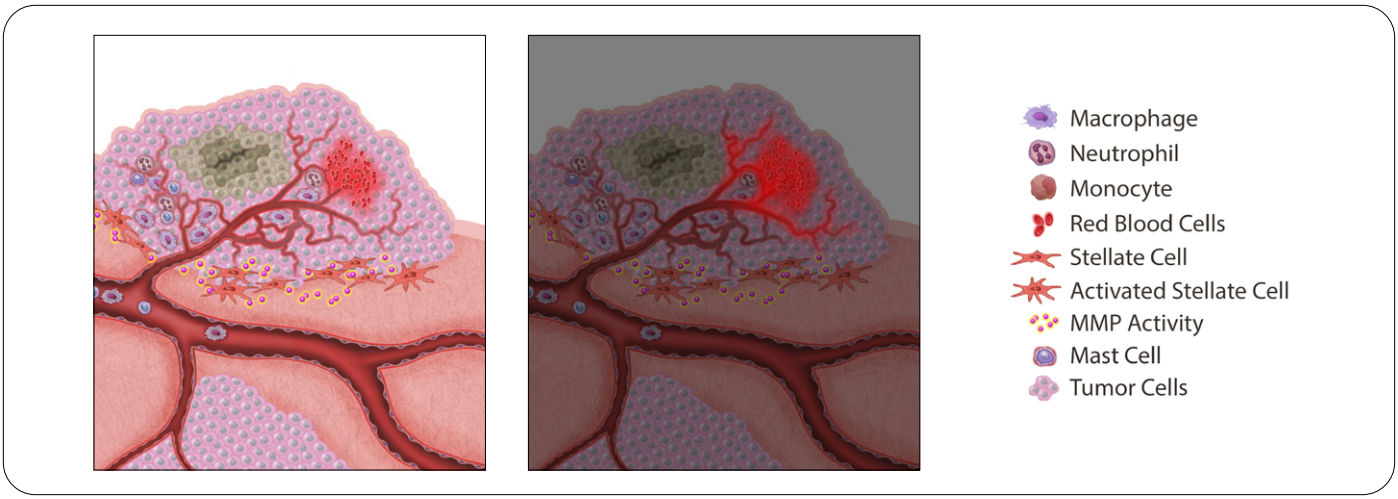

Figure 1. Deregulated angiogenesis is a key pathological event in cancer, providing nutrients and oxygen to assist tumor growth. IVISense Vascular probe fluorescent imaging of neo-vasculature is represented in the figure on the right.

What is IVISense™ Vascular fluorescent probe?

IVISense Vascular probes are fluorescent NIR *in vivo* blood pool imaging agents. At early timepoints, IVISense Vascular probes remain in the blood and can provide a measure of vascular burden. At later timepoints, IVISense Vascular probe accumulates in areas of vascular leak due to either inflammatory edema or to leaky neo-vasculature. As many inflammatory diseases such as arthritis are marked by alterations in blood flow or oxygenation at the tissue or cellular level, IVISense Vascular probe can provide a means to non-invasively quantify relevant physiological processes, including blood flow and perfusion, as well as detect early changes in vascular permeability and tumor leakiness as indicators of tumor vasculature.

How are IVISense Vascular probes used?

Here we show two case studies demonstrating possible applications of IVISense Vascular fluorescent probes

Case study 1 Oncology

Monitoring tumor development in a mammary fat pad model using implanted 4T1 tumor cells

Tumors were established by injecting 4T1 mouse mammary carcinoma cells into the flanks of mice. The tumors were allowed to grow for two weeks prior to administration of either a VGFR-2 blocker or vehicle control. 24 hours after the VGFR-2 blocker was administered, mice were injected with IVISense Vascular probe and imaged. The fluorescent imaging results indicate that a reduction in vascular disruption was measurable, thereby indicating a diminished neo-vascularization process that would otherwise typically occur in and around tumors. In this example, the use of optical imaging allowed the subtle changes in neovascularization to be observed days before standard caliper tumor measurements. The early molecular events captured by optical imaging provide new insights into molecular mechanism and early events in tumor development, treatment, and compound efficacy.

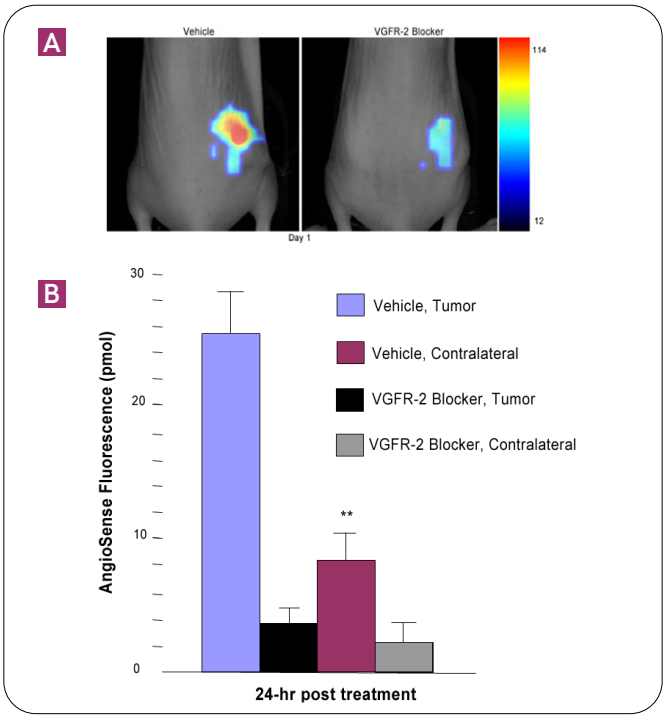

Figure 2. (A). Control untreated and VGFR-2 blocker treated mammary fat pad tumors were visualized using IVISense Vascular fluorescent probe at 24-hours after control or blocker treatment. (B). Quantification of image data showing significantly reduced VEFG-2 presence in mice treated with a blocker. (Imaged using FMT® 2500).

Case study 2 | Oncology

Monitoring arthritis progression and treatment using IVISense Vascular fluorescent probe

In models of arthritis, including immunization with collagen or systemic injection of anti-collagen antibodies, an anti-collagen immune response leads to inflammation and edema, as well as tissue and bone destruction in the joint. These are routinely monitored by measuring changes in paw swelling. Currently, the efficacy of potential anti-inflammatory and anti-arthritic therapies are most often tracked by measuring changes in paw swelling, subjective clinical scoring, and histopathology. In addition to these standard measurements, IVISense Vascular probes can be used to non-invasively detect and monitor early subtle changes in underlying edema that are part of the inflammatory processes.

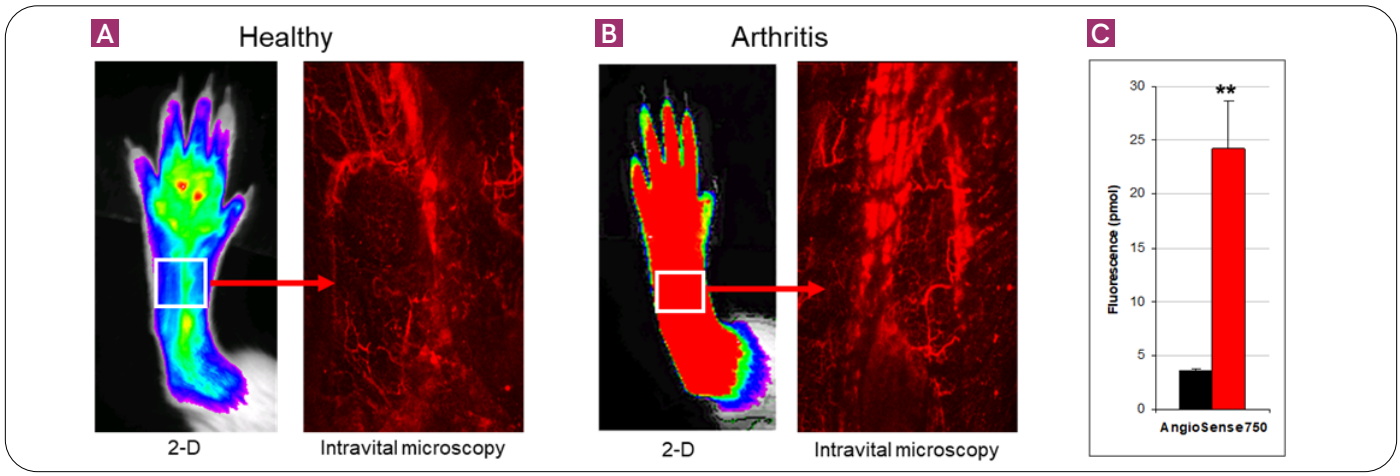

Figure 3. Following induction of arthritis in a collagen antibody induced arthritis model (CAIA), IVISense Vascular probe was administered. The figures above show probe accumulation in (A) healthy paw from a non-arthritic mouse and (B) paw from a collagen Ab injected mouse with developing arthritis. Figure (C) shows that IVISense Vascular probe accumulation is significantly higher in the collagen antibody treated mouse as compared with a control healthy paw. (Imaged using FMT 2500).

Use IVISense Vascular probes as part of a complete experimental solution package

Revvity provides complete *in vivo* imaging solutions including reagents, instrumentation and support expertise that can help you monitor and design experiments to understand the progression of diseases and their related processes, or to evaluate the potential therapeutic efficacy of drugs targeting the underlying mechanisms involved in disease.

IVISense Vascular NIR fluorescent probes are available in two wavelengths; 680 and 750, and are designed to evaluate vascular changes to better understand various disease states or provide valuable information on effects of drug candidates earlier in the development process.

Cat #	Product	
NEV10054EX	IVISense Vascular 680	Imaging of vascularity, perfusion, and vascular permeability. IVISense Vascular 750 (NEV10011EX)
NEV10011EX	IVISense Vascular 750	remains localized in vasculature for 0-4 hrs; accumulates in tumors and arthritic joints at 24 hr.

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