

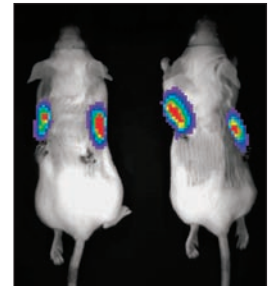
OVERVIEW SHEET

Applications in Biofilm Research

Caliper has developed a rapid, continuous method for in vivo real-time monitoring of biofilms, through non-invasive imaging of bioluminescent bacteria. Luciferase-engineered strains developed by Caliper Life Sciences constitutively produce light without the need for stimulation or excitation, making viable cells easily detectable.

The Features:

- **Improved data statistics:** The non-invasive procedure provides the ability to image the same animals over time, improving statistical analysis by providing an internal control.
- **More predictive data:** Improves data collection for in vivo animal models by sensitive real-time screening of medical device materials and/or drug compounds.
- **Quantitative monitoring of biofilms:** In vivo without the need for exogenous sampling and culturing.
- **Rapid and user friendly results:** Data collection is frequently accomplished in seconds to minutes. This can accelerate drug development at the animal model step.
- **Infections:** Could be studied with clinically relevant doses as low as 10^3 CFU/device.
- **Biofilm development and response to therapy:** With the ability to follow disease progression for weeks within the same animal.
- **Efficacy:** Allows examining efficacy or relapse and resistance development to therapeutic agents.



P. aeruginosa Xen 5 colonized on catheters, imaged on Day 20

In Vivo Models

Currently Available: Subcutaneous Catheter Model

An in vivo mouse model of device-related biofilm infection is established by subcutaneous implantation of either pre- or in vivo-colonized catheters with bioluminescent, biofilm-forming pathogens. Caliper's optical imaging technology and biofilm-forming pathogens engineered to express light offer a method for studying chronic biofilm infection, pathogen burden and metabolic activity of biofilms, non-destructively, and directly on a support matrix. The model is useful for the study of pathogenesis and in vivo efficacy of therapeutic agents against both Gram-positive and Gram-negative bacterial pathogens in real-time. The imaging procedure can be repeatedly performed, thereby reducing the overall number of animals used, allowing each animal to act as its own control over time, overcoming the problem of animal-to-animal variations. The methodology is especially appealing for the analysis of efficacy of anti-microbial agents in vivo, as the effectiveness of the compound can be rapidly monitored without the need for exogenous sampling and culturing.

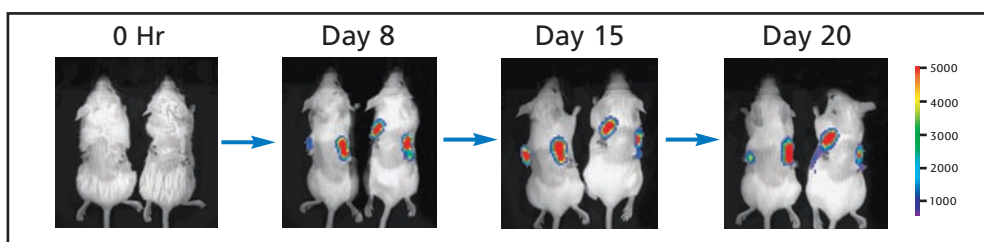
Rat Endocarditis Model

This is a bioluminescent adaptation of an established model, in which luminescent pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* are used to infect rats with implanted cardiac catheters. Caliper's technology can quantitatively monitor biofilm formation by these bioluminescent bacteria by repeated non-invasive imaging of the original animals throughout the disease course.

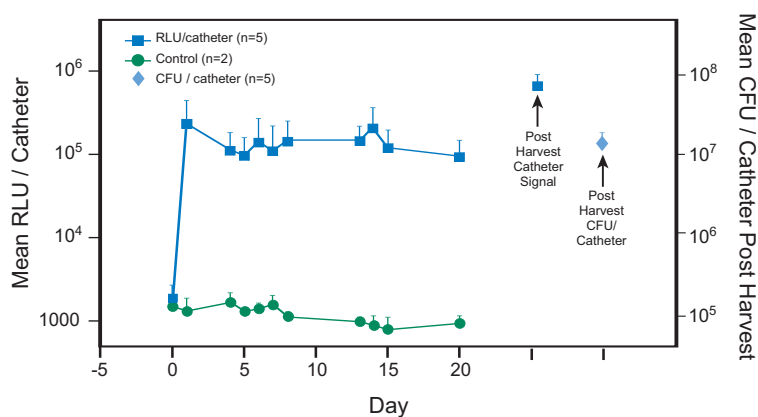
In Vitro Models

Currently Available: Biofilm Formation on Catheter Surfaces

Caliper's optical imaging technology and bioluminescent bacterial pathogens offers an efficient in vitro monitoring method to rapidly and effectively assess biofilm formation, prevention of colonization or efficacy of therapeutic agents on biofilm bacteria. The method provides information regarding physiological activities of bacteria within biofilm in real-time, thus allowing for optimizing of biofilm research.



Biofilm formed on catheters colonized by bioluminescent *S. aureus* Xen 29 can be quantified in vivo with Caliper's IVIS Imaging System.



Note: Bioware® microorganisms and derivatives thereof may only be used as a research reagent and not for any diagnostic, therapeutic, or commercial application. In vivo imaging in mammals is covered by one or more U.S. and foreign patents controlled by Caliper, including the following: U.S. patent numbers 6,217,847 and 5,650,135 and European Union patent number 0861093. A license from Caliper Life Sciences is required to practice under these patents.



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