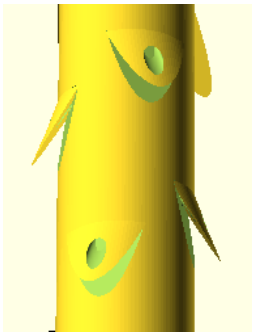
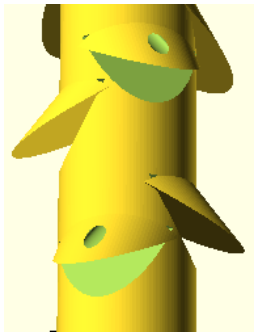
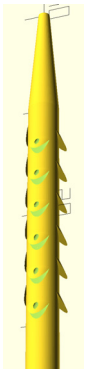
# Supplemental materials

Pedersoli F, et al, "Bioinspired intratumoral infusion port catheter improves local drug delivery in the liver"

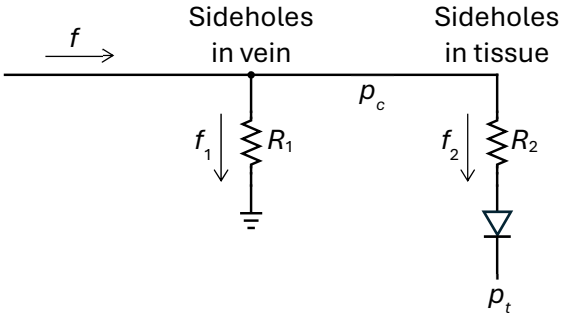
## Parametric catheter model

Variations of the barbed sidehole catheter are automatically generated by modifying the parameters:

| | | | | |
|---|---|---|---|---|
| Sidehole diameter | 0.1 mm | 0.2 mm | **0.4 mm** | 0.6 mm |
| |  |  |  |  |
| Sidehole position | tip | **middle** | base | off barb |
| |  |  |  |  |
| Sidehole / barb angle | 35° | **40°** | 45° | 50° |
| |  |  |  |  |
| Barb spiral angle | **100°** | 120° | 130° | 150° |
| |  |  |  |  |

## Physical model of intratumoral infusion

Drug is infused into a multi-sidehole catheter in a tumor. Some of the sideholes are in low resistance blood vessels, and some sideholes are embedded in tumor tissue. Drug flow into tumor can be modeled as a simple circuit with 2 resistors and a diode:




| | |
|---|---|
| $f$ | flow rate (ml/min) |
| $r$ | resistance of all sideholes (mmHg · min/ml) |
| $t$ | fraction of sideholes in tumor tissue |
| $p_t$ | tissue pressure (mm Hg) |
| $p_c$ | catheter pressure (mm Hg) |

Then:

$R_1 = r/(1-t)$

$R_2 = r/t$

$f = f_1 + f_2$

$f_1 = p_c/R_1$

$$f_2 = \begin{cases} 0 & \text{if } p_c < p_t \\ (p_c - p_t)/R_2 & \text{otherwise} \end{cases}$$

Solving this system of equations,

$$p_c = \begin{cases} fr + p_t t & \text{if } fr > p_t(1-t) \\ fr/(1-t) & \text{otherwise} \end{cases}$$

Then, the fraction of drug infused into tumor is:

$$f_2/f = \begin{cases} t - p_t(t - t^2)/(fr) & \text{if } fr > p_t(1-t) \\ 0 & \text{otherwise} \end{cases}$$

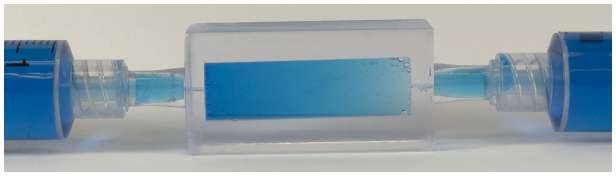
Higher sidehole resistance (smaller sideholes) and higher flow rate (pulsatile flow) results in higher pressure in the catheter, which overcomes the tissue pressure, resulting in more drug delivery into tumor. In the best case scenario, high pressure in the catheter results in uniform flow through each sidehole. In the worst case scenario, low pressure in the catheter (less than tissue pressure) results in zero drug delivery into tumor tissue, and all drug flows into intratumoral veins instead. This equation accurately predicts local drug retention in both gel and in pig liver (Figure 5).

## Quantitative photography

To quantify methylene blue concentration in photographs, injected gels were photographed in a light box with standard lighting. Raw image files were converted to bitmaps with 16 bits per color channel. Pixel values ($r$,$g$,$b$) were converted to methylene blue concentrations using the formula:

$$\text{Methylene blue concentration} = \begin{cases} 0 & \text{if } b = 0, \text{ or } r > b \\ (1 - r/b)^{\gamma} & \text{otherwise} \end{cases}$$

Methylene blue absorbs light mostly in the red channel, and the blue channel is used to normalize for local light levels. To determine the gamma correction exponent (γ), we photographed a linear gradient of known methylene blue concentrations. Using OpenSCAD, we attached two luer connectors to a linear gradient ranging from 1 to 10 mm of thickness, and 3D printed this in clear plastic, using stereolithography (Xometry). The 3D printed gradient was filled with a known concentration of methylene blue:



This linear gradient allowed us to generate a calibration curve, and pick γ to match the known concentrations:

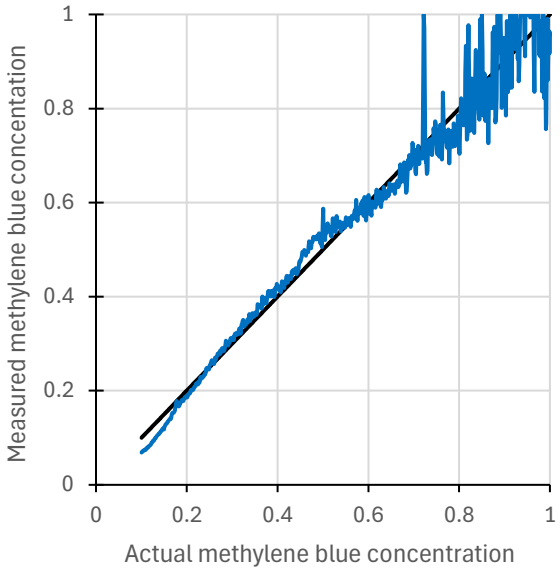



Image processing was performed using Photoshop and Mathematica.