A microfluidic reciprocating intracochlear drug delivery system with reservoir and active dose control

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Electronic Supplemental Information

Planar polyimide fluidics fabrication

The planar fluidics -- the reciprocating flow pump, T-junction, and drug reservoir-- were fabricated from machined and laminated polyimide sheets. We have described the fabrication method in detail elsewhere[44]. Briefly, the polyimide films, of thickness 25–125 μm (Kapton, Dupont, Wilmington DE), were machined using a milling machine (Quickcircuit 7000, T-Tech, Norcross GA). Layers were laminated together with thermoset adhesive film (R/flex 1000, Rogers Corp., Rogers CT) at controlled temperature and high pressure.

Reciprocating flow pump fluidics

To provide a stable mounting surface for the reciprocating flow pump, the polyimide fluidic assembly (25.4 × 12.7 × 0.9 mm) was laminated to an aluminum baseplate. The diaphragm consisted of 25.4 μm thick polyimide film. The dimensions of the displacement chamber (6.5 mm in diameter × 483 μm deep) were dictated by the model. The fluidic channel (cross-sectional dimensions 500 × 483 μm) extended 13 mm from the displacement chamber, then split into 2 short segments leading to the drug loading port and the infuse-withdraw port, 2.7 mm and 1.5 mm long respectively. At each port, the fluidic path passed through a normally open valve structure, which was not used in these experiments, then exited the device at a machined socket. A short segment of 28-gage stainless steel hypodermic tubing was inserted into a each socket then bonded to the laminated polyimide assembly with epoxy (Epoxy 907, Miller-Stephenson, Danbury CT), to provide a convenient fitting for tubing connections.

Reciprocating flow pump actuator

The solenoid actuator (Ø11 × 13 mm, Bicron, Canaan CT) was mounted to the aluminum baseplate of the polyimide reciprocating pump fluidic assembly. The actuator has a DC resistance of 31.8 Ω at room temperature. The actuator shaft was fitted with a custom machined acetal head, 3.5 mm in diameter, with a spherical profile to conform to the shape of the deflected diaphragm. The actuator was powered either by a power supply (Model E3631A, Agilent, Santa Clara CA) controlled by a computer running Labview (National Instruments, Austin TX), or by custom electronics in the packaged animal-mountable system described in "System control and packaging."

Cannula and T-junction

In the complete controllable dose system, the reciprocating pump was connected to the drug reservoir and cannula through a T-junction (see **Error! Reference source not found.**b). The T-junction was fabricated from laminated machined polyimide. Its design minimized internal fluid volume (175nL) and facilitated the placement and securing of the cannula during implantation in

the animal. Sockets, sized for the insertion of 360 µm OD polyetheretherketone (PEEK) tubing (IDEX Health & Science, Oak Harbor WA), were machined at each port of the T-junction. The PEEK-polyimide joints were sealed with epoxy. One branch of the T-junction connected to the proximal segment of the cannula with a 2.8 cm length of PEEK tubing with an inner diameter of 75 µm. This length was found to be the minimum required for deft handling during insertion of the cannula into the cochlea. The internal volume of the fluid path between the T-junction and the cannula outlet determines the amount of residual drug that is infused in each cycle; hence, the small inner diameter of the PEEK tubing was chosen to minimize this volume. The other branches of the T-junction connected to the infuse-withdraw port of the reciprocating pump with 8cm of PEEK tubing with an inner diameter of 150 µm, and to the drug reservoir with 16 cm of PEEK tubing with an inner diameter of 100 µm. These tubing lengths were selected to facilitate surgical handling and skull mounting. The lengths and inner diameter dimensions were also used to tune the relative resistances in the fluid network so that the fluid preferentially flows through the infuse-withdraw line and the cannula during the infuse-withdraw stage, and not through the reservoir loop. The use of designed passive resistances here enabled operation of the system without the need for active valves.

The cannula was designed to be inserted into the cochlea through a drilled cochleostomy (175 µm in diameter). The implanted portion of the cannula was made from a 12 mm length of polytetrafluoroethylene tubing (PTFE Sub Lite tubing, 101 µm ID × 201 µm OD, Zeus Inc., Branchburg NJ) that had been treated with fluorinated etchant (FluoroEtch, Acton Technologies, Pittston PA) to promote adhesion to epoxy. The PTFE tubing was connected to the aforementioned 2.8 cm length of PEEK tubing with a sleeve made of a short length of medical grade PVC tubing (Tygon S-54-HL PVC tubing, 0.25 mm ID × 0.76 mm OD, Saint-Gobain, Île-de-France, France), and the joints were sealed with epoxy.

Fluid connections

To assemble the various components into networks, PEEK-to-PEEK and PEEK-to-stainless steel tubing connections were made using short lengths of Tygon R-3603 tubing (4-8 mm in length, 0.25 mm ID × 2.07 mm OD) as sleeves. These sleeves were also used as temporary shutoff valves for testing by pinching the tubing closed with small clamps. The inlet of the drug loading pump was connected to the drug reservoir and the outlet to the reciprocating pump with 17.5 mm and 15 mm lengths of the Tygon R-3603 tubing, respectively. As an added measure avoid entraining air, critical seals at tubing connections (those which experienced pressure transients below ambient) were further sealed with epoxy (Epoxy 907, Miller-Stephenson, Danbury CT) to fill any possible gaps between the Tygon and the PEEK or stainless steel tubing. The need for this precaution was not tested rigorously. After filling the network with a syringe, the fill port was either sealed off with a clamp, or closed with a cap made from a sealed length of the Tygon R-3603 tubing.