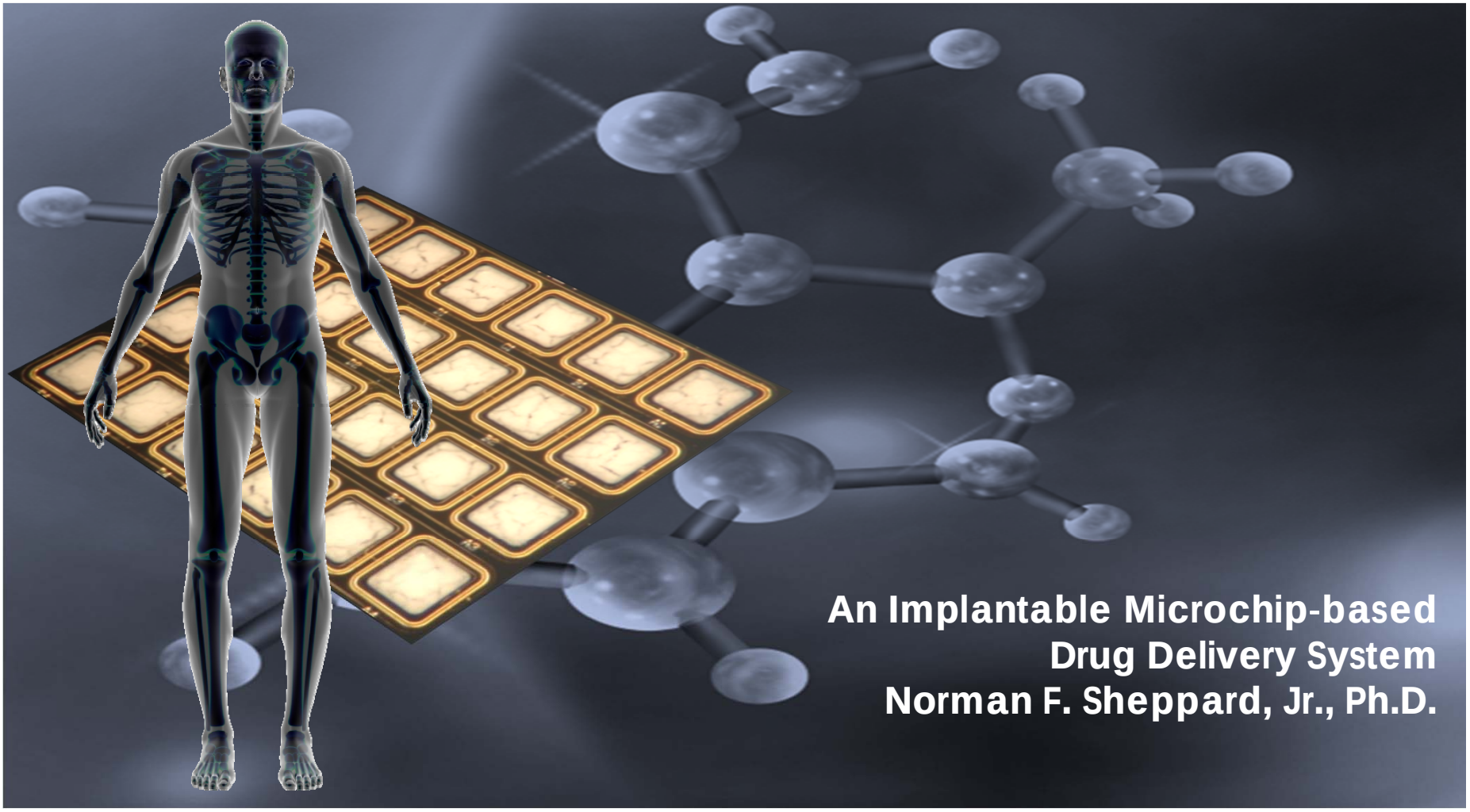
MICROCHIPS™ ELECTRONIC DRUG DELIVERY

Enabling Remote Medicine & the Networked Patient



An Implantable Microchip-based Drug Delivery System

- **Microchip Drug Delivery**
  - Microreservoir Technology
  - Drug Formulation and Filling
  - Low-temperature Hermetic Sealing
- **Implantable Device Design**
- **First Human Testing**

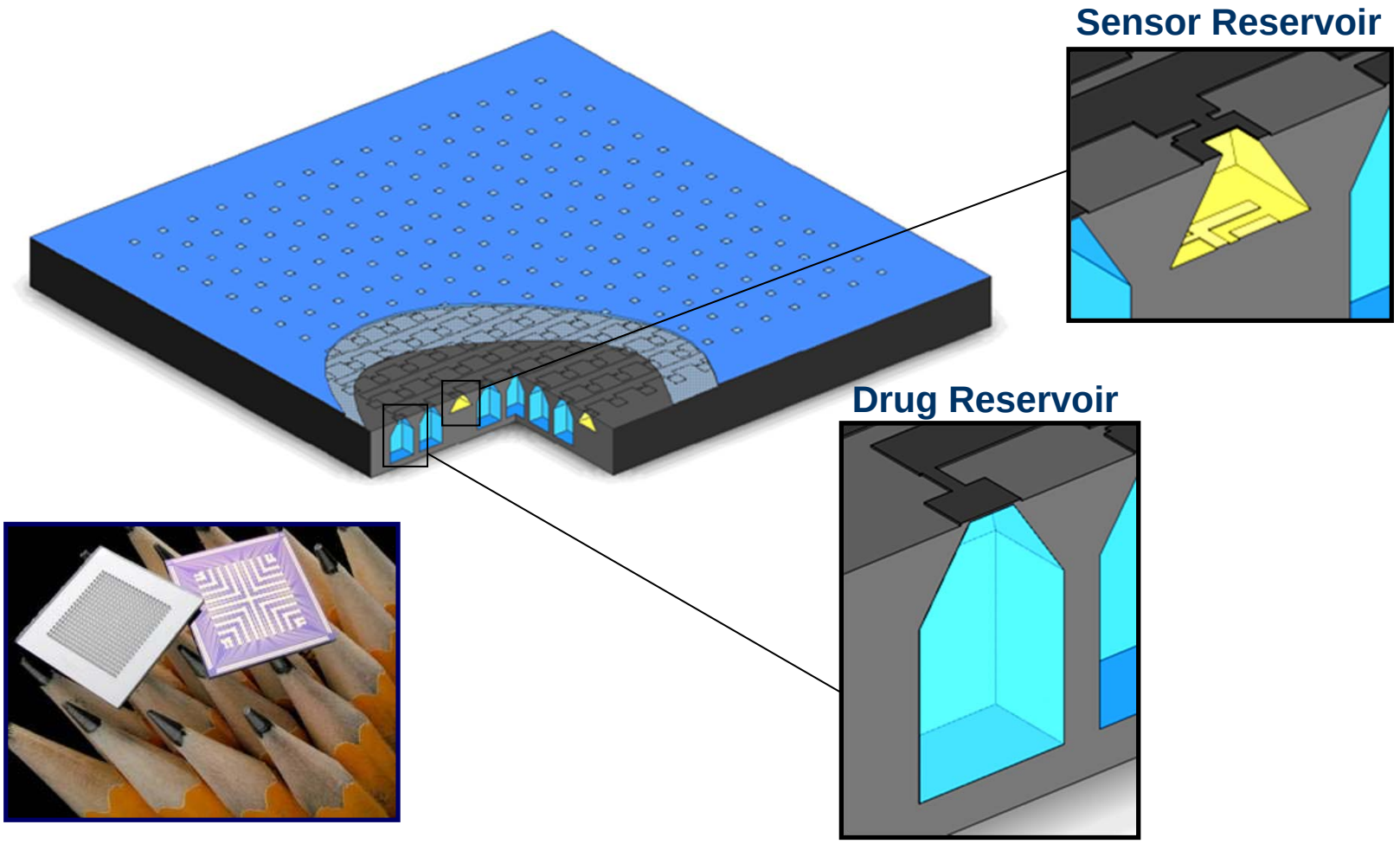
Company

MicroCHIPS, located in Boston, develops implantable drug delivery and biosensing products.

- Formed to commercialize microreservoir array IP developed at MIT (Langer & Cima labs)
  - Long term protection of drugs
  - Release of drug triggered by an electronic signal
- Extensive IP portfolio
  - Improvements to MIT technology
  - Low-temperature hermetic sealing

Microreservoirs for Drug Delivery and/or Biosensing

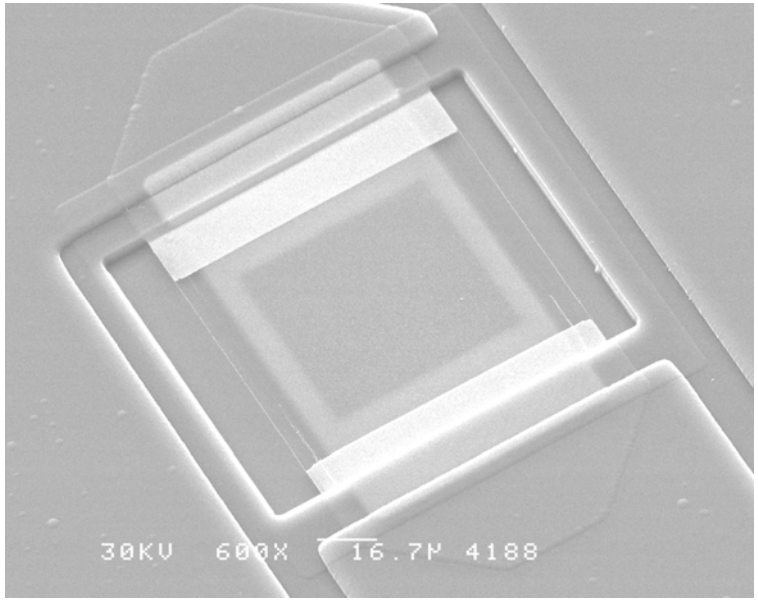
- MEMS technology used to create reservoirs in silicon substrate



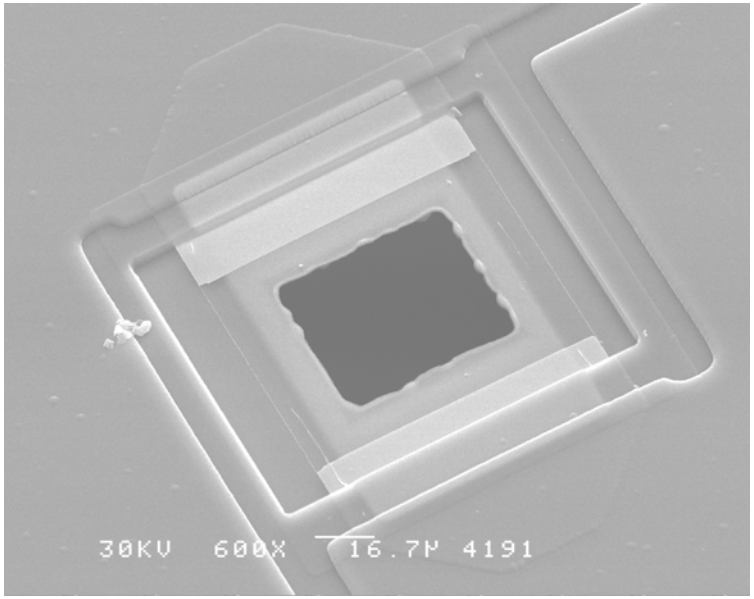
Microreservoirs Opened Electronically

- Aperture in the silicon connects reservoir to “outside world”
- Aperture sealed with submicron metal film
- Current pulse removes film & exposes reservoir contents

Before Activation

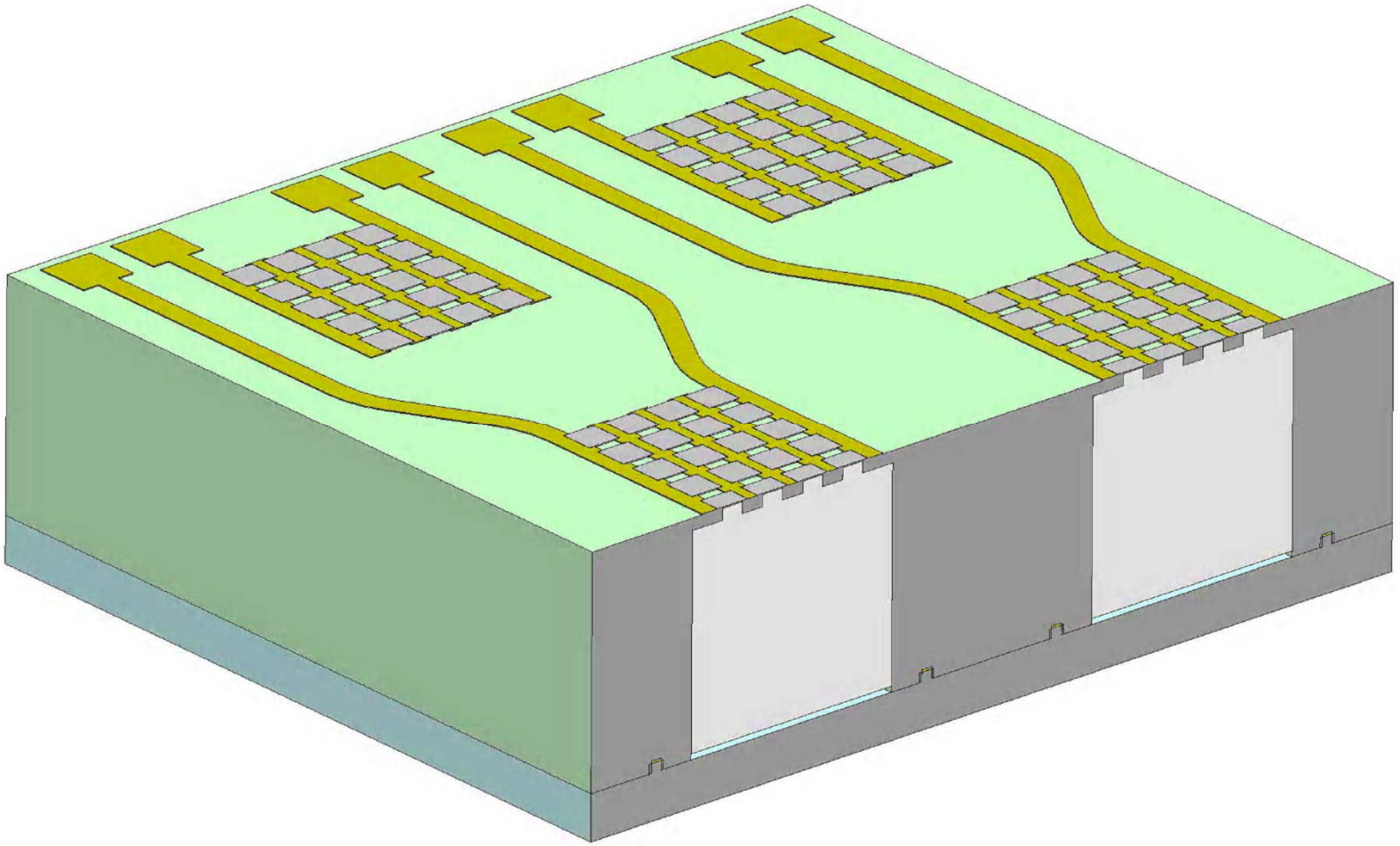


After Activation



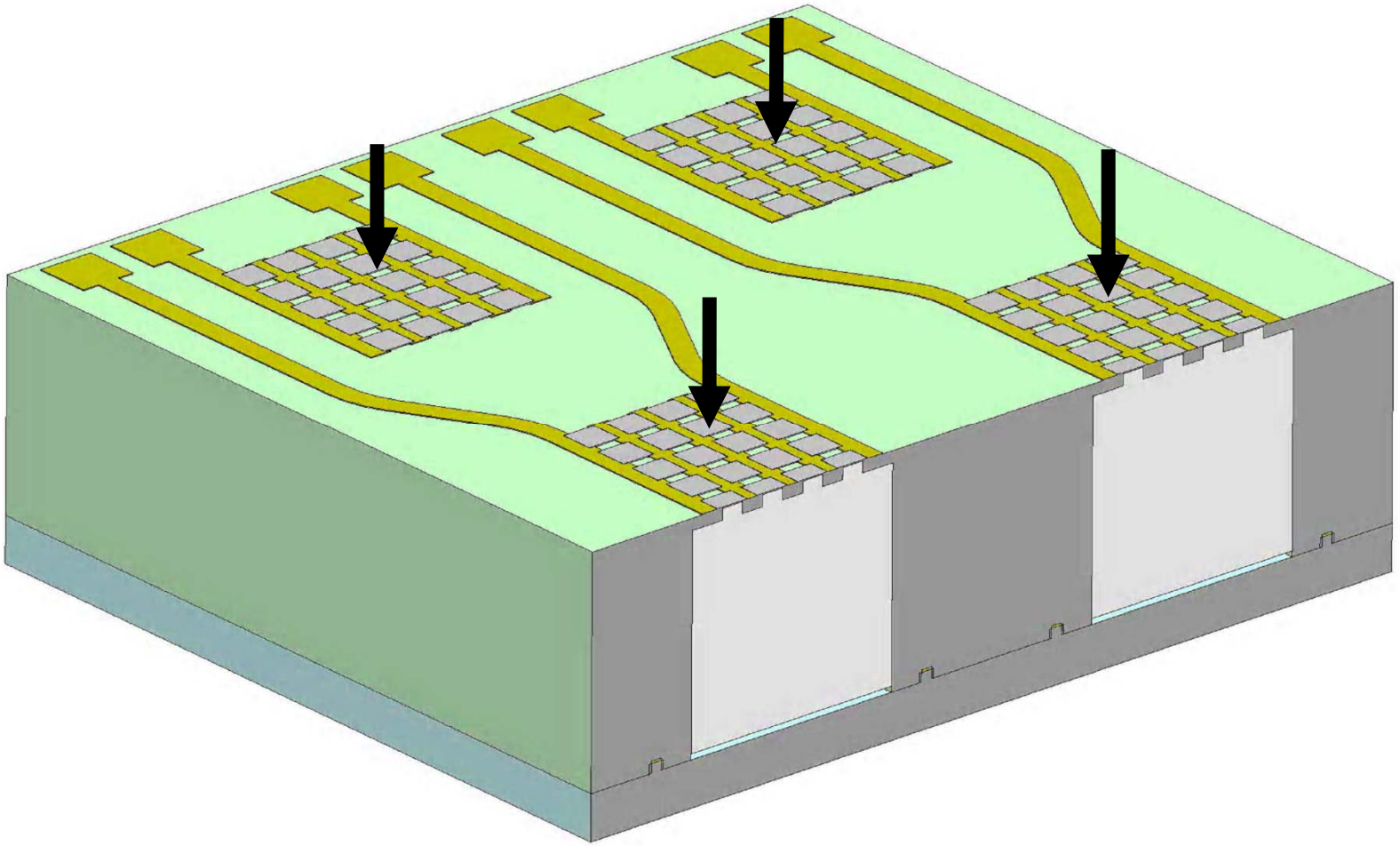
Microchip Drug Delivery

Drugs stored in microreservoirs can be delivered on a predefined schedule, on condition, or on demand.



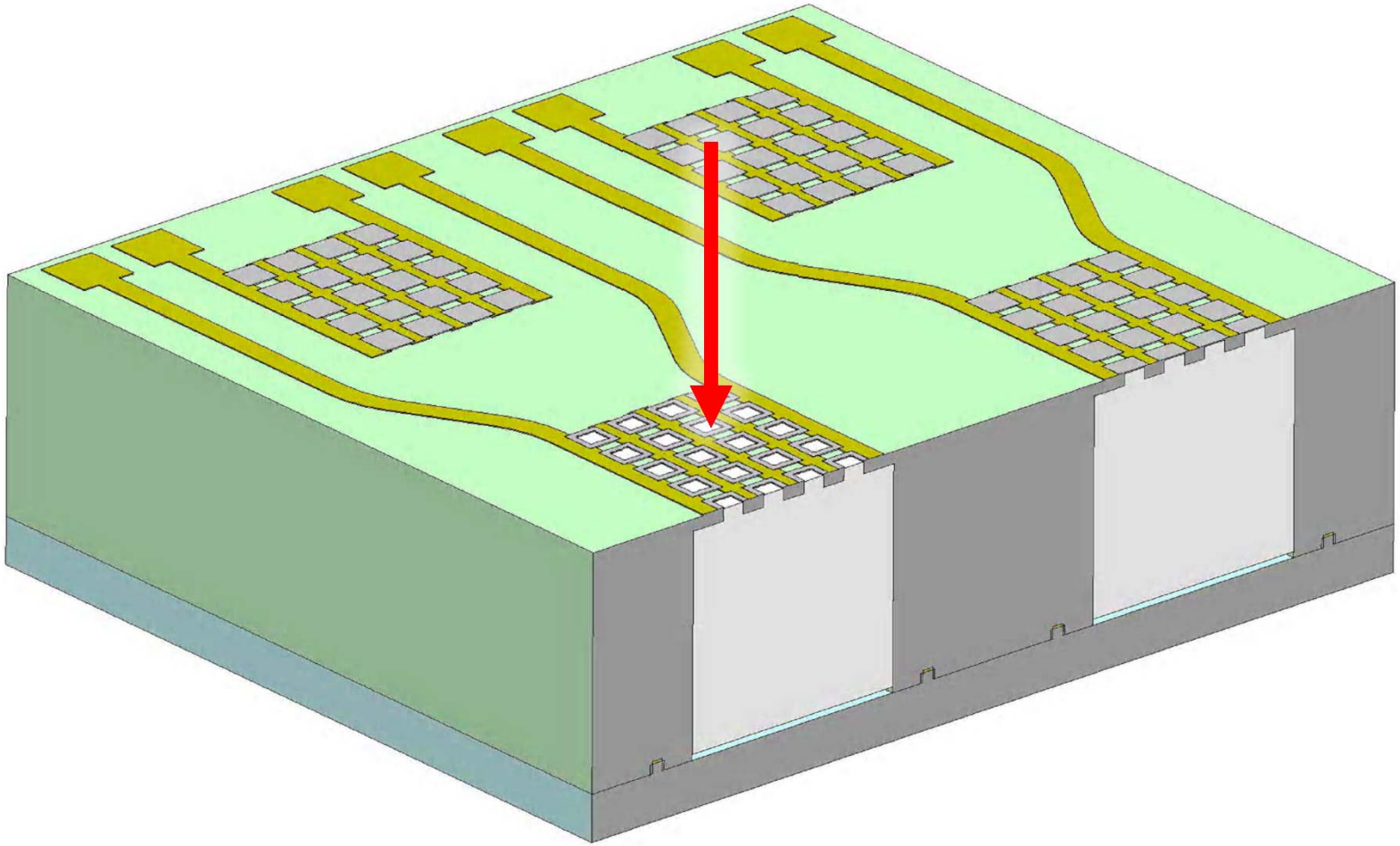
Microchip Drug Delivery

Step 1. At implant, all drug reservoirs in array are sealed.



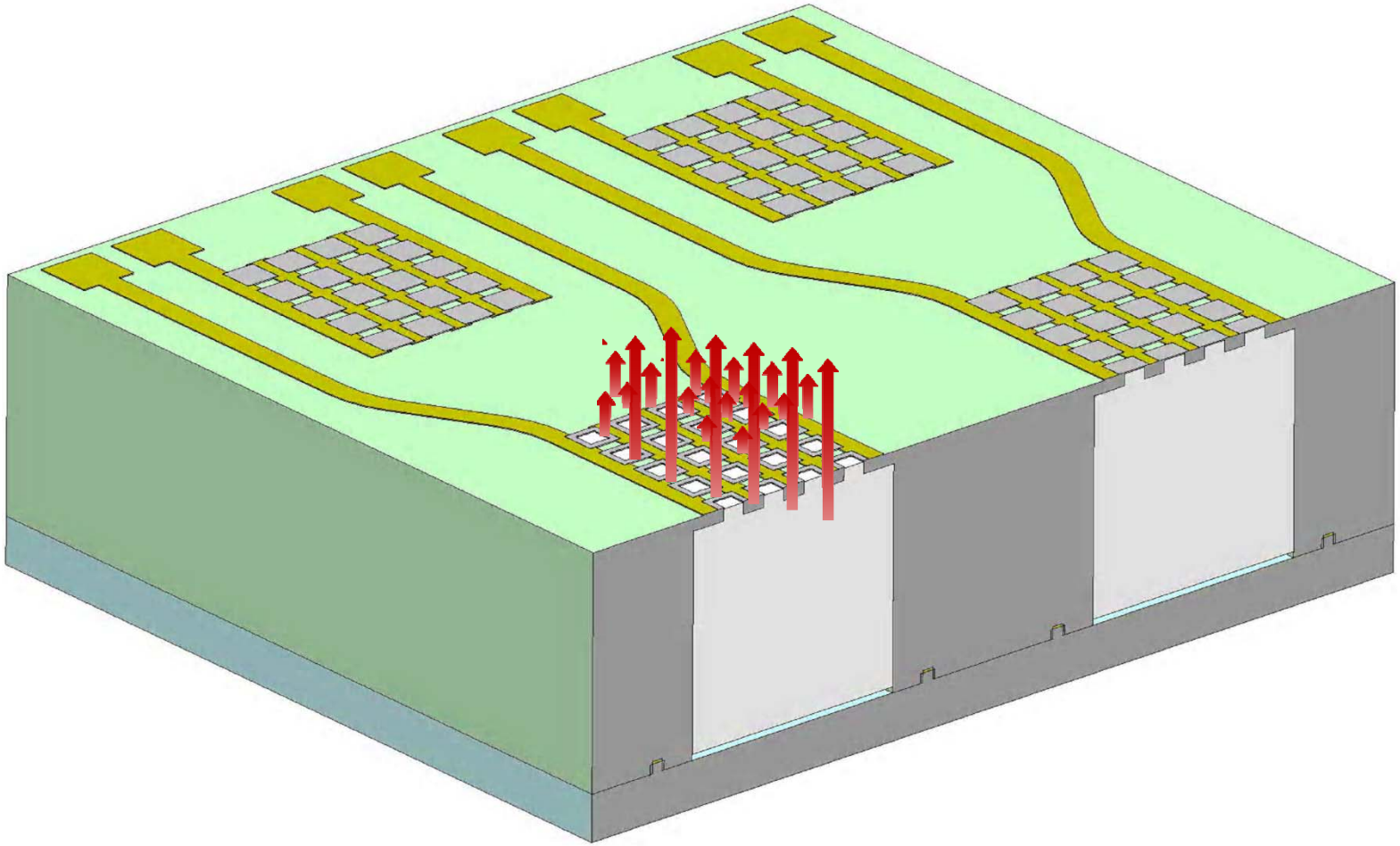
Microchip Drug Delivery

Step 2. First drug reservoir is actively opened on schedule.



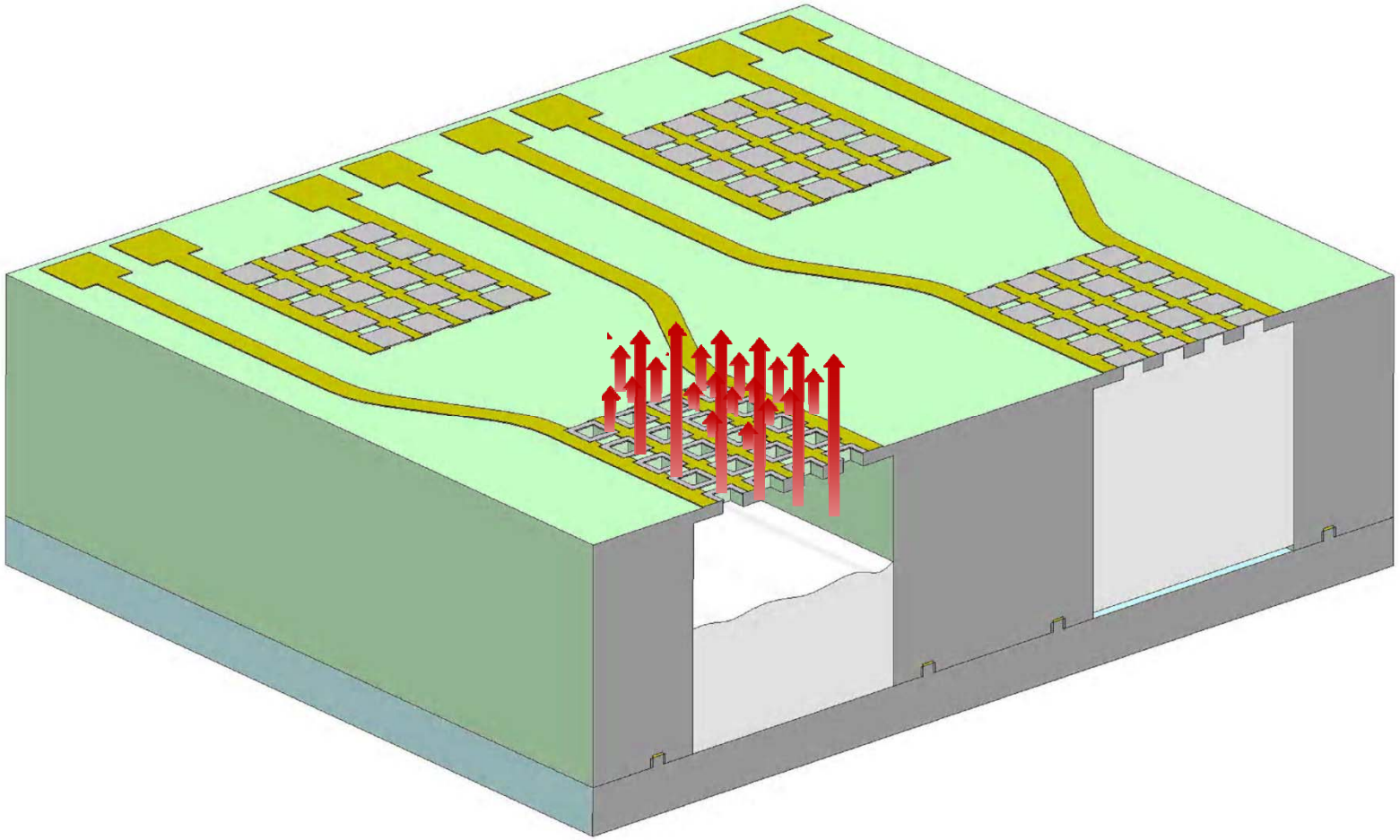
Microchip Drug Delivery

Step 3. Drug begins to release from the reservoir.



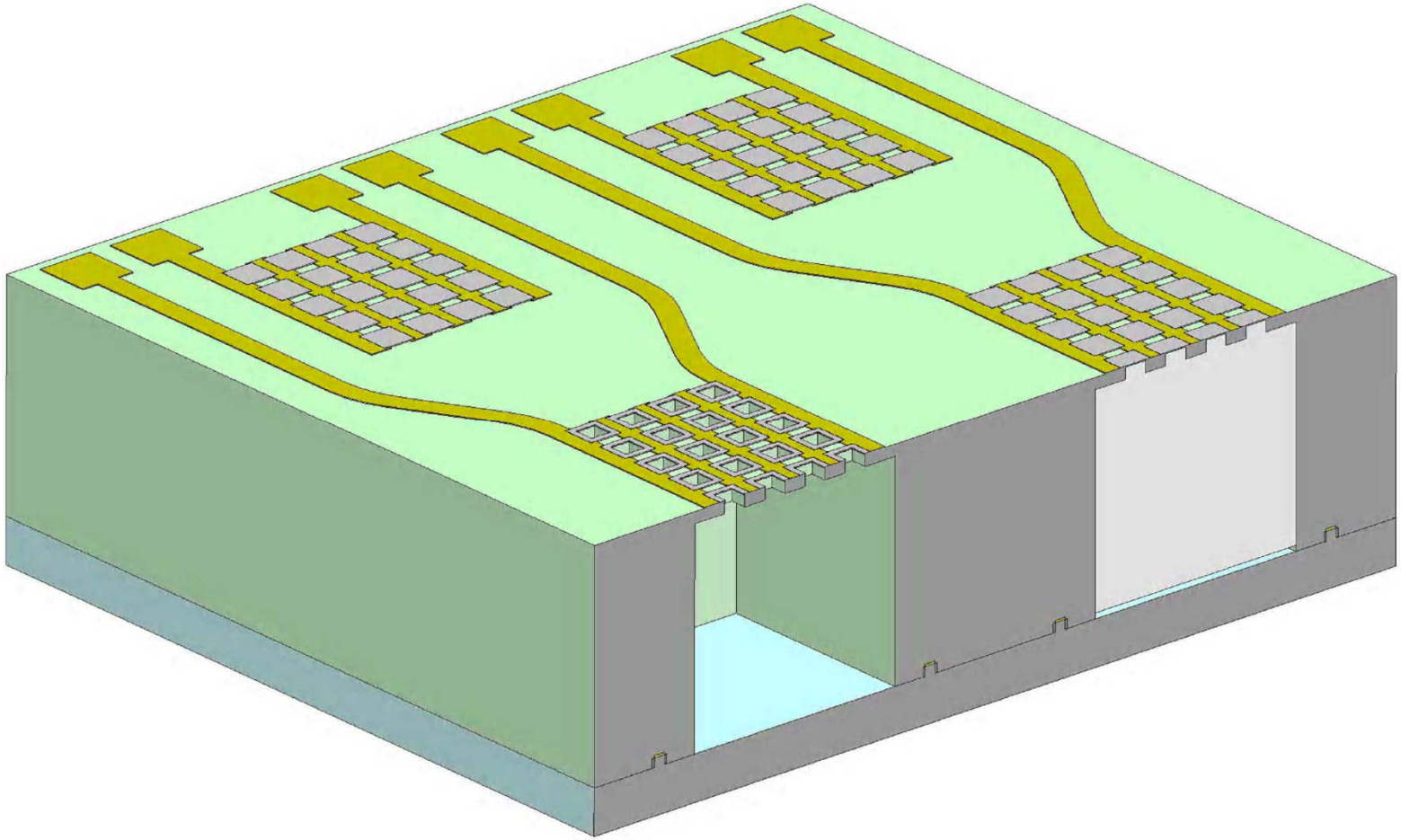
Microchip Drug Delivery

Step 4. Drug releases from the reservoir at a rate determined by the composition of the drug formulation and the area of the apertures.



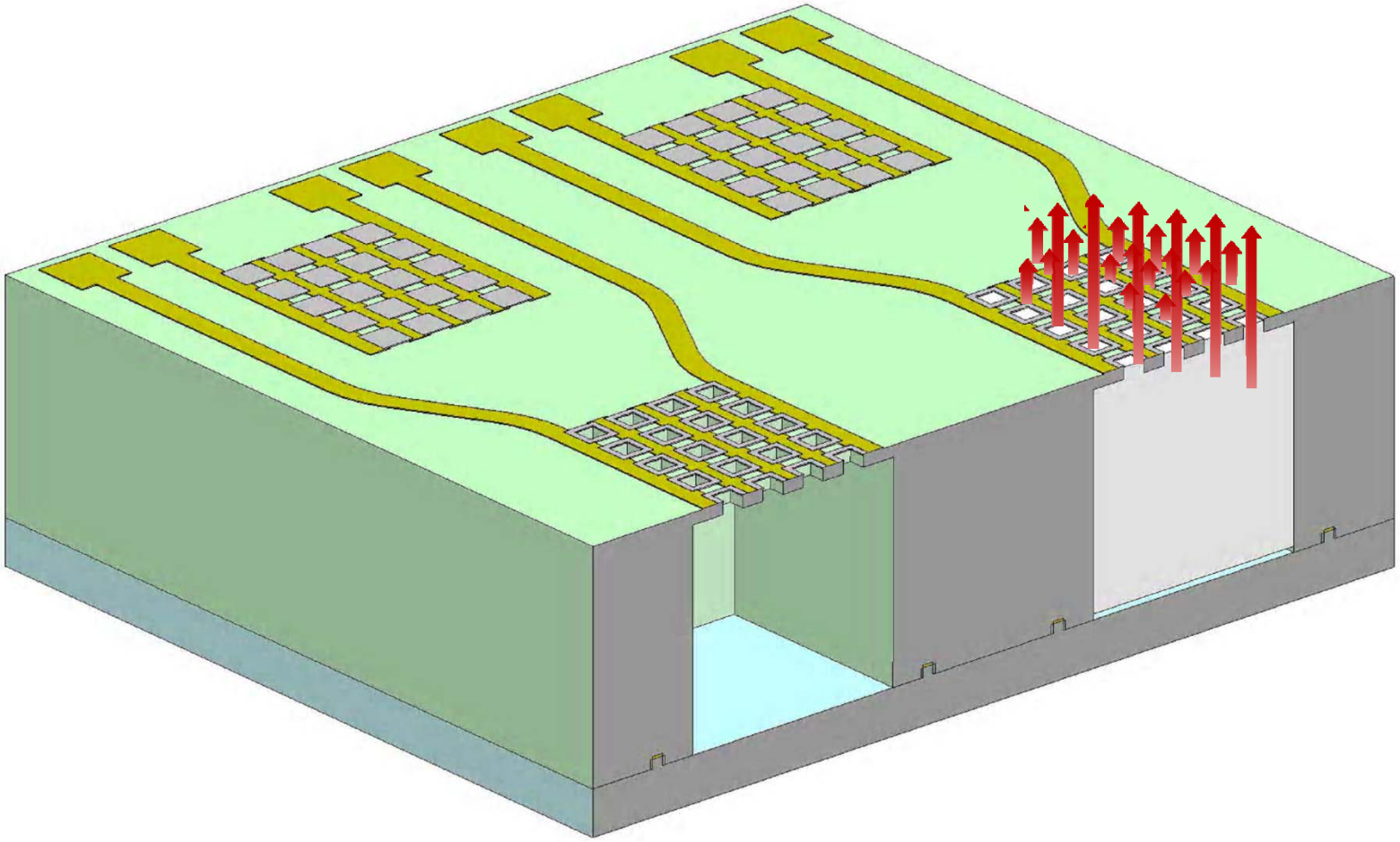
Microchip Drug Delivery

Step 5. After the drug reservoir is empty, the next dose can be delivered from another reservoir.



Microchip Drug Delivery

Step 6. Drug releases from the second reservoir.



Drug Formulation and Filling

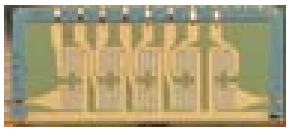
- Drug payload is formulated as a solution with stabilizers.
- Loaded into microchip reservoirs using custom robotic dispenser.
- Freeze-dried to preserve stability.

Hermetic Sealing - Compressive Cold Weld (CCW)

- A true hermetic seal is required to protect drug, sensors from exposure to moisture during long-term implantation.
- Low temperature (≤ 98.6˚F) process required to prevent denaturation of protein drugs, enzymes used in sensors.

Implantable Drug Delivery Device

Drug-loaded microchips are mounted to the surface of a pacemaker-like control system.



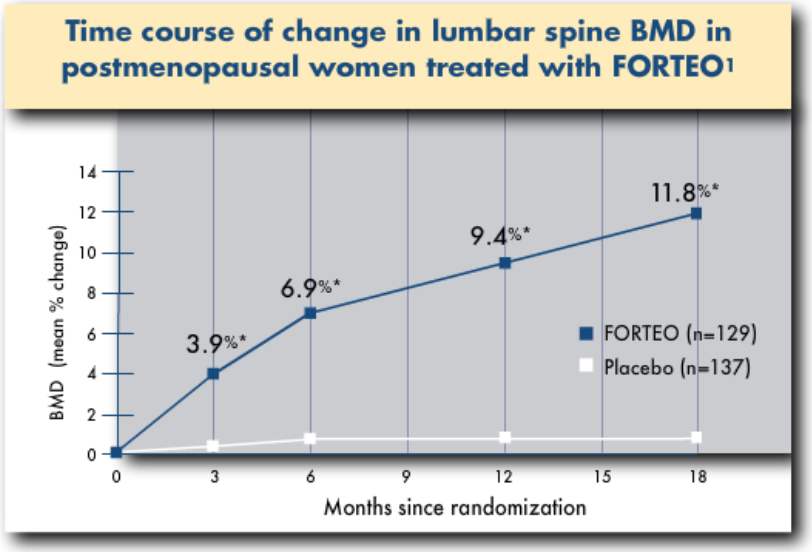
Filled & Sealed Drug Delivery Microchips

Drug Delivery Implant

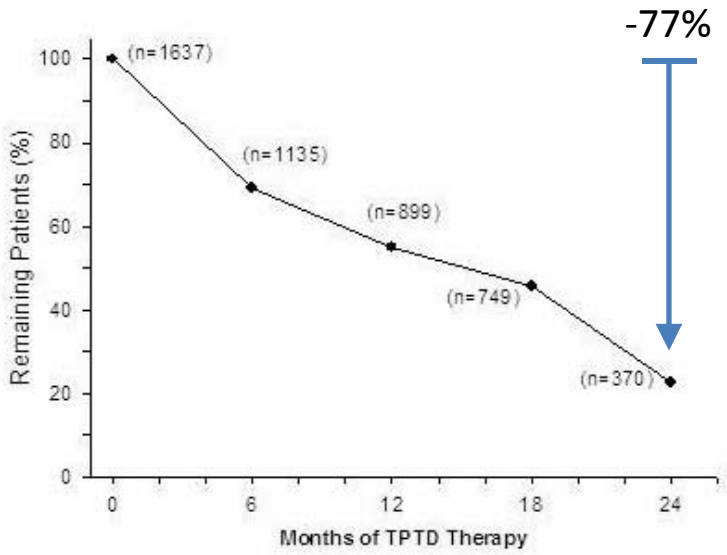
- microprocessor
- 128kB memory
- custom microchip control ASICs
- MICS band transceiver
- custom antenna
- hermetic, biocompatible enclosure
- implant-grade battery

Osteoporosis Treatment – Background

- Parathyroid hormone (PTH) is an effective treatment, and only approved anabolic (bone-building) drug
- Eli Lilly's FORTEO™ yields 10% - 15% increase in bone mineral density (BMD) over the course of 18 month therapy
- Daily subcutaneous injection results in poor compliance



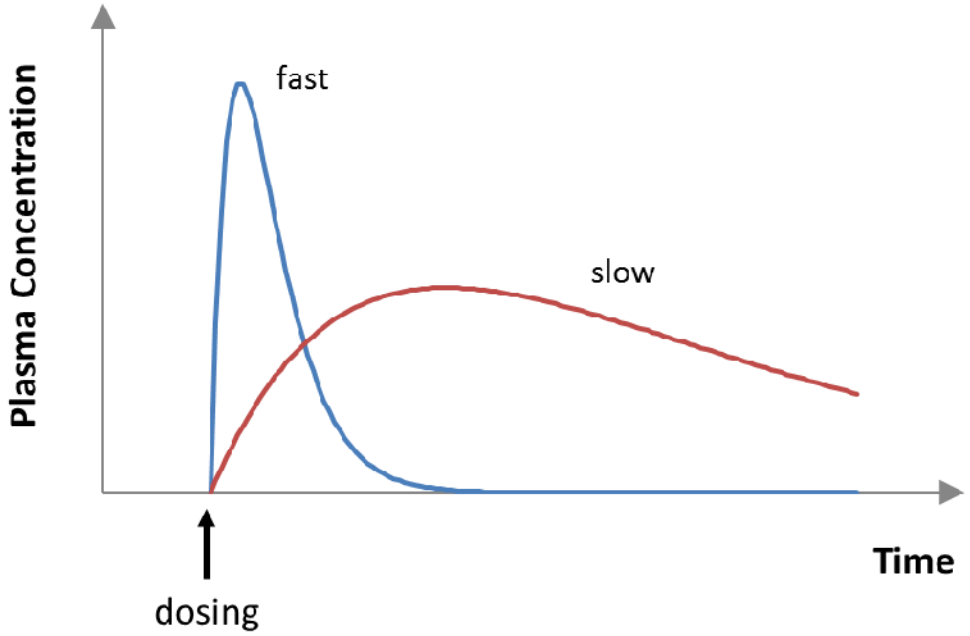
(http://www.forteohcp.com/Pages/efficacy-rapid-bmd.aspx)



(Abstract SA395, presented at ASBMR 30th Annual Meeting)

PTH Pharmacokinetics

- Pharmacokinetics (PK) describes the processes of drug adsorption, distribution, metabolism and excretion.
- Characterized by measuring the concentration of drug in the bloodstream following administration.
- Parathyroid hormone builds bone only when delivered in a pulsatile manner.



Microchip Implant Delivery of Parathyroid Hormone

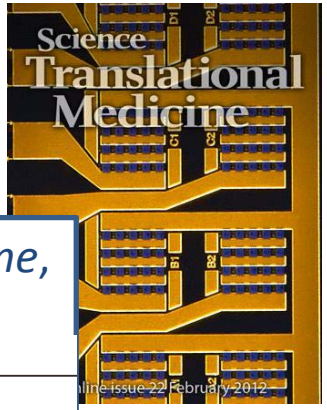
- Implanted device will improve compliance, lead to better outcomes.
- Questions to be answered by clinical study:
  - How will pharmacokinetics compare to a subcutaneous injection, particularly after the formation of a fibrous tissue capsule?
  - How will patients accept the device?

First Human Testing of Microchip Drug Delivery

- Device
  - 20 reservoir microchip implant
  - 40 microgram doses of hPTH(1-34)
- Patient population
  - postmenopausal women between 65 and 70
- Study design
  - eight week healing period after implant
  - four week microchip dosing period w/ four PK procedures
  - four PK procedures with FORTEO as control
- Additional measures
  - bone growth markers
  - tissue capsule histology

First Human Testing - Key Results

- Equivalent therapeutic efficacy as Forteo injections
- Similar increase in bone formation blood marker, P1NP
- More consistent doses than Forteo injections
- Great patient acceptance
  - Could not feel the device
  - Willing to have another device implanted
  - 100% Compliance
- Complete study results published



Science Translational Medicine,
Published February 22, 2012

RESEARCH ARTICLE

DRUG DELIVERY

First-in-Human Testing of a Wirelessly Controlled Drug Delivery Microchip

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MicroCHIPS Drug Delivery Implant

- Therapeutic Benefits
  - 100% compliance with no patient or caregiver actions required
  - Drug is automatically delivered at the prescribed time
  - Drug is delivered with less variability than an injection
  - Drug can be delivered at opportune times to reduce side effects
  - Different dosing per device to enable weaning on and off the medication
  - Different drugs can be stored – “pharmacy on a chip”
  - Drug can be stored in lyophilized form for long term stability

Summary

- Silicon microreservoir technology protects drugs and biosensors, releases them on demand
- Filling and sealing processes are compatible with temperature sensitive biological materials
- True hermetic seal ensures long-term stability in implantable device applications
- First human test of implantable parathyroid hormone delivery device successful
- Numerous drugs are possible candidates for microchip delivery to treat chronic disease