Piezoelectric Patch & Pump for Drug Delivery in Tumors

BMEn 5151
Final Project
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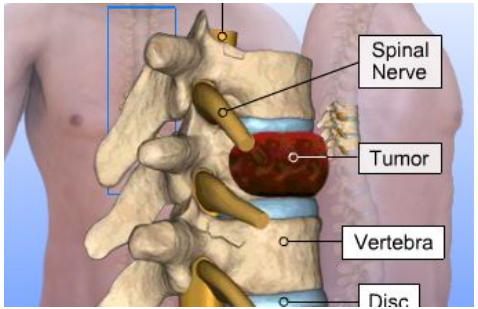
Purpose of the Device

- Drug delivery to inoperable tumors
  - Using a patch coupled with drug delivery to shrink tumors that can't be removed such as spinal tumors, or tumors integrated with necessary blood vessels
- Application especially to tumors that are accessible but poor vascularity for drug delivery through the blood
- Growth specific drug delivery
  - Reduce the excess chemotherapy delivered and focus it on the parts of the tumor that are growing



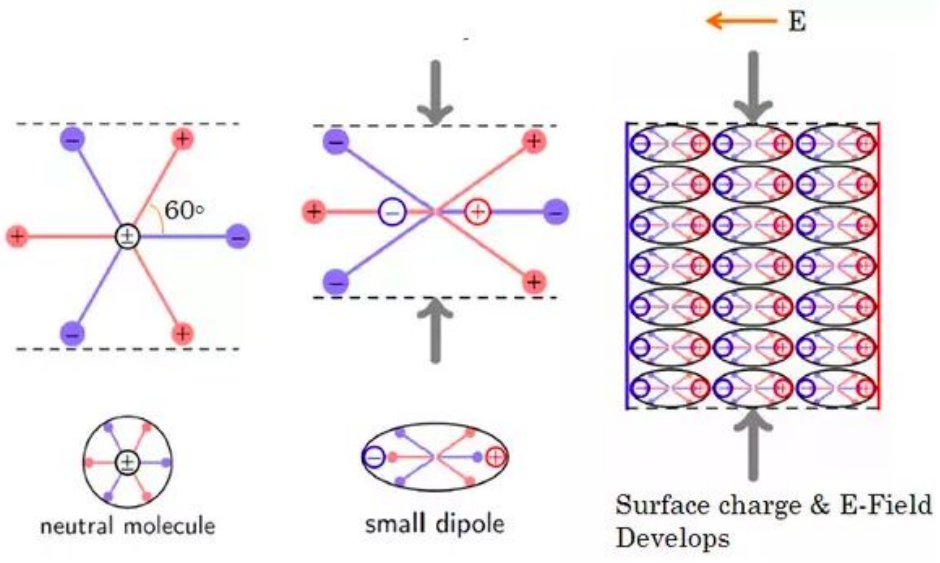
[7]

Overview of Piezoelectric Materials

- Many materials display this characteristic
  - Natural: Cane sugar, quartz, topaz
  - Artificial: barium titanate and lead zirconate titanate
- Two different pathways exists for the properties of these materials to be exploited for engineering purposes
- Direct Piezoelectric effect (discovered first)
  - Mechanical strain produces voltage
- Indirect Piezoelectric effect
  - External electric field produces strain

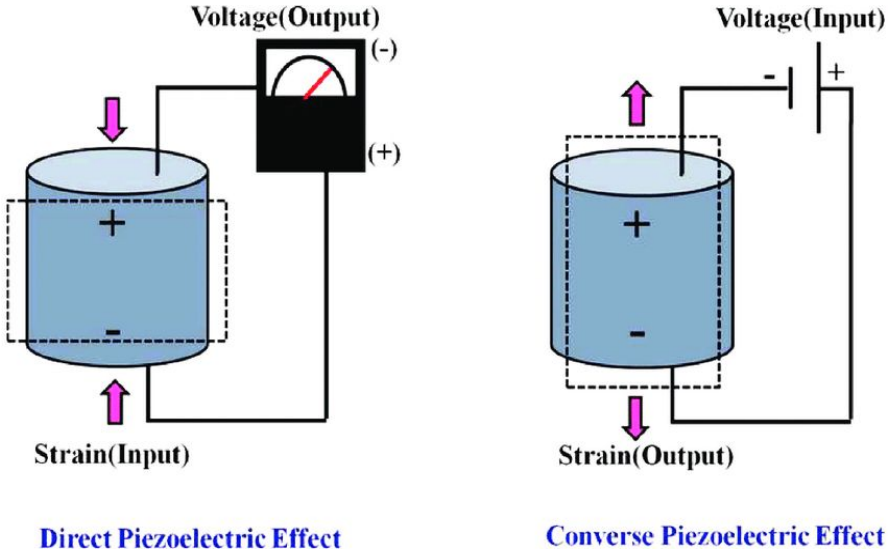
[10]

https://www.worldatlas.com/articles/quartz-facts-geology-of-the-world.html



Molecular representation of direct piezoelectric effect. Reverse effect occurs from asymmetric displacement of anions and cations.

https://www.quora.com/How-does-a-piezoelectric-igniter-work

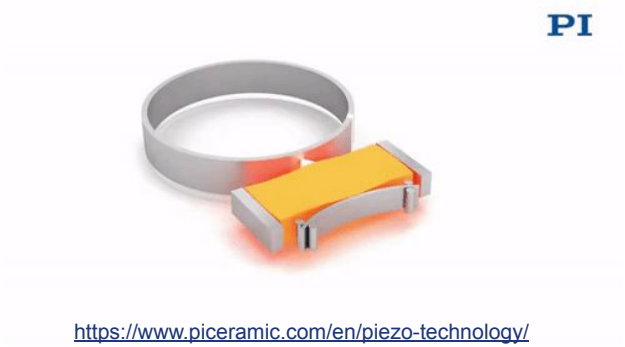


Illustrating direct and indirect effect. Voltage output and strain output directly proportional to their respective inputs.

https://www.researchgate.net/figure/Direct-and-converse-piezoelectric-effect_fig2_329228323

What is it Good For?

- Direct effect equips material with an intrinsic battery
- Indirect effect has many diverse uses
  - Lighters, sensors, printers, speakers, microphones…
- Useful for pumps and motors
  - Many different variations of motors and pumps exist that are driven by piezoelectric materials
  - Rely upon the vibration/deformation of a material to cyclically drive movement



https://www.piceramic.com/en/piezo-technology/

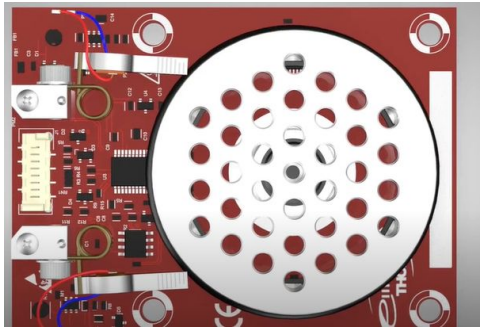
- A visualization taken from a commercial distributor of piezoelectric motors and pumps (PI)
- Ultrasonic rotary motor
  - Excellent control, simple design, readily miniaturized, good holding torque, low temperatures and power consumption

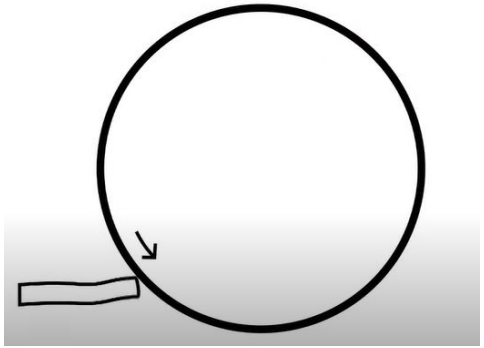
[11]

Fabrication

Components:

- Piezoelectric material - measuring the tumor growth
- Piezoelectric material - converting the growth voltage to motor
- Ultrasonic rotary motor
- Drug storage and emission

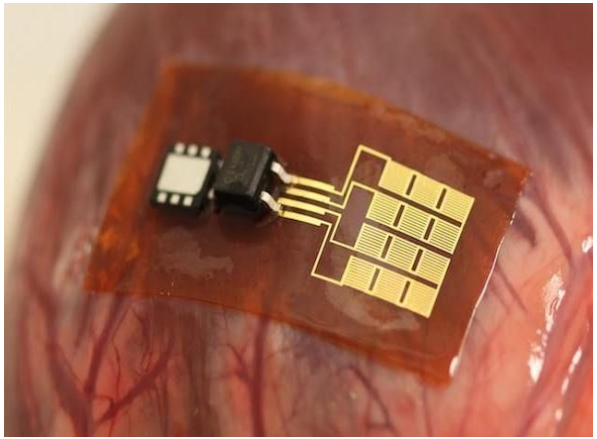




[1]

PZT Ribbon Fabrication

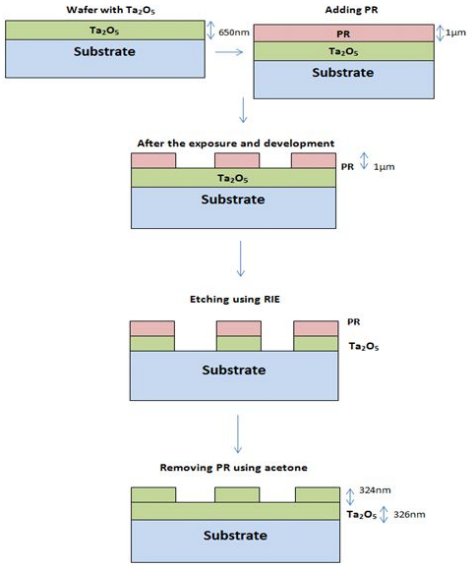
- Lead zirconate titanate (PZT) for the piezoelectric material
  - Commonly used in medical devices for getting energy[2]
  - Harnesses native movement from body ex. Lungs and heart
- Fabrication process of PZT ribbons with electrodes
  - Top electrode of Au/Cr formed by electron beam evaporator
  - Coat wafer with photoresist and patterned photolithography defines electrode areas
  - Au Cr layers etched with gold etchant
  - PZT ribbons created by wet chemical etching with HNO3, BHF, H20 through a hard baked mask of PR (photoresist) [2]



[2]

PZT Ribbon Fabrication Cont.

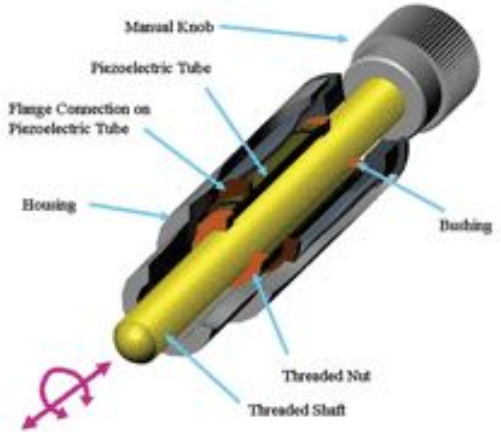
- Hard baking with a sequence of varying temperatures and time
- The bottom Pt/Ti electrode patterned by wet chemical etching with HCl, HNO3, and DI water through a hard baked mask
- PZT layers protected by PR during removal of sacrificial layer SiO2 with HF.
- Hard baked photoresist mask removed in an acetone bath [2]
- Transfer to PDMS stamp and conformally contacted top of the ribbons
- Device retrieved by peeling the stamp away from the Si wafer and transferred on a film of PI (polyimide)
- Electrode holes made by patterning with photoresist then using reactive ion etching



[5]

Piezoelectric Motor Pump

- Voltage from PZT ribbon electrodes connected to piezoelectric motor pump
- Voltage to the piezoelectric material in the pump will control the rotor speed
- The higher the speed the more drug administered
- The drug will be dispensed similar to a syringe plunger
- Drug reservoir will be surrounding the device to minimize space



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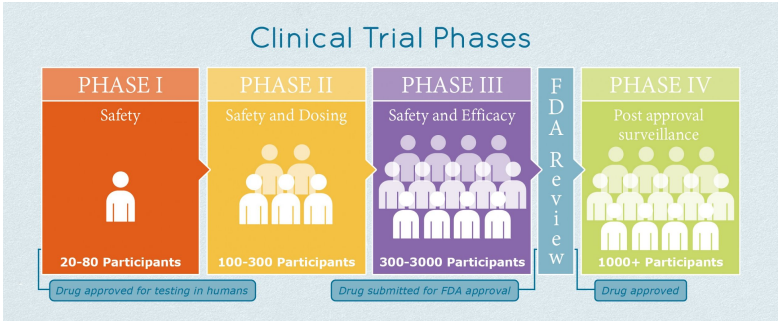
Testing Methods

- Need to test that the device releases drug
  - Create model tumor, place the device onto it and inflate the model tumor
  - This is conducted in solution with an indicator for the chosen drug
  - Can use this method to measure release rate over time
- Need to test that the device releases more drug in correlation with more growth
  - Repeat the above routine with models inflated to different sizes
  - Measure concentrations of indicator over time to analyze drug release rate as well
- Potential in vitro testing using tumor tissue samples as well

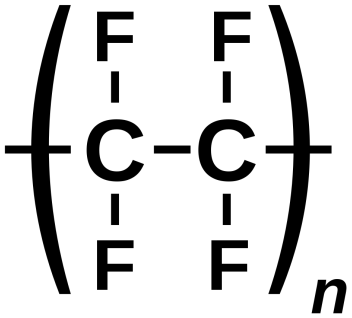
Testing Methods Part 2

- Need to test for biocompatibility
  - Conduct tests based on ISO 10993 standards for device biocompatibility [4]
    - Cytotoxicity, device leachability tests, sensitization assay testing, immune response testing
- Clinical Testing
  - Animal studies
    - Determine how much drug/potency needs to be released to shrink actual tumor tissue
  - Human clinical trials



[6]

Biocompatibility



- Considerations:
  - Need a good anti-fouling surface
  - Also need a good insulator, since a voltage is created with the piezoelectric material creates a voltage
  - Need general compatibility and durability as well (i.e. non-corroding, non-toxic)
- Fluoropolymer coating such as PTFE (Polytetrafluoroethylene)[9]
  - Good anti-fouling surface
  - Also a good insulator, commonly used in ICD's
  - Nontoxic and commonly implanted
  - Good corrosion and chemical resistance
  - FDA Approved

Limitations

- Small Window of application (i.e. tumors that can be reached surgically, but cannot be removed)
- Sensors cannot discriminate between pressure from the actual tumor or other factors (i.e. movement, infection)
- Can only load with a finite amount of drug, may need to be restocked
- Will require both a careful implant and explant surgery
- Need a base release rate so that drug is still delivered as tumor shrinks

Citations

[1] Thorlabs, Inc. “The Elliptical Technique of the Piezo Resonant Motor” *Thorlabs* June 2017.

[2] The American Ceramic Society. “PZT Flexible Thin Films for Biologically Powered Medical Devices

[3] Murillo et al. “Optimization of a Piezoelectric Energy Harvester and Design of a Charge Pump converter for CMOS-MEMS Monolithic Integration

[4] Pacific BioLabs. “Biocompatibility.”

[5] Murugaiya et al. “Etch Process Development of Tantalum Pentoxide Using Photoresist” *Researchgate.* Mat 2013

[6] IDL Collective. “Clinical Trial Phases” https://www.ildcollaborative.org/resources/phase-iii-ipf-clinical-trials

[7] Spine Physicians Institute. “Spinal Tumors Overview.” https://spinephysiciansinstitute.com/conditions-view/spinal-tumors/

[8] Fred Haas “Tiny Piezoelectric Motor Enhances Nanoscale positioning” *Electronic Products* December 2004

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[9] AFT Fluorotec Limited. “What is PTFE?” *AFT Fluorotec*.

[10] M. S. Vijaya, *Piezoelectric Materials and Devices*. Boca Ranton, FL: CRC Press, 2013.

[11] J. Wallaschek, “Piezoelectric Ultrasonic Motors,” *Journal of Intelligent Material Systems and Structures*, vol. 6, no. 1, pp. 76–80, Jan. 1995.

Questions?