Hydro-Bandaid

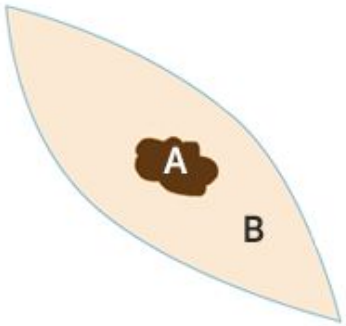
Nakyung Lee, Qingyuan Liu, Ayako Ohoka, Arushi Sardana, Aaron Schwartz-Duval, Veronika Sowers

Melanoma

What it is	**Most dangerous** form of skin cancer originating from the pigment-producing melanocytes in the bottom layer of the epidermis
Causes	Unrepaired DNA damage to skin cells (usually from **ultraviolet radiation**) → genetic mutations → skin cells multiply rapidly
Diagnosis	**ABCDEs** of melanoma - asymmetry, border, color, diameter, evolving **Biopsy**

Stages and Current Treatments

Stage 0 (in situ)	Melanoma only in top surface layer of epidermis Has not metastasized	**Wide-local excision surgery**
Stage 1	Melanoma less than 2 mm thick Has not metastasized	**Wide-local excision surgery**
Stage 2	Melanoma between 1 mm and around ~4 mm thick Has not metastasized	**Wide-local excision surgery**



- Skin cancer and a small margin of healthy tissue around it is cut out
- Edges of wound are sutured
- Tissue sent to pathologist for processing and margin evaluation
- Recovery rate depends on size and site of cancer

Significance

Melanoma

- ~73,870 diagnosed in 2015
- ~9,940 deaths in 2015
- Incidence of melanoma has been increasing for the past 30 years
- Recurrence occurs 10 or more years after initial treatment in more than 1 in 20 patients

Surgical Site Infection

- 3 in every 100 patients who have surgery develop a surgical site infection
- Most common health-associated infection
- ~157,500 occurrences a year
- 98,987 deaths by healthcare associated infection in 2002

Our Approach: Hydro-Bandaid

- Focusing on patient recovery post wide-local excision surgery
- Sticky degradable hydrogel patch with microneedle for diffusion into skin
- Layered assembly of alternating hydrogels with environmentally sensitive structure
- Offers controlled release of therapeutics

  Imiquimod- prevents recurrence

  Antibiotics- prevents infection

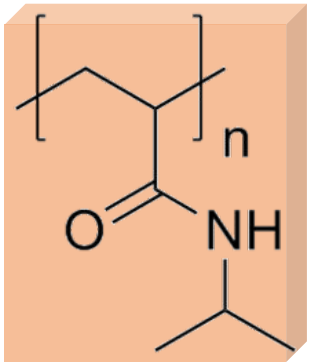
  Interferon- boosts immune system

  Anticoagulants- prevents blood-clotting

Temperature and pH Dependance

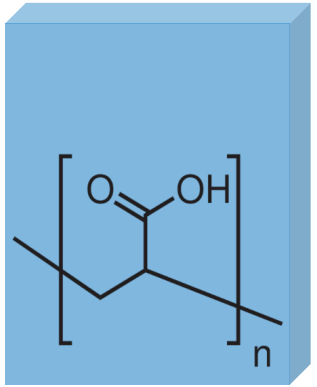
poly(n-isopropylacrylamide) – Temperature Sensitive

- Modifiable with cellulose
- Skin~34°C, Internal Body Temp=37°C



poly(acrylic acid) – pH Sensitive

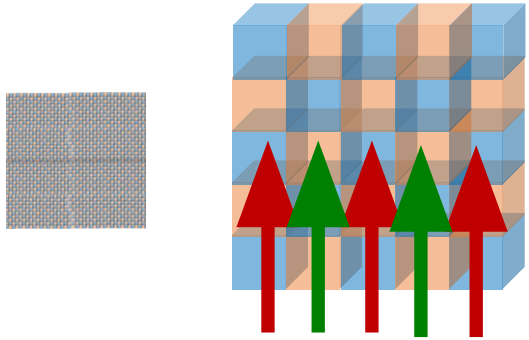
- Modifiable with cellulose
- Skin~5.5, Blood=7.4, Tumor=6.0-6.8

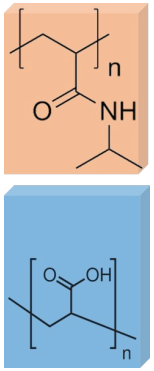


Layered Assembly versus Hybrid Gel

Hybrid Gel

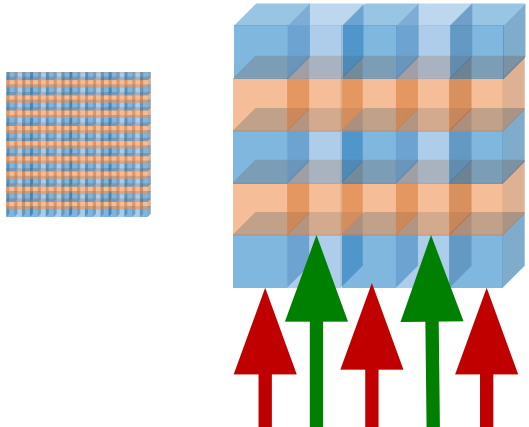
- Uneven dissolution/ release of therapeutic
- Non-uniform diffusion gradient of heat and protons





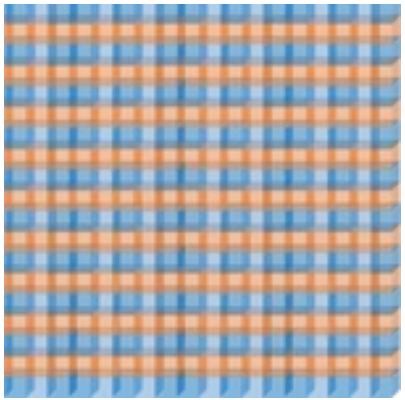
Layered Assembly

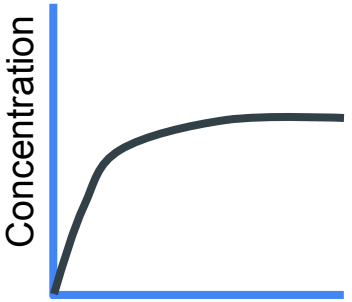
- Each layer provides “insulation” against the affector of the next layer
- Superior control for directional release through two mechanisms
- Separate tunable distinct modes of release for each layer



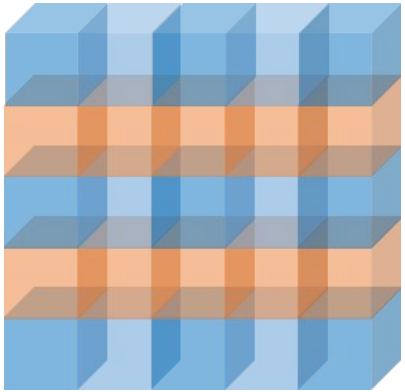
Thick versus Thin Layered Assembly

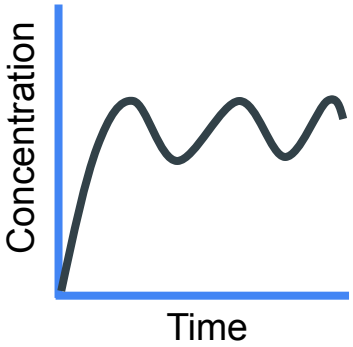
Thin layers will result in a more stable release of therapeutic, but the “insulation effect” will be diminished



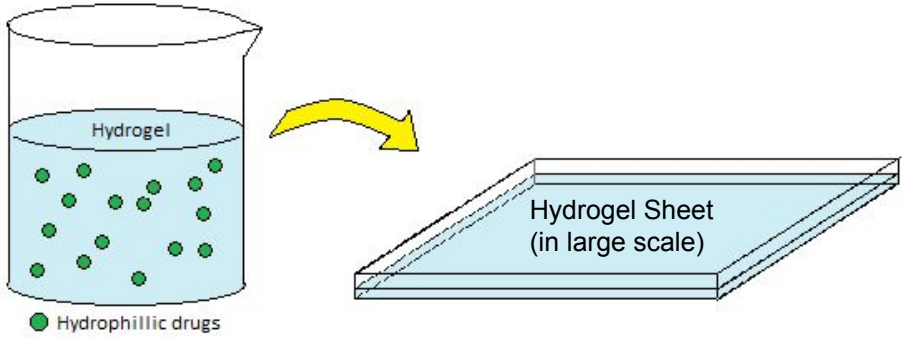


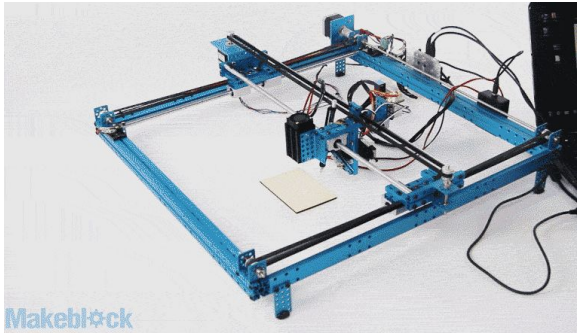
Thick layers will result in a more pulsatile release of therapeutic controlled therapeutic release





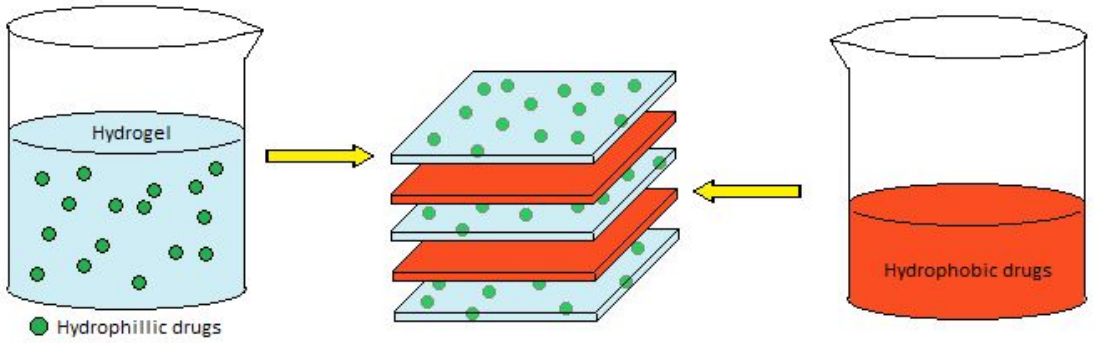
Fabrication / Methods



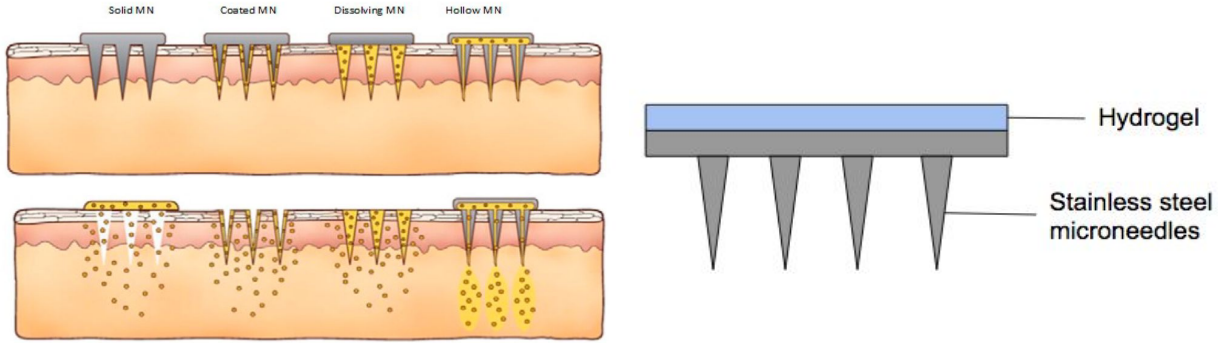


- Hydrogel can be prepared in large-scale sheets □ Mass production possible
- Cut into desired size using x-y directional laser cutter

Fabrication / Methods



- Layers of hydrogel and drug stacked up
- Hydrogel with drug incorporated in goes on top of the metal micro-needle



- Painless microneedles
- Stainless steel

Testing: Material

Physical Characterization

- Strip extensiometry
- Compression
  - Tensile modulus
- SEM

Drug Release

- Beaker containing 37˚C pH 5.5 citrate buffer covered by dialysis membrane
- Read drug concentration in the solution overtime with UV/V is over various timepoints

Testing: In vitro

Direct Contact Test:

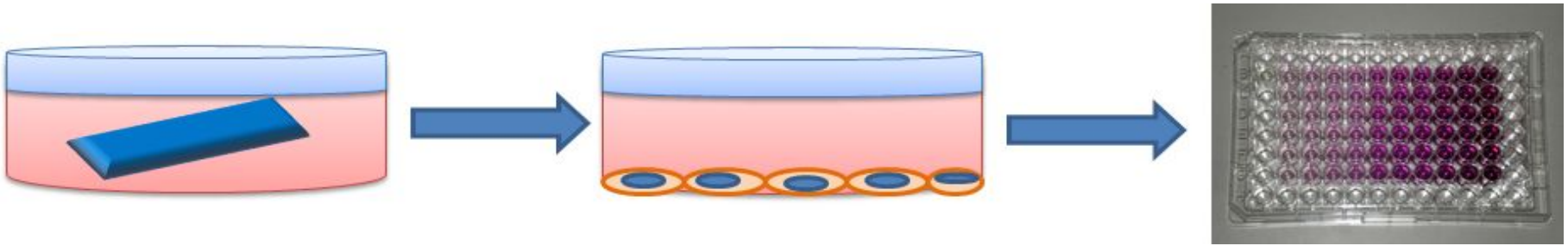
- Place hydrogels in well plate containing PCS-201-012 human dermal epithelial cells

→ Live/Dead Assay

Elution:

- Place hydrogels in culture media in a well plate, then remove media after 24 hours
- Take media to culture PCS-201-012 cells

→ Cell assays: MTT, LDH, WST

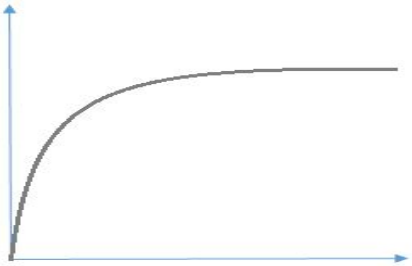


Testing: In vivo

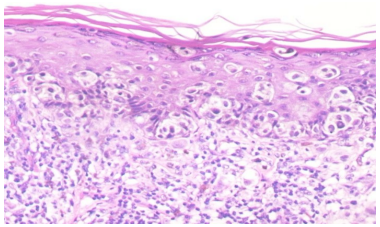
Inject C32 melanoma cells into hairless guinea pig (HGP), remove most of tumor

Adhesion of Hydro-Bandaid to excision site

- Drug release study from examining concentration in blood
- Histopathology
  - Inflammation
  - Vascularization
  - Fibrosis



skin sample



Summary

- Wide-local excision surgery most common treatment for melanoma
- Recovery can be extensive and long
- Hydro-Bandaid offers controlled release of therapeutics to accelerate recovery and prevent recurrence at primary site
- Future applications: controlled release of antibiotics and/or sterilization agents

  -Topical postoperative infection control

  -Steroid treatment

  -Nicotine withdrawal remedy