Localizing Chemotherapeutic Drug Release to Treat Stage III Colorectal Cancer

Team TUMOR

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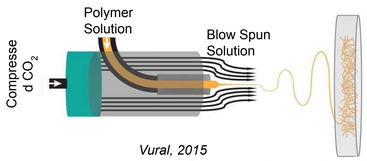
Research Problem

- Colon cancer has a 33% recurrence rate despite aggressive treatment
- Treatment typically includes surgical resection followed by systemic chemotherapy, which has adverse side effects.[3]
- Sutures could be supplemented by a polymer surgical sealant to localize treatment

Research Questions

- How can we use a surgical sealant to provide localized chemotherapy and mitigate systemic side effects?
- How can we examine the effects of chemotherapeutic drugs on surgical sealant properties?

Approach



Vural, 2015

Solution blow spinning (SBS) involves running a dissolved polymer solution through an airbrush. The solvent evaporates rapidly, depositing polymer fibers on the desired surface.[1]

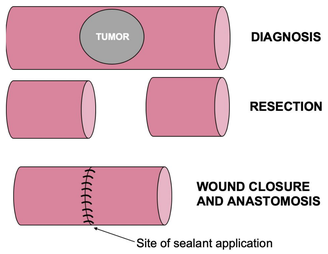
Benefits of SBS:

Resection

- Permits high degrees of freedom and ease of use

Chemotherapy

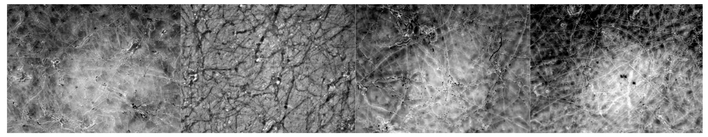
- Allows direct deposit of chemotherapeutic agents at resection sites
- Maximizes efficacy of treatment while minimizing collateral cell damage in the body



Surgical Resection and Closure (Atalla, 2019)

In the conducted experiments, the biodegradable polymer poly(lactide-co-caprolactone) (PLCL) was tested at two molecular weights (40 and 80 kDa) in conjunction with the chemotherapy drug capecitabine.

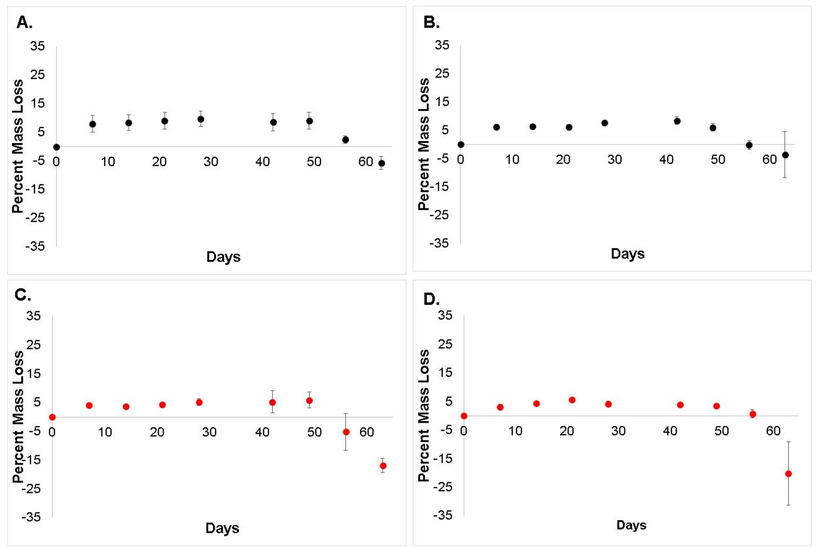
Surgical Sealant Morphology



40kDa PLCL without Drug (Control) | 40kDa PLCL with Drug | 80kDa PLCL without Drug (Control) | 80kDa PLCL with Drug

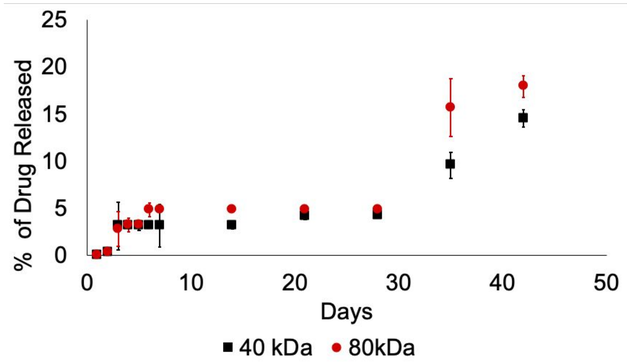
Capecitabine was soluble in PLCL at both molecular weights. When sprayed, incorporation of drug did not alter the ability to form fibers or physical properties of the fiber.

Surgical Sealant Degradation



80 kDa PLCL did not degrade to the extent to which 40 kDa PLCL did in physiological conditions within a 60 day period. The increase in mass within the 12 week period was attributed to water uptake by the polymer. The degradation occurred complementary to the wound healing timeline.

Chemotherapeutic Drug Release



Both 40 and 80 kDa PLCL and capecitabine exhibited a delayed release profile. Chemotherapy begins 1 week to 2 months after surgical resection.[2] The start of significant drug release begins in both molecular weights within this time period.

Future Directions

The chemotherapeutic did not affect the mechanical and physical properties of the surgical sealant. This demonstrates that its function as a surgical sealant may not be altered by drug incorporation. These fiber mats exhibit a delayed release, which indicates possible implications in cancer treatment via surgical resection. This release pattern complements the normal waiting period[2] by allowing intestinal healing to occur before post-operative chemotherapeutic treatment.

Other biodegradable synthetic polymers will be tested to determine if similar drug release patterns are observed. This may provide insight into the mechanisms behind the delayed release in PLCL trials. Pull-off adhesion testing will also be performed to further assess the mechanical strength of different polymers. These studies will allow us to determine the drug-release properties of the polymers in order to develop a functional drug delivery system.

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References