Engineering an Embolization Device for Localized and Sustained Release of a Chemotherapeutic Agent

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Introduction

Clinical Problem

- Bortezomib (BTZ), a cytotoxic drug that has a highly limited therapeutic window, encapsulated in nanoparticles (NPs) can be released for 1 month [1-2]. At the injection site, the NP retention is only 14 days due to rapid clearance by the body, so the BTZ release timeline does not match the NP retention timeline [2].
- The swine study showed that the nanofiber-reinforced macroporous hydrogel composite (NMHC) can occlude blood vessels (Fig. 1). When swollen, the NMHC easily fragments, so in transarterial chemoembolization (TACE), tumor exposure to the NMHC increases.

Proposed Solution

- BTZ-NPs can be embolized into tumor vessels with the NMHC (Fig. 2)

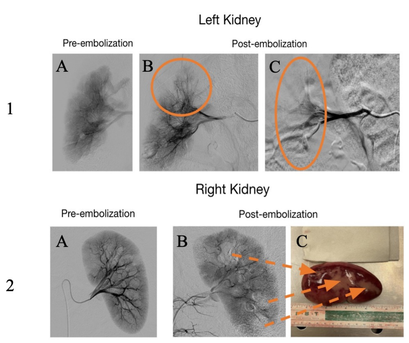

Figure 1. Results of swine study.

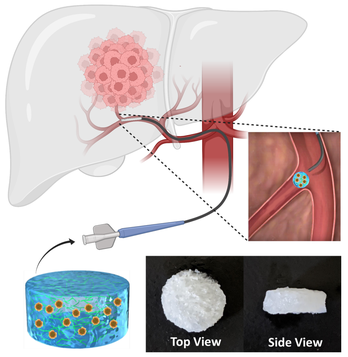

Figure 2. Schematic of solution.

Objectives

- The engineering design of this project is a component, the NMHC, that can be loaded with nanoparticles (Fig. 3).

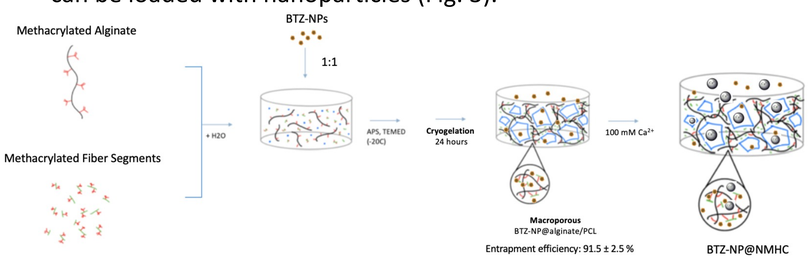

Figure 3. Schematic of NMHC synthesis and NP-loading procedure.

To evaluate the NMHC as an embolization platform to enhance nanoparticle retention and localization,

1. Test release kinetics of BTZ from the NMHC,
2. Evaluate nanoparticle entrapment kinetics,
3. Characterize mechanical properties of the BTZ-NP@NMHC.

BTZ Release Kinetics

Methods

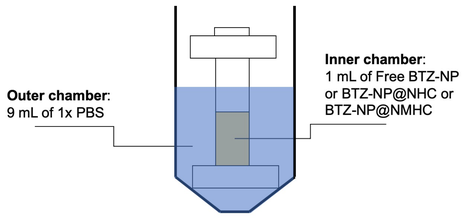

Figure 4. *In vitro* releasing device to model BTZ release from NMHC.

- The negative control is free BTZ-NPs, and the positive control is the hyaluronic acid-based nanofiber-reinforced hydrogel composite (NHC).
- BTZ concentration in outer chamber is measured using high-performance liquid chromatography (Fig. 4).

Results

- The NMHC does not affect the BTZ release kinetics from the NPs.
- The release curves of the NMHC nearly overlap with the curves for free BTZ-NPs and the NHC (Fig. 5).

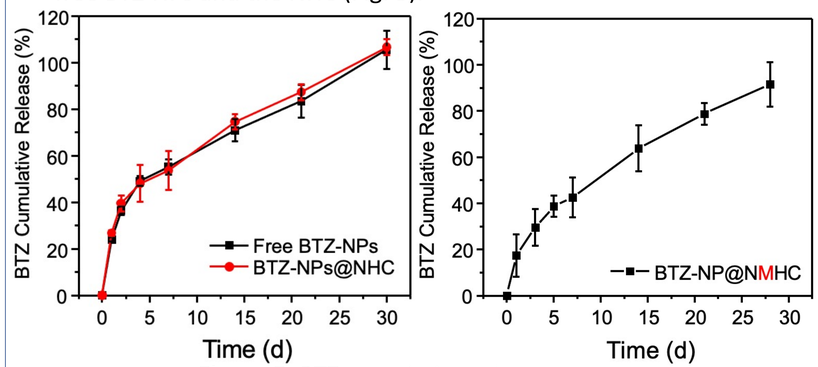

Figure 5. BTZ cumulative release curves.

Mechanical Properties

Methods

- The swelling ratio and shear storage modulus (G') of the NMHC and BTZ-NP loaded NMHC were measured.

Results

Loading Condition	Swelling Ratio	Storage Modulus
NMHC	12.96 ± 2.14	3.32 ± 0.36 kPa
BTZ-NP@NMHC	12.02 ± 0.69	3.46 ± 0.18 kPa

- The NP-loading procedure does not affect the mechanical properties of the NMHC. Running t-tests for both metrics indicated no significant difference in the different NP-loading conditions.

Nanoparticle Entrapment Kinetics

Methods

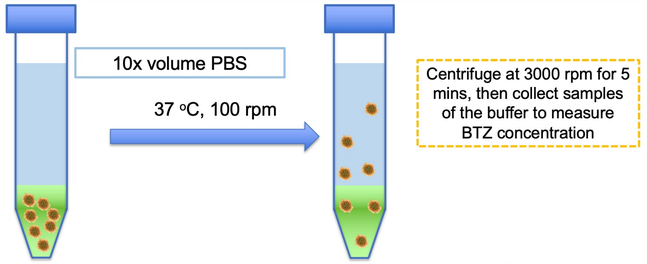

Figure 6. *In vitro* releasing device to model NP release from NMHC.

- BTZ concentration in the buffer solution is measured using high-performance liquid chromatography (Fig. 6).

Results

- The BTZ-NPs can be entrapped in the NMHC for about 2 weeks. Around 90% of the total BTZ NPs are released by Day 14 (Fig. 7).

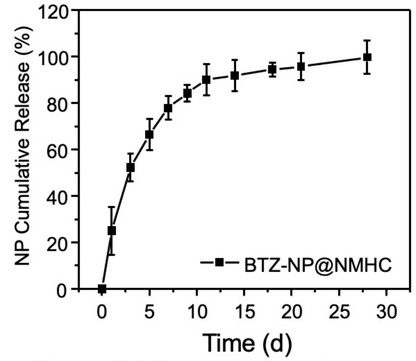

Figure 7. NP cumulative release curve.

Conclusion & Future Directions

- The NMHC as a TACE platform is confirmed. The NMHC can retain NPs for another 14 days for the sustained release of BTZ.
- Future directions would encompass further improving the entrapment efficiency and kinetics timeline.

Reference and Acknowledgements

1. Dou, Q., and Zonder, J. (2014). *Current Cancer Drug Targets,* 14(6), 517–536.
2. Li, L., Zhang, Y. et al. (2022). *Hepatology*. [under review]

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