Abstract
Safe and efficient delivery of hydrophilic drugs across the ocular surface still poses a great challenge in the ophthalmic field. Corneal collagen crosslinking (CXL) is the standard treatment for keratoconus. The conventional method (C-CXL) however requires surgical removal of corneal epithelium to permit sufficient accumulation of riboflavin in the stroma. Therefore, strategies for the transepithelial delivery of riboflavin have been developed, aiming to save patients from the post-surgical complications. Nonetheless, most transepithelial formulations suffer from limited stromal absorption owing to the barrier properties of the epithelium. In this study, we intend to employ ultrasound at low-intensity low-frequency (LILF) to induce sonoephoretic transepithelial delivery of riboflavin. Parameters such as riboflavin concentration, ultrasound mechanical index, dwell-time and ocular surface area exposed were optimized to enhance the corneal permeability to riboflavin. Histological studies were also performed to examine the safety of LILF ultrasound. We optimized that LILF ultrasound at 40 kHz, MI = 0.4 and 30 minute dwell-time with corneoscleral region exposed to 0.5% riboflavin was able to achieve corneal riboflavin amount, 114.33 ± 21.3 μg/g tissue (N = 9) which is approximately 10 times greater than the therapeutic range reported in C-CXL, 15 to 20 μg/g tissue. The safety tests revealed minor exfoliation of the superficial epithelium, and dissolution of intercellular junction complex. Despite the significant enhancement of riboflavin absorption, our mechanical test demonstrated 1.1-fold improvement of Young’s modulus post-CXL, which is lower than C-CXL in giving 1.7-fold improvement. We also discovered an alternative entrance of riboflavin to the stroma via limbal passage, which may be enhanced with the application of ultrasound. In conclusion, LILF ultrasound can enhance the corneal permeability to riboflavin without causing severe damage to the deeper tissue layers. This suggests the potential applications of LILF ultrasound in promoting topical delivery of small, hydrophilic therapeutic molecules in treating keratoconus and other ocular surface diseases.

Date: 12 Aug 2019 (Monday)
Time: 10:00am
Venue: Room 4582 (Lifts 27-28)

Examination Committee:
Prof. Terence T W Wong (Chair)
Prof. Ying Chau (Supervisor)
Prof. Angela R H Wu

All are welcome!