Localized Topical Delivery of 5-Fluorouracil via Mammary Papilla (Nipple)
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Purpose
This study is aimed at determining the feasibility of topical delivery of 5-fluorouracil (5FU) through the mammary papilla.

Methods
In-vitro studies were performed in a vertical Franz diffusion cell using excised porcine and human mammary papilla. 5FU (MW= 130 Da; Log P= -0.89) was used as a model anti-cancer agent for the study. Effect of treatment time and keratin plug removal was studied to optimize the delivery through the mammary papilla. Penetration of 5FU through mammary papilla was compared with the surrounding breast skin. Female Sprague Dawley rats were used for in-vivo studies where topical delivery through the mammary papilla was compared with transdermal and intravenous delivery of 5FU. Quantitative analysis of 5FU was performed by radioactive counts from 14C- 5FU.

Results
Upon 6 hrs of treatment 5FU formed a depot in the mammary papilla and the drug was slowly transported from the depot up to 48 hrs. Removal of the keratin plug by simple application of an alcohol swab increased the 5FU penetration through the mammary papilla by more than 7 folds. In addition, keratin plug removal decreased the lag time for 5FU from 17.96 ± 3.80 hours to 8.76 ± 1.46 hours. Penetration of 5FU through porcine mammary papilla was comparable to human mammary papilla. Moreover, permeation of 5FU via mammary papilla was higher than that via the surrounding breast skin by approximately 2 folds. In-vivo studies showed that topical delivery via mammary papilla led to significantly higher (~ 2 folds) retention of 5FU in mammary tissues with very minimal systemic exposure compared to transdermal and intravenous delivery.

Conclusion
The results suggest that mammary papilla is a potential route for drug delivery, directly to the breast. Overall the findings from the study can be used to develop localized delivery strategies for breast cancer.