

Lytic Effects Of Water On Bladder Cancer Cells – Implications For Continuous Bladder Irrigation After TURBT

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INTRODUCTION

- Recurrence of NMIBC after TURBT is observed in 40-80% of patients
- Intraoperative spillage of cells can lead to tumour cell re-implantation and local recurrence
- Intravesical chemotherapy is effective at reducing recurrence, but is underutilised due to high cost and toxicity
- Bladder irrigation with water as opposed to saline may be a comparable alternative to chemotherapy as it causes osmotic cytolysis in addition to mechanical dilution to remove remaining viable cells

AIMS

1. To determine the time course of osmotic effects of water on bladder cancer cells *in vitro* and *in vivo*
2. To determine whether water is able to lyse cancer cell lines other than bladder cancer *in vitro*
3. To determine what degree of contamination by urine or blood nullifies the effects of water's osmolytic properties

METHOD

IN VITRO

- Two bladder cancer cell lines (HT1197, HT1376) were exposed to water, 0.9% saline or 1.5% glycine
- Cell counts were performed with trypan blue exclusion in triplicate at regular intervals for 5h
- These experiments were repeated for colorectal (LIM2405, KM23), ovarian (COV434), and renal (SKRC52) cancer cell lines
- HT1197 & HT1376 were also exposed to varying concentrations of NaCl to determine if increases in osmolarity would impede water's efficacy

IN VIVO

- 23 patients received saline or water irrigation for 3h post-TURBT
- Hourly 200mL washout samples were collected for cell counting at 0, 1, 2, and 3 hours post-TURBT
- Selected patient samples were sent for immunohistochemistry (IHC)

RESULTS

IN VITRO (Figures 1 & 2)

- Water caused 100% cell lysis within 20 minutes
- Both saline- and glycine-irrigated samples had viable cells remaining at 5h
- Similar results were achieved on all 4 other cancer cell lines
- Gradation study showed that an increase to 0.045% NaCl would impact the osmotic functions of water

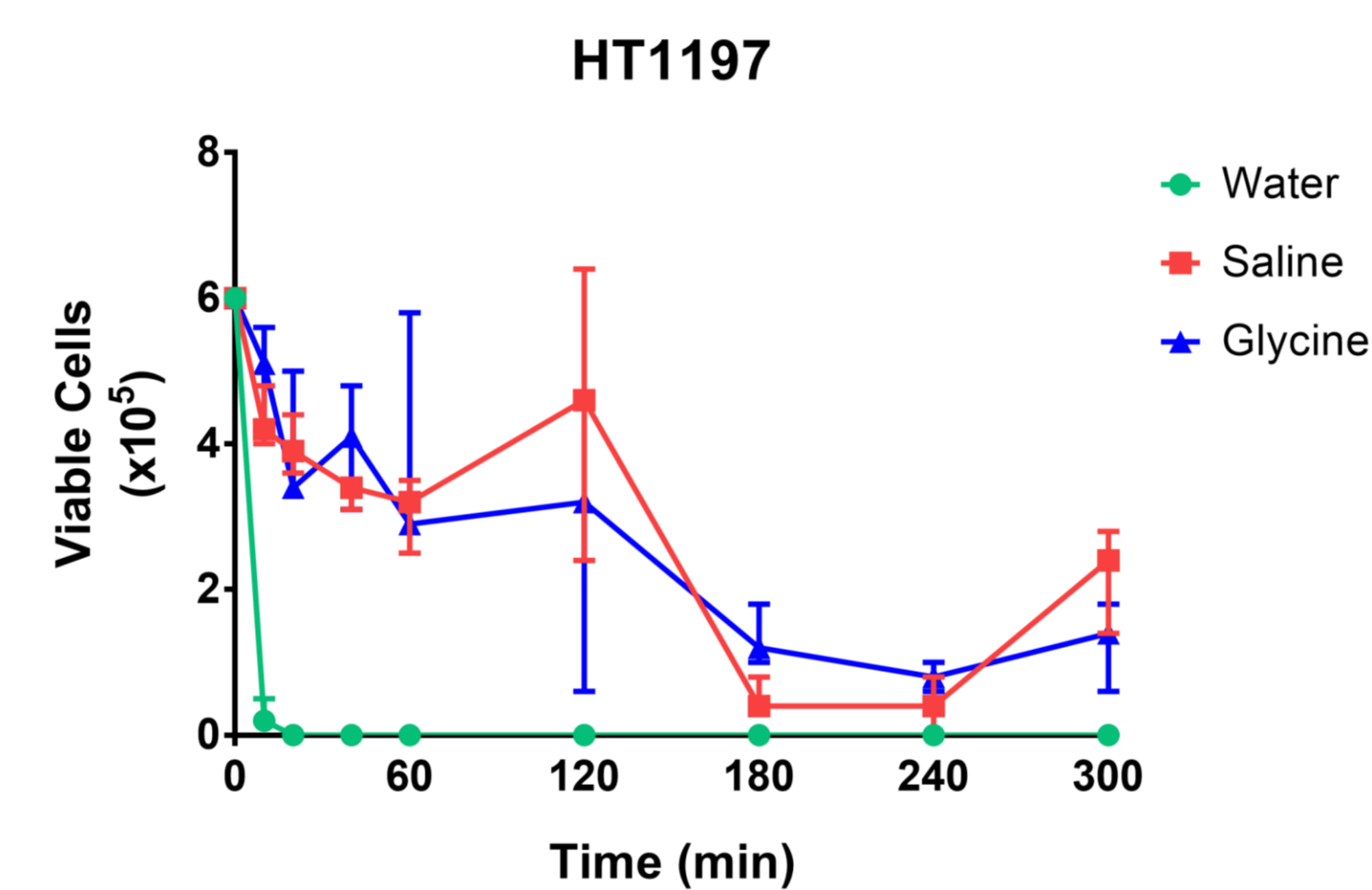


Figure 1. Viable cell numbers for bladder cancer cell line HT1197 when exposed to water, saline or glycine for up to 5 hours.

IN VIVO (Figure 3)

- 14 patients received water irrigation *in vivo*
 - Time 0 (median) = 14×10^3 cells
 - 1 hour onwards (median) = 0 cells
- 9 patients received saline irrigation *in vivo*
 - Time 0 (median) = 40×10^3 cells
 - 3 hours (median) = 20×10^3 cells
 - Median cell count never reached zero

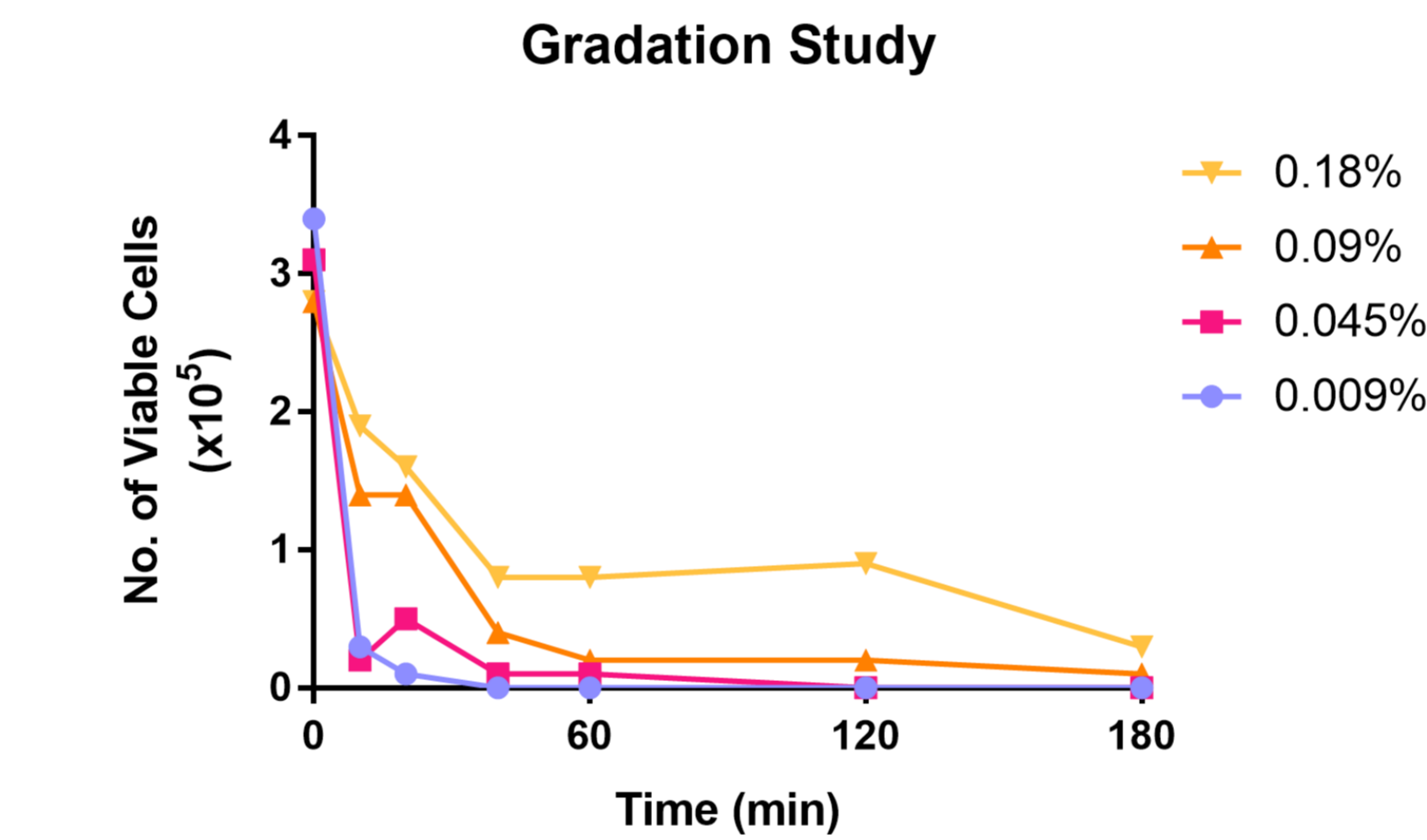


Figure 2. Viable cell numbers for bladder cancer cell line HT1197 when exposed to decreasing concentrations of NaCl. Data represents median values of n = 3 measures

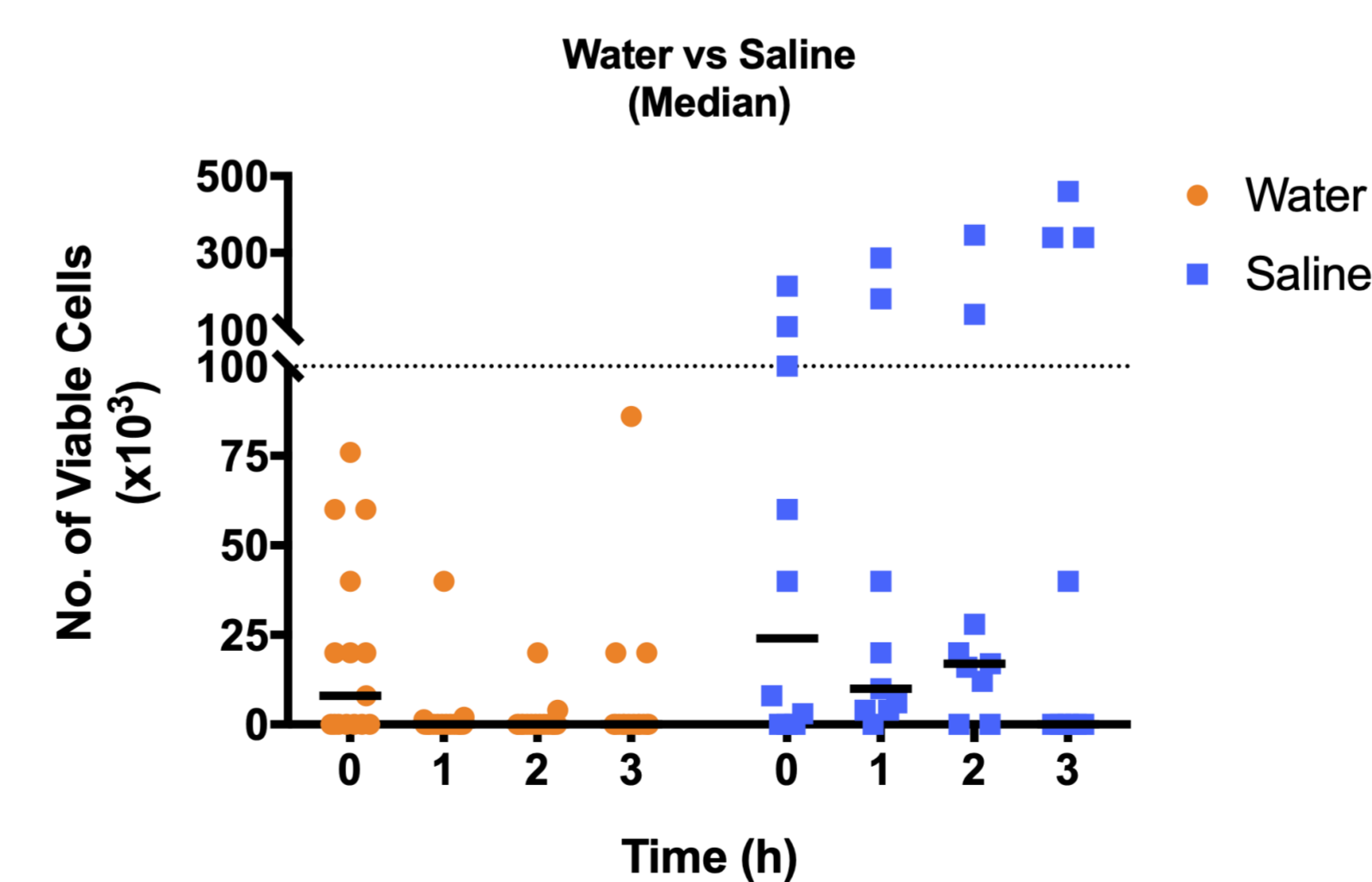


Figure 3. Water vs saline *in vivo*

RESULTS CONT.

- IHC (Figures 4 & 5) on *ex vivo* samples showed significant numbers of bladder epithelial cells in saline-irrigated patients and low numbers in water-irrigated patients
- Cytokeratin 7 (CK7) shows bladder epithelial cells in brown

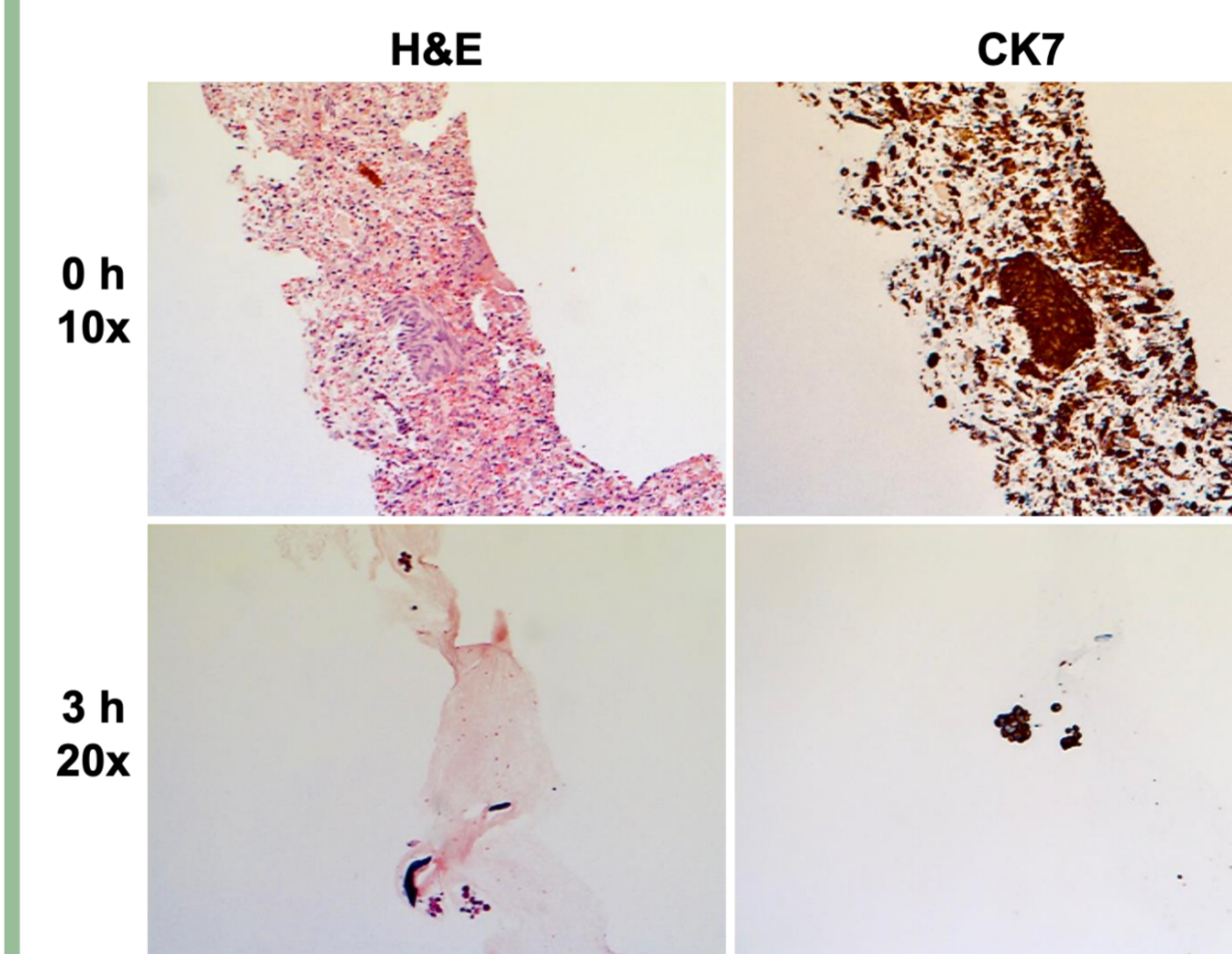


Figure 4. IHC for a saline-irrigated patient

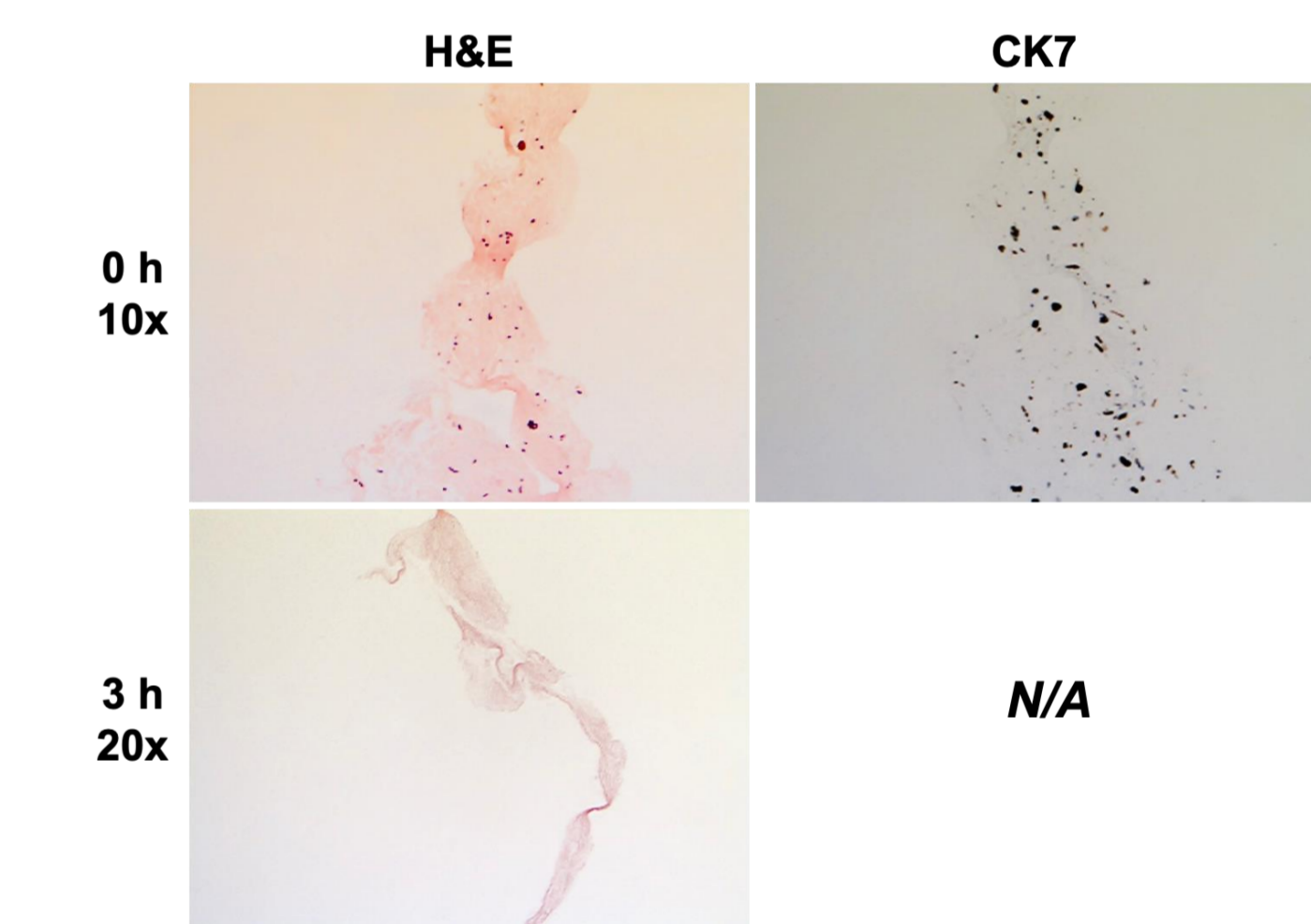


Figure 5. IHC for a water-irrigated patient

CONCLUSIONS

Water is able to rapidly lyse bladder cancer cells *in vitro* and *in vivo*. A short 3-hour period of water irrigation post-TURBT may be an effective intervention to reduce bladder cancer recurrence

- Water is able to lyse viable cells in at least 4 other cancer cell lines
- An increase from 0% NaCl (pure water) to 0.045% NaCl is sufficient to alter the efficiency of cytolysis

ACKNOWLEDGEMENTS

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