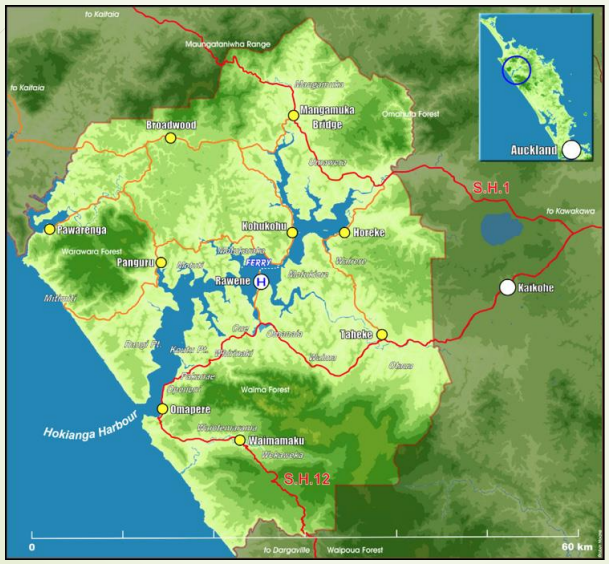
Reflections on my Bladder Problems

A tale of being a patient, denial as a coping strategy and the costs involved, with pointers to perhaps a better option.

Rural - 1

Rural - 2

Rural - 3



The Element **Water**: from a dream May 2004

Timeline for my Prostate Surgery & Follow-up

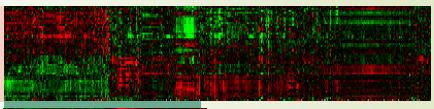
DATE	PROCEDURE	COMMENTS	DIRECT	TRAVEL
Thursday, 28 April 2005	First attack Acute Retention, in Wellington, catheterised, Home on plane with urine bag.		$0.00	$0.00
Saturday, 30 April 2005	Removed catheter. Started on alpha blocker.			
Sunday, 23 October 2005	My 60th Birthday	In the Cook Islands		
Saturday, 12 November 2005	Acute retention again	Consultation with Urologist privately. U/S huge prostate.		
Monday, 14 November 2005	TURP @ Mercy Hospital	Superficial Papillary "Transitional Cell Carcinoma" Grade I found	$12,000.00	NIL
Saturday, 19 November 2005	My 60th Birthday Party.	Back Home		
Thursday, 1 December 2005	Follow-up visit	Histology confirmed Urogenital Carcinoma	$600.00	$440.80
Thursday, 18 May 2006	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Friday, 24 November 2006	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Tuesday, 23 May 2006	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Friday, 24 November 2006	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Tuesday, 8 May 2007	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Monday, 26 May 2008	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Wednesday, 27 May 2009	Follow-up Cystoscopy: Suspicious area seen, Biopsied: No recurrence.		$600.00	$440.80
Friday, 6 November 2009	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Thursday, 17 February 2011	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Wednesday, 9 May 2012	Follow-up Cystoscopy	In Auckland	$600.00	$440.80
Tuesday, 28 May 2013	Follow-up Cystoscopy	In Auckland	$900.00	$440.80
Thursday, 17 July 2014	Follow-up Cystoscopy	In Whangarei	$500.00	$255.00
Thursday, 16 July 2015	CxBladder follow-up test	At Home	$368.00	$0.00
Thursday, 14 July 2016	CxBladder follow-up test	At Home	$368.00	$0.00
Wednesday, 7 June 2017	CxBladder follow-up test	At Home	$368.00	$0.00
Monday, 9 July 2018	CxBladder follow-up test	At Home	$368.00	$0.00
			$21,472.00	$5,544.60

Cxbladder Test: Theory behind detection of UC

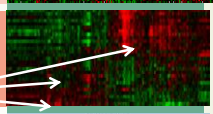
- The test quantifies biomarker mRNA from exfoliated & lysed cells from tumor of the urinary tract (urothelial carcinoma)
- Whole cells are not required for test to be conducted.
- Specific mRNA biomarkers that show differential gene expression between tumor and normal urothelium are detected

Gene Expression Microarrays (from bladder tissue)

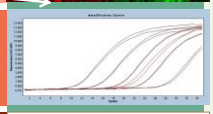
30,000 genes: Bladder tumour vs bladder normal tissue



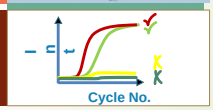
Genes selected for their change in expression in tumour tissue compared with normal tissue



PCR validation of leading genes (1016 candidates)



Select gene candidates that are specifically and reproducibly expressed in tumour urine samples as detected by PCR



5 Gene Signature: Multiplex RT-qPCR

PCR = Polymerase Chain Reaction

10 Years and 3500 patients for development

Cxbladder uses five proprietary biomarkers

- **MDK:** Principally involved in cell proliferation, migration, and angiogenesis in cancer cells
- **HOXA13:** Principally involved in cell differentiation and the morphogenesis and differentiation of the genitourinary tracts
- **CDC2 (CDK1):** Cyclin dependent kinase. Essential to mitotic cell cycle: cell proliferation
- **IGFBP5:** Acts as an anti-apoptotic gene
- **CXCR2:** Mitigates neutrophil migration to areas of inflammation

- Apoptosis = death of cells which occurs as a normal & controlled part of organism's growth & development.

Detection and Management of Urothelial Cancer

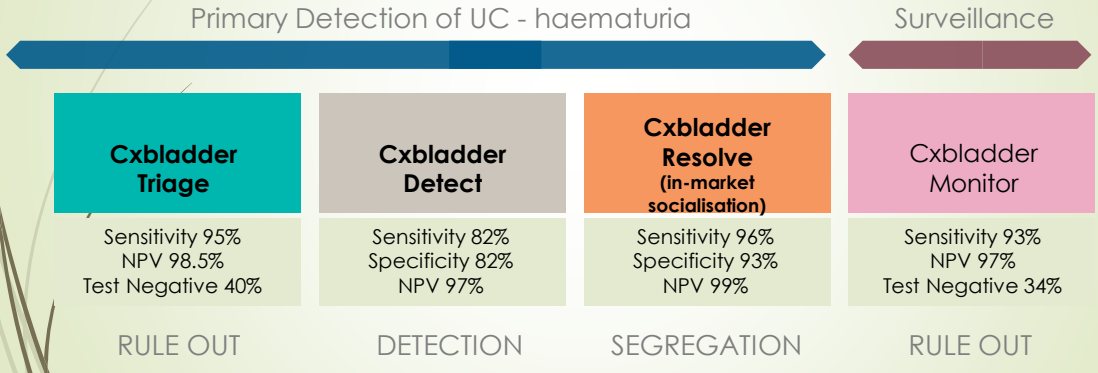
	Cxbladder Triage	Cxbladder Detect	Cxbladder Monitor
Patient Presentation	Primary Detection	Primary Detection	UC Surveillance
Patient Type Examples			
Chronic Microscopic haematuria	X	X	
Young, non-smoker, no occupational exposure	X	X	
Gross Haematuria*	X	X	
Atypical Cytology		X	
Discrepant Result		X	
Renal Insufficiency		X	
Surveillance for UC Recurrence			X

*No visible blood in collection tube

X = Optimized for these patient type examples

Cxbladder Performance

High sensitivity and high Negative Predictive Value (NPV) provide the greatest confidence to RULE OUT the disease when it is not present



Cxbladder – Primary Detection (haematuria)

Cxbladder Triage

Cxbladder Triage is a RULE OUT test combining the power of genomic biomarkers with extra phenotypic and clinical risk factors to accurately identify patients with haematuria who have a low probability of bladder cancer. Cxbladder Triage is intended to reduce of the number of patients needing an expensive and invasive work-up for bladder cancer, is designed for use by GP's prior to urology referral.

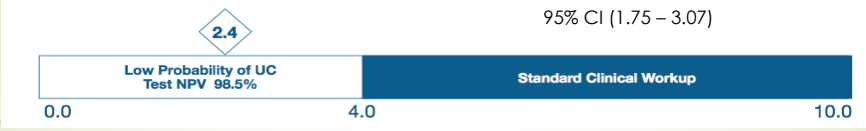
Cxbladder Detect

Cxbladder Detect enables the non-invasive detection of bladder and other urinary tract cancers from a small volume of a patient's urine. Cxbladder Detect optimises both sensitivity and specificity to provide clinicians with a quick, cost effective and accurate measure of the presence of the cancer as an effective adjunct to cystoscopy. Cxbladder Detect is designed for use by urologists as part of a urological workup.

Cxbladder Triage

Accurately segregates low probability patients from high grade and late stage disease

Cxbladder Triage Test Output



Cxbladder Triage Score <4.0	This test has a Negative Predictive Value (NPV) of 98.5%, and a Sensitivity of 95.1%. Low probability of urothelial carcinoma (UC).
Cxbladder Triage Score ≥4.0	Continue with the clinician-directed standard clinical workup to establish if urothelial carcinoma (UC) is present.

- Test Sensitivity: 95.1% NPV: 98.5%

Value Propositions

- Triage out low risk patients that may not require a full workup
- Replace the need for other urine-based tests in primary workup
- Enables patient prioritisation in high throughput settings

Cxbladder Triage now adopted by some DHBs in NZ

Canterbury DHB Health Pathways case study:

- Cxbladder to replace cytology in the primary care referral
- Cxbladder Triage provided, as well as imaging (USS or CT) – ordered by GP
- Cxbladder Triage sample collection done at the local labs,; sent to Dunedin
- Only patients with +ve Cxbladder Triage or +ve imaging are referred to urology
- Initial CDHB study showed 1/3 of ALL haematuria patients could avoid cystoscopy
- **For Cxbladder Triage –ve haematuria assessments, the risk of not performing a cystoscopy is negligible. CDHB data as follows:**
  - Cxbladder Triage sensitivity was 95.5%, NPV 98.6%
  - Pathway (Cxbladder + imaging) sensitivity was 97.7%, NPV 99.3%
  - 32% of all haematuria patients are Cxbladder –ve = no cystoscopy

Cxbladder Monitor – Surveillance for recurrent UC

Cxbladder Monitor combines genomic biomarkers measured from a small quantity of a patient's urine with patient-specific clinical factors to better monitor bladder cancer patients for recurrence of the disease.

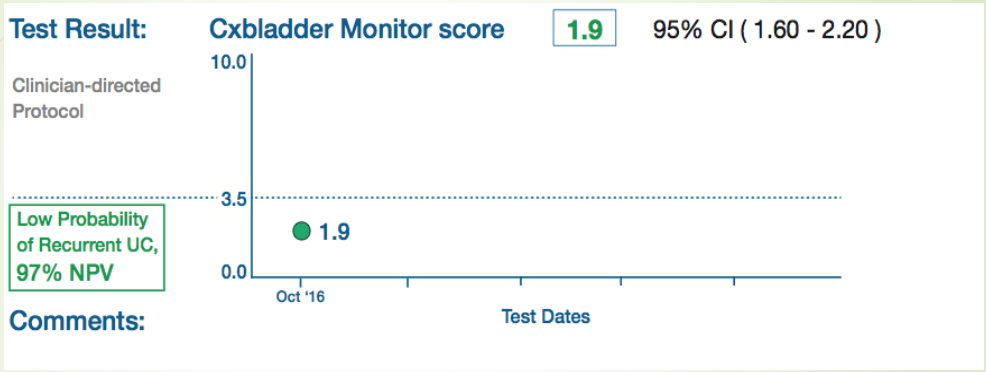
Bladder cancer has a high recurrence rate post treatment (50-80%) and requires life-long surveillance.

Cxbladder Monitor accurately identifies patients with a prior history of UC whose Cxbladder score shows that they have a low probability of recurrent UC.

Applications

- Increase the interval of check cystoscopies with non-invasive testing (low grade)
- Complement cystoscopy to increase surveillance intensity for UC recurrence (high grade)
- Reduce cystoscopy burden on elderly / frail patients or those with co-morbidities

Cxbladder Monitor - Test Output



Cxbladder Monitor Score ≥ 3.5	A clinician-directed protocol to determine the presence of recurrent UC, is warranted.
Cxbladder Monitor Score < 3.5	This test has a Negative Predictive Value (NPV) of 97%, and a sensitivity of 93%. Low probability of recurrent UC.

Cxbladder Monitor: Waitemata DHB case study

- Cxbladder Monitor offered to surveillance patients at WDHB
- Eligibility based on Urothelial Carcinoma history – prior low-grade disease, annual check cystoscopy
- Cxbladder Monitor test alternated between annual check cystoscopies
- Sample collection done at the local labs; sent to Dunedin
- Patients with -ve Cxbladder Monitor (Low Probability) have cystoscopy deferred by 12 months to their next scheduled clinic visit
- Initial WDHB study showed 75% of patients could avoid cystoscopy
- **Flow-on benefits are better patient outcomes:**
  - Maintain surveillance intensity with non-invasive testing
  - Free up hospital resources – staff, theatres
  - Fewer invasive procedures for patients (some are elderly, frail, or have other comorbidities)

The Cxbladder test – can be done in the privacy of your own bathroom.