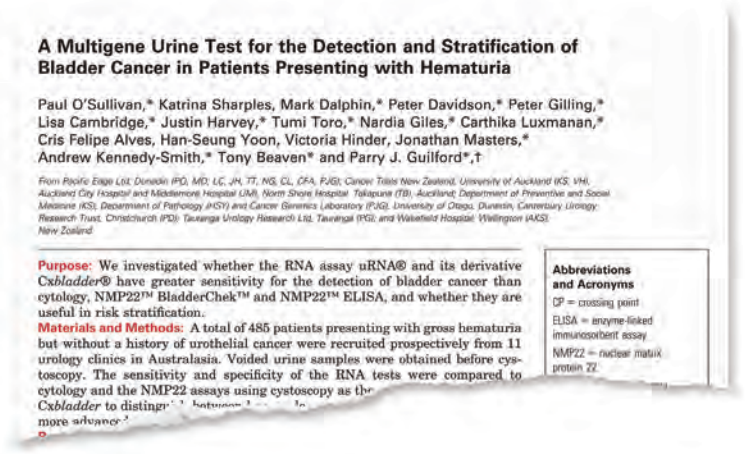
# Cxbladder™ Clinical study

## Introduction to clinical study

The Cxbladder cancer detection test has been validated by a multicentre clinical study. This study was conducted on a prospective cohort of 485 patients with a recent history of gross haematuria, who were under-going investigation for possible urological cancer[1].

## Overview

- Eligible consenting patients provided a freshly voided mid-stream urine sample prior to cystoscopy, for Cxbladder, the NMP22 tests (ELISA and BladderChek) and urine cytology analysis.
- NMP22 ELISA and urine cytology tests were analysed at an independent, accredited testing laboratory.
- NMP22 BladderChek tests were conducted at each clinical site.
- The presence of urinary tract urothelial carcinoma (UC) was determined by biopsy and histopathological examination within a three-month period following study registration.
- Patients who were not diagnosed with UC at three months, but positive for Cxbladder, were followed up at one year to determine disease and survival status.



**A Multigene Urine Test for the Detection and Stratification of Bladder Cancer in Patients Presenting with Hematuria**

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**Purpose:** We investigated whether the RNA assay uRNA® and its derivative Cx*bladder*® have greater sensitivity for the detection of bladder cancer than cytology, NMP22™ BladderChek™ and NMP22™ ELISA, and whether they are useful in risk stratification.

**Materials and Methods:** A total of 485 patients presenting with gross hematuria but without a history of urothelial cancer were recruited prospectively from 11 urology clinics in Australasia. Voided urine samples were obtained before cystoscopy. The sensitivity and specificity of the RNA tests were compared to cytology and the NMP22 assays using cystoscopy as the [illegible] Cx*bladder* to distinguish [illegible] more advanced

**Abbreviations and Acronyms**

CP = crossing point

ELISA = enzyme-linked immunosorbent assay

NMP22 = nuclear matrix protein 22

O'Sullivan et al: A multigene urine test for the detection and stratification of bladder cancer in patients presenting with hematuria, J Urol 2012; 188: 741-747

## Summary of clinical study outcomes:

- Outperformed comparative tests as an adjunct to cystoscopy.
- Negative Predictive Value (NPV) of 97%.
- Detected 100% of T1-T3, Tis and upper tract tumours.
- Detected 97% of high-grade tumours.
- Detected 68% of Ta tumours as compared to cytology at 35%.
- Distinguished between low grade Ta tumours and other detected UCs with a sensitivity of 91% and specificity of 90%.
- Robust to BPH, cystitis/UTI, haematuria secondary to warfarin, prostatitis and urolithiasis.
- Detected six urothelial carcinoma not identified by cystoscopy during the clinical work-up but confirmed at the 12 month follow-up:
  - 1 x T2 single renal pelvis.
  - 1 x Unk multiple high grade bladder tumours.
  - 1 x T2 single high grade bladder tumour.
  - 3 x Renal pelvic / distal uteric tumours (detected by CT; not path confirmed).
- Overall Sensitivity of 82%.

[1] An incidental recruitment strategy was employed.

# Cxbladder™

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Cxbladder is more reliable and objective than many other urine-based cancer detection tests. With its high sensitivity, Cxbladder makes an effective adjunct to cystoscopy.

## Key clinical study results

| | Cxbladder | Cytology | NMP22 BladderChek | NMP22 ELISA |
|---|---|---|---|---|
| **Tumour stage** | | | | |
| Tis | **100%** | 100% | 0% | 0% |
| Ta | **68%** | 35% | 38% | 35% |
| T1 | **100%** | 69% | 50% | 75% |
| T2 | **100%** | 100% | 22% | 67% |
| T3 | **100%** | 100% | 50% | 100% |
| **Tumour Grade**[1] | | | | |
| Low grade | **69%** | 28% | 41% | 31% |
| Mixed grade[2] | **100%** | 100% | 25% | 75% |
| High grade | **97%** | 83% | 38% | 69% |
| **Tumour Multiplicity** | | | | |
| Single | **79%** | 52% | 33% | 44% |
| Multiple | **92%** | 77% | 62% | 77% |
| **Tumour Location** | | | | |
| Bladder | **80%** | 56% | 40% | 48% |
| Upper Tract | **100%** | 50% | 0% | 75% |
| **Overall Sensitivity** | **82%** | 56% | 38% | 50% |
| **Specificity** | **85%** | 96% | 96% | 88% |

[1] WHO/ISUP 1998
[2] Mixed grade indicates the presence of a high grade and a low grade tumour

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