

Multi-domain quantitative recovery following Radical Cystectomy for patients within the iROC (Robot Assisted Radical Cystectomy with intracorporeal urinary diversion versus Open Radical Cystectomy) Randomised Controlled Trial: The first 30 patients

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1 **Multi-domain quantitative recovery following Radical Cystectomy for patients within the**
2 **iROC (Robot Assisted Radical Cystectomy with intracorporeal urinary diversion versus**
3 **Open Radical Cystectomy) Randomised Controlled Trial: The first 30 patients**

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41 interpretation of the data.

42

43 **Take Home Message**

44 We analysed recovery after radical cystectomy using multiple domains reflecting
45 mobilisation (steps per day), exercise capacity (chair to stand), disability, HRQOL and health
46 economics. We found most patients recovered most of their physical capacity by 12 weeks
47 of surgery.

48

49 **Tweet**

50 Activity trackers help measure recovery after major surgery

51

52

53 **Letter**

54 Many patients develop complications after Radical cystectomy (RC) [1]. Reductions in
55 morbidity have occurred through centralization, technical improvements [2] and perhaps
56 through Robot-assisted RC (RARC). Whilst RARC is gaining popularity, there are concerns
57 about oncological safety [3], extra-corporeal reconstruction [4] and RCTs find little
58 difference [5]. We are conducting a prospective RCT comparing open RC and RARC with
59 mandated intra-corporeal reconstruction (iROC [6]). Within this trial we quantify recovery
60 using multiple domains: personal activity trackers, the 30 second Chair Stand Test (CST30),
61 and qualitative questionnaires of disability (WHODAS 2.0), HRQOL (EORTC QLQ-C30 and
62 QLQ-BLM30 [6]) and health economics (EQ-5D-5L).

63

64 Given that little is known of these tools in this setting, we included an internal analysis when
65 the first 30 patients reached the primary outcome (90 days after RC). This was reached 209
66 days after the first recruitment and included 28/30 who underwent their allocated RC
67 (supplementary figures, supplementary table 1). The average time to discharge was 11.0
68 days (st dev. \pm 5.7), and following discharge 20/28 (71%) patients visited their GP or A&E,
69 and 5/28 (18%) were readmitted to hospital. Within 90 days of surgery, the average
70 duration out of healthcare was 76.6 ± 6.7 days. Post-operative complications were seen in
71 15/28 patients, including; Clavien-Dindo Grade 1 in 5/28, Grade 2 in 7/28 and grade 3a/3b in

72 3/28 (11%, supplementary tables). Baseline compliance varied from 22/28 (79%) for activity
73 trackers, 24/28 (86%) for CST30, 27/28 (96%) for WHODAS 2.0, 27/28 (96%) for QLQ-C30, to
74 28/28 (100%) for EQ-5D-5L. The observed values (figure 1) matched the general population
75 (e.g. average WHODAS 2.0 score (15%) was within 78% of general population, CST30
76 (average 13) was similar to that for >65 year old males and >60 year old females [7]) or were
77 slightly lower (age matched Canadian men and women walked 7,869 and 6,970/steps per
78 day, respectively [8]). Compliance with activity trackers and CST30 improved during
79 recruitment as the trial staff became experienced with collection during the perioperative
80 period.

81

82 Each measure deteriorated after surgery (figure 2). At day 5 (POD5) the average number of
83 daily steps was 1840 ± 1348 ($32 \pm 22\%$ baseline) and CST30 was 8.3 ± 5.3 ($62.0 \pm 38\%$ baseline).
84 Activities levels improved such that by week 5 walking reached $74 \pm 32\%$ of the baseline
85 (4294 ± 2370 steps/day) and CST30 reached $96 \pm 35\%$ baseline ($12 \pm 4.3/30$ seconds). By week
86 12 many patients had returned to their baseline level of activity (average steps/day
87 6375 ± 3246 , $99 \pm 47\%$ baseline and CST30 13 ± 5 , $108 \pm 33\%$). Patient reported qualitative
88 disability scores contrasted activity levels. At week 5, WHODAS 2.0 disability reached
89 $26 \pm 22\%$ (which was 2.9 ± 3.3 fold higher than at baseline), before returning to pre-operative
90 levels in most patients by week 12 (0.9 ± 1.1 fold baseline). Changes in EQ-5D-5L scores rating
91 'health today'(Q6) and QLQ-C30 (Q29: overall health and Q30: QOL in past week)
92 questionnaires mirrored activity levels with lower scores in week 5 (EQ-5D-5L $84 \pm 17\%$, QLQ-
93 C30(Q29) $80 \pm 22\%$ and QLQ-C30(Q30) $78 \pm 23\%$ of baseline) that recovered to baseline by
94 week 12 ($93 \pm 17\%$, $98 \pm 16\%$ and $93 \pm 16\%$, respectively). Patients seeking medical review after
95 discharge (GP, A&E or hospital admission) averaged fewer daily steps at week 5 (medical
96 review: 4069 ± 2526 vs. no review: 4743 ± 2132) and week 12 (5535 ± 1786 vs. 6724 ± 3703), and
97 had lower absolute CST30 numbers at the same times (week 5: 11.2 ± 4.3 vs. 13.0 ± 4.4 and
98 week 12: 13.2 ± 5.5 vs. 13.5 ± 3.1), although the low sample size precluded meaningful
99 statistical comparison. We hypothesised that multiple domains are needed to robustly
100 measure recovery after RC and that accurate measurement will allow a meaningful
101 comparison between open RC and RARC. Correlation of baseline data revealed no significant
102 associations between measures of activity, qualitative disability or QOL data (Pearson
103 correlation all $p > 0.08$). Average daily steps was not correlated to CST30 ($r = -0.08$, $p = 0.7$ in 20

104 patients) and was closest to the QLQ-C30 domain reflecting QOL ($r=0.41$, $p=0.08$). In this
105 small sample size, one could hypothesise that daily steps reflect actual activity whilst CTS30
106 is a measure of lower limb strength and exercise capacity (which may not be used).

107

108 In conclusion, we report multi-domain measurements of recovery after RC. Our measures
109 appear well tolerated by patients, are applicable to routine practice, are likely to be useful
110 within our RCT and in the RC pathway.

111 **Figure legends**

112 Figure 1. Distribution of multi-domain measurements at recruitment (baseline).

113 Figure 2. Multi-domain measurements of RC recovery over the first 26 weeks after RC.

114 Supplementary figure 1. Recruitment within iROC. a). Consort diagram of iROC feasibility
115 phase recruitment and b). histogram of length of stay and primary outcome measure (days
116 alive out of hospital/healthcare).

117 Supplementary figure 2. Recruitment within iROC.

118 Supplementary Table 1. Patients and tumours within the iROC feasibility phase.

119 Supplementary table 2. Complications seen after surgery.

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123 **References**

- 124 [1] Leow JJ, Cole AP, Seisen T, Bellmunt J, Mossanen M, Menon M, et al. Variations in the
125 Costs of Radical Cystectomy for Bladder Cancer in the USA. *Eur Urol.* 2018;In Press.
- 126 [2] Pang KH, Groves R, Venugopal S, Noon AP, Catto JWF. Prospective Implementation of
127 Enhanced Recovery After Surgery Protocols to Radical Cystectomy. *Eur Urol.* 2018;73:363-
128 71.
- 129 [3] Ng CK, Kauffman EC, Lee MM, Otto BJ, Portnoff A, Ehrlich JR, et al. A comparison of
130 postoperative complications in open versus robotic cystectomy. *Eur Urol.* 2010;57:274-81.
- 131 [4] Desai MM, Gill IS. "The devil is in the details": randomized trial of robotic versus open
132 radical cystectomy. *Eur Urol.* 2015;67:1053-5.
- 133 [5] Tan WS, Khetrupal P, Tan WP, Rodney S, Chau M, Kelly JD. Robotic Assisted Radical
134 Cystectomy with Extracorporeal Urinary Diversion Does Not Show a Benefit over Open
135 Radical Cystectomy: A Systematic Review and Meta-Analysis of Randomised Controlled
136 Trials. *PLoS One.* 2016;11:e0166221.
- 137 [6] Catto JWF, Khetrupal P, Ambler G, Sarpong R, Khan S, Tan M, et al. Robot Assisted
138 Radical Cystectomy with intracorporeal urinary diversion versus Open Radical Cystectomy
139 (iROC): protocol for a randomised controlled trial with internal pilot phase. *BMJ Open.* 2018;
140 In revision
- 141 [7] Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength
142 in community-residing older adults. *Res Q Exerc Sport.* 1999;70:113-9.
- 143 [8] Colley RC, Garriguet D, Janssen I, Craig CL, Clarke J, Tremblay MS. Physical activity of
144 Canadian adults: accelerometer results from the 2007 to 2009 Canadian Health Measures
145 Survey. *Health Rep.* 2011;22:7-14.
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148 Supplementary table 1. Patient features within the iROC feasibility phase.

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150

	n	%
Sex		
Male	23	76.7%
Female	7	23.3%
Age		
Average \pm st. dev.	67.9	\pm 11.7
>75	10	33.3%
ASA		
1	5	16.7%
2	12	40.0%
3	4	13.3%
Missing	9	30.0%
Reconstruction		
Ileal conduit	22	73.3%
Neobladder	5	16.7%
Missing	1	3.3%
BMI		
Average \pm st. dev.	27.01	\pm 3.4

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154

155 Supplementary table 2. Complications seen after surgery.

156

Patient	Grade of complication	Detail
2	Grade II	Systemic sepsis, ileus, blocked catheter
3	Grade II	Infection of unknown origin
6	Grade I	Wound - Hernia
7	Grade I	Gastrointestinal - ileus and emesis
8	Grade IIIb	Surgical - Incisional hernia. Small bowel obstruction
10	Grade II	Wound - Wound infection
11	Grade II	Genitourinary - Urosepsis and renal failure
13	Grade I	Gastrointestinal - Diarrhoea
19	Grade II	Cardiac - Arrhythmia
20	Grade I	Scrotal swelling. Anaemia not requiring transfusion
21	Grade IIIb	Obstructed common Bile Duct. Urinary infection.
26	Grade I	Gastrointestinal - Constipation
27	Grade IIIb	Cardiac - Myocardial infarction
31	Grade II	Ileus. TPN line.
34	Grade II	Oral Thrush

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