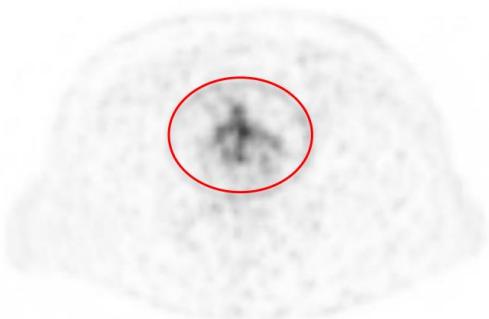
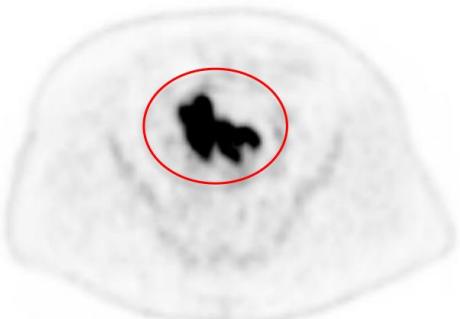
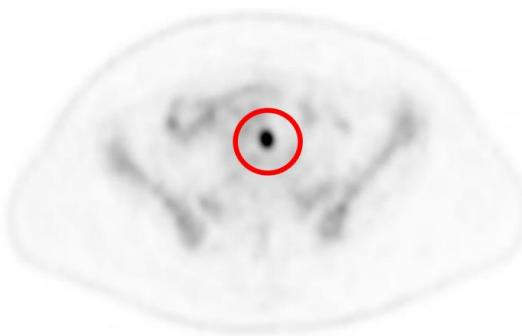
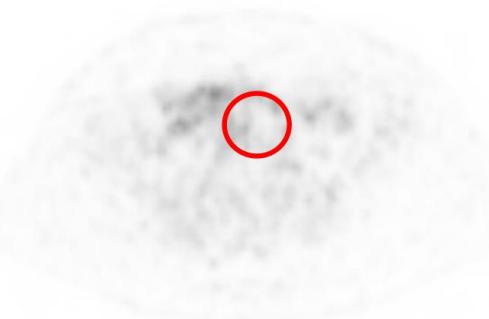
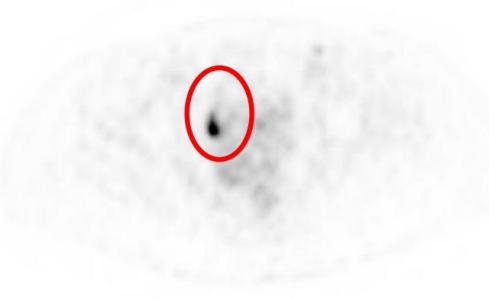
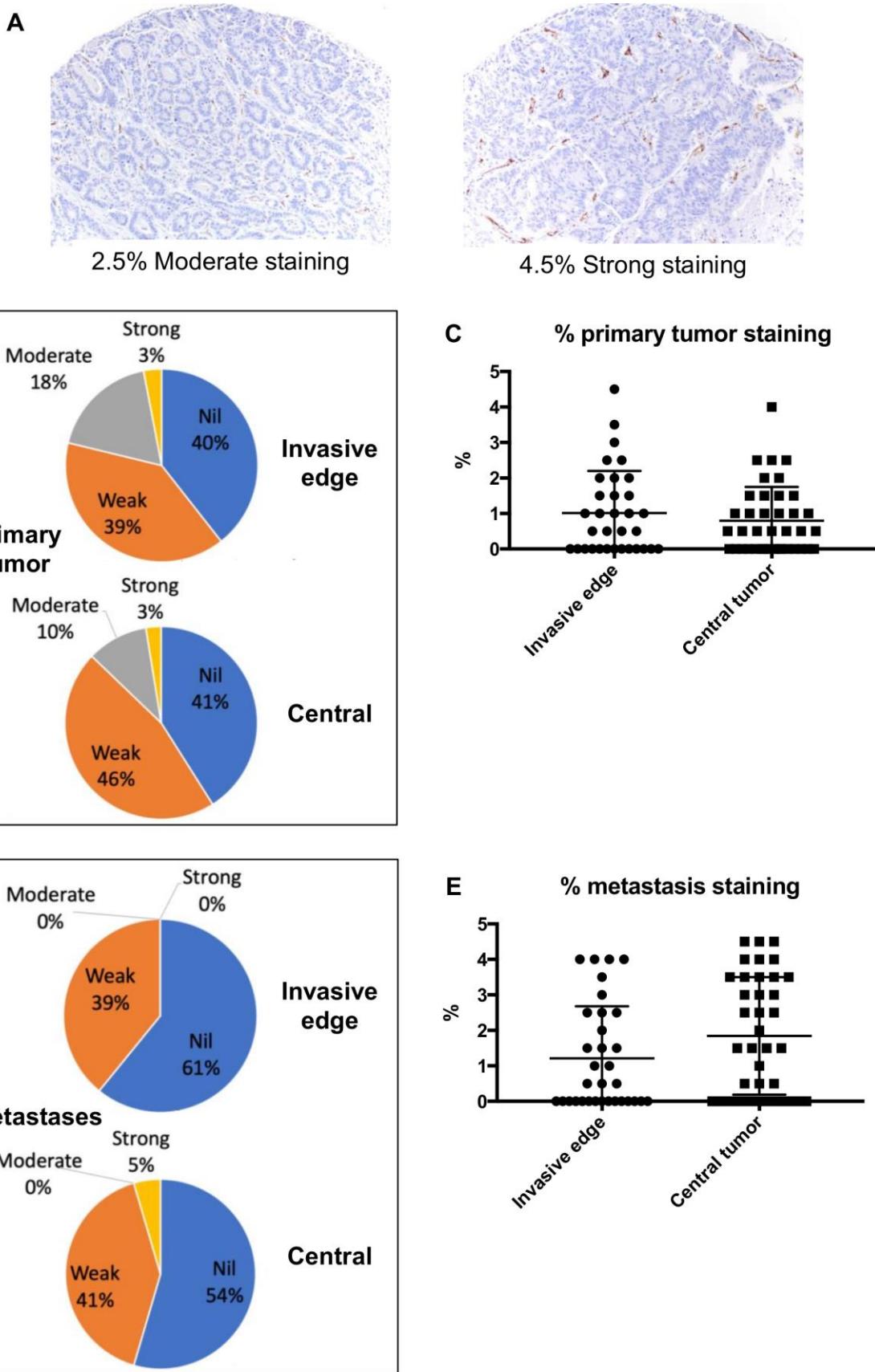


^{68}Ga -PSMA-11 PET**A****FDG PET****B****C**

SUPPLEMENTAL FIGURE 1. Representative ^{68}Ga -PSMA-11 PET and FDG PET axial images demonstrating low SUV_{max} in malignant lesions of patients imaged with ^{68}Ga -PSMA-11 PET (left) versus high SUV_{max} of the same lesions during FDG PET (right). **A** Primary sigmoid colorectal cancer of patient 7; **B** Pelvic lymph node metastasis of patient 8; **C** Lateral side wall pelvic lymph node metastasis of patient 8.



SUPPLEMENTAL FIGURE 2. **A** Representative images of PSMA staining of primary CRC tumor cores displaying 2.5% of cells with moderate staining and 4.5% of cell with strong staining. **B** Intensity of PSMA staining of central tumor and invasive edge cores of primary CRC tumors. **C** Percentage of whole tumor staining in central tumor and invasive edge cores of primary CRC tumors with mean +/- SD displayed. **D** Intensity of PSMA staining of central tumor and invasive edge cores of CRC metastases. **E** Percentage of whole tumor staining in central tumor and invasive edge cores of CRC metastases with mean +/- SD displayed.

Supplemental Table 1. Inclusion and exclusion criteria of ^{68}Ga -PSMA-11 PET-CT pilot study participants

Inclusion criteria:	Exclusion criteria:
<p>1. ≥ 18yo, male or female</p> <p>2. Histologically confirmed colorectal non-mucinous adenocarcinoma (not signet ring/mucinous)</p> <p>3. Metastatic colorectal cancer</p> <p>4. Patient of RBWH or Redcliffe Hospital Health Services</p> <p>5. No current or recent chemotherapy, external beam radiation, immunotherapy, radiological, angiogenesis inhibitors up to four weeks prior for all therapies except angiogenesis inhibitors bevacizumab for at least eight weeks;</p> <p>6. Adequate hemopoietic (58):</p> <ul style="list-style-type: none"> i. Absolute neutrophil count $>1.5 \times 10^9/\text{L}$ ii. Platelets $>150 \times 10^9/\text{L}$ iii. Hemoglobin $>5.6 \text{ mmol/L}$ <p>7. Adequate hepatic function (total bilirubin not more than twice the upper limit of normal (ULN), aspartate transaminase/alanine transaminase not more than three times ULN) (58)</p> <p>8. Adequate renal function (serum creatinine not more than twice ULN, Cockcroft clearance $>50 \text{ ml/min}$) (58)</p> <p>9. No known problems of peripheral venous access</p> <p>10. Able to provide informed, signed consent</p>	<p>1. Concurrent malignancies, except non-melanoma skin tumors or stage 0 (<i>in situ</i>) cervical carcinoma (59)</p> <p>2. Cardiac disease with NYHA classification III or IV or any other illness significantly affecting the patient's clinical condition</p> <p>3. Eastern Cooperative Oncology Group performance status two or greater (58,59)</p> <p>4. Participation would delay imminent conventional treatment</p> <p>5. Pregnant or breast feeding (59)</p> <p>6. Patient without capacity</p> <p>7. Lives a distance from Brisbane Herston Imaging Research Facility (HIRF) requiring extensive travel</p> <p>8. Administered a radioisotope within five half-lives before intended ^{68}Ga-PSMA-11 imaging (59)</p> <p>9. Patients with allergies to PSMA agent</p> <p>10. Patient with a concurrent or history of PC or raised PSA indicating prostatic malignancy</p> <p>11. Unable to lie flat for imaging</p>

Supplemental Table 2. Characteristics of study participants

Characteristic	Total number of patients
Age - mean (SD)	62.1 (+/-10.1)
Male:female	6:4
Primary tumor site	Right colon n=3 Left colon n=1 Sigmoid n=1 Rectosigmoid n=1 Rectum n=3 Not identified n=1
Location of metastases	Abdominal/pelvic LN n=4 Bone n=2 Liver n=4 Lung n=4 Peritoneal/omental n=1 Soft tissue n=1
Histological grade	Mod diff n=8 Poorly diff n=2
Therapy before imaging	Adj CTx n=2 LCCRTx n=1 Pall CTx n=2

*Adj CTx, adjuvant chemotherapy; LCCRTx, long course neoadjuvant chemoradiotherapy; LN, lymph nodes; mod diff, moderately differentiated; n, number of patients; pall CTx, palliative chemotherapy; poorly diff, poorly differentiated.

Supplemental Table 3. Patient demographics

Patient	Gender	Age	Primary location	Metastasis sites	Tumor histological grade	TNM stage	Microscopic inv	Mismatch repair proteins	BRAF/KRAS	Neoadj/adj prior to imaging	Surgical resection
1	F	69.9	R colon	Liver	Mod-diff	T4aN1bM1aR0	VI, LI, TB	Intact	NT	Nil	R hemi
2	M	76.3	Not identified	Lung	Mod-diff	TxNxM1a (biopsy only)	Biopsy only	NT	NT	Nil	Nil
3	M	65.3	Rectal	Lung Liver Iliac LN Omental	Mod-diff	T4aN0M1aR2	PI, TB	Intact	NT	Pall CTx	TATME
4	M	71.0	Rectal	Lung	Mod-diff	T3N2bM1cR0	VI, TIL	NT	KRAS mutation	Pall CTx	APR R hep
5	F	68.0	R colon	Lung Thoracic wall Pararenal	Mod-diff	T4aN1bM1cR0	VI, LI	Intact	NT	Nil	R hemi
6	M	59.3	Rectosigmoid	Primary tumor Locoregional LN Adrenal Retroperitoneal LN Bone	Mod-poorly diff	TxNxM1c (biopsy only)	Biopsy only	NT	BRAF mutation	Nil	Nil
7	M	49.8	Sigmoid	Primary tumor Mesenteric LN	Mod-diff	T4aNxM1c (biopsy only)	Biopsy only	Intact	NT	Nil	Nil

				Retroperitoneal LN Liver							
8	F	43.8	R colon	Primary tumor Locoregional LN Pelvic LN	Poorly-diff	TxNxM1c	Biopsy only	Intact	Intact	Nil	Nil
9	M	55.8	L colon	Bone	Mod-diff	T3N1aM1b	TB	NT	NT	Adj CTx	HAR Pulm lob
10	F	61.6	Rectal	Liver	Mod-diff	TxNxM1a	Biopsy only	Intact	KRAS mutation	Adj CTx, neoadj LCCRTx	Nil

*adj, adjuvant; APR, abdominoperineal resection; CTx, chemotherapy; HAR, high anterior resection; hemi, hemicolectomy; hep, hepatectomy; LCCRTx, long course chemoradiotherapy; LI, lymphatic invasion; LN, lymph nodes; mod diff, moderately differentiated; neoadj, neoadjuvant; NT, not tested; pall CTx, palliative chemotherapy; PI, perineural invasion; poorly-diff, poorly differentiated; pulm lob, pulmonary lobectomy; TATME, transanal total mesorectal excision; TB, tumor budding; TIL, tumor infiltrating lymphocytes; VI, venous invasion.

Supplemental Table 4. ^{68}Ga -PSMA-11 SUVmax and tumor:liver background

Patient	Tumor/metastatic site	PSMA SUVmax	Tumor:liver b/g ratio	FDG SUVmax
1	Liver	5.6♦	1.8	10.8
2	Lung	3.3■	0.7	-
3	Lung	9.3	1.2	-
	Liver	10.1	1.3	
	Iliac LN	3.9	0.5	
	Omental	3.2	0.4	
4	Lung	5.6	0.5	-
5	Lung	2.3	0.4	15
	Thoracic wall	3.3	0.5	13
	Pararenal	4.3	0.7	20
6	Primary tumor	5.4	0.6	-
	Locoregional LN	2.9	0.3	
	Adrenal	NA	NA	
	Retroperitoneal LN	5.8	0.6	
	Bone	18.7	2.1	
7	Primary tumor	8.0	1.1	43.7
	Mesenteric LN	3.5	0.5	6.3
	Retroperitoneal LN	NA	NA	3.3
	Liver	NA	NA	8.3
8	Primary tumor	10.4	1.4	23.7
	Locoregional LN	4.7	0.6	19.1
	Pelvic LN	10.4	1.4	23.4
9	Bone	5.6	1.1	-
10	Liver	NA	NA	22.0

*NA, lesions not avid; LN, lymph node; ♦, only partial lesion avidity; ■, some lesions not avid; -, imaging not available or not performed.

Supplemental Table 5. Lesion count of ^{68}Ga -PSMA-11, FDG AND ceCT

Patient	Tumor/metastatic site	FDG no. of lesions	ceCT no. of lesions	PSMA no. of lesions	Number of missed lesions by PSMA	% missed lesions
1	Liver	1	1	1♦	0	100
2	Lung	25	13	9	16	64
3	Lung	OD	16	10	6	37.5
	Liver		4	1	3	75
	Iliac LN		1	1	0	0
	Omental		1	1	0	0
4	Lung	NP	21	2	19	90.4
5	Lung	3	6	2	4	66.7
	Thoracic wall	1	1	1	0	0
	Pararenal	1	1	1	0	0
6	Primary tumor	1	1	1	0	0
	Adrenal	1	1	0	1	100
	Bone	12	2	6	6	50
7	Primary tumor	1	1	1	0	0
	Mesenteric LN	3	3	1	2	66.7
	Retroperitoneal LN	5	5	0	5	100
	Liver	1	0	0	1	100
8	Primary tumor	1	1	1	0	0
	Locoregional LN	1	1	0	1	100
	Pelvic LN	2	2	0	2	100
9	Bone	1	1	1	0	0
10	Liver	9	9	0	9	100

*no., number; LN, lymph nodes; ♦, only partial lesion avidity; OD, outdated scan, NP, scan not performed.

Supplemental Table 6. Days from ^{68}Ga -PSMA-11 PET

Patient	FDG PET-CT	ce-CT
1	+1	-27
2	-90	+1
3	-1206	-82
4	NA	-16
5	-41	-54
6	-8	-13
7	-13	-28
8	-7	-38
9	-45	-1
10	-252	-216
Median	-41	-27.5

*NA, not applicable – scan not performed

Supplemental Table 7. Total number of primary tumor and metastasis sites of independent cohort of patients included in TMA

Site	Total number of samples
Primary tumors	
L colon	14
R Colon	9
Rectal	14
Metastasis sites	
Bladder	1
Bone	1
Brain	3
Liver	26
Lung	6
Omentum	2
Ovary	1
Soft tissue	3
Spleen	1

Supplemental Table 8. Individual patient demographics of TMA

Patient	Primary tumour site in TMA	Individual metastasis sites in TMA	Initial T stage	Initial N stage	Initial M stage
1	Rectal	Liver	3	1	0
2	Rectal	Liver, Brain	3	0	0
3	Rectal	Lung, Lung	3	0	0
4	L colon	Liver	3	1	1
5	L colon	Liver	2	1a	1a
6	R colon	Liver, Liver	3	1b	0
7	Rectal	Liver	4a	2a	1
8	L colon	Liver	3	2b	1
9	Rectal	Lung	2	0	1
10	Rectal	Lung	3	0	0
11	L colon	Liver	3	0	0
12	Rectal	Liver	3b	2b	1a
13	Rectal	Liver, Lung, Spleen, Bladder	3	0	0
14	L colon	Liver	3	0	0
15	R colon	Liver	4a	2a	1
16	Rectal	Bone, Liver	3c	1	0
17	Rectal	Liver	2	0	0
18	R colon	Liver	4a	1b	1a
19	R colon	Liver	4a	0	1
20	L colon	Liver	3	1b	1
21	R colon	Omentum	4a	1a	0
22	L colon	Liver	3	0	0
23	Rectal	Brain	3	0	0
24	Rectal	Liver	2	1a	0
25	L colon	Soft tissue	4	0	0
26	L colon	Ovary	3	1a	
27	L colon	Omentum	4	1b	1b
28	R colon	Liver	4a	0	1
29	L colon	Liver	2	1a	1
30	Rectal	Brain	3	0	0
31	L colon	Lung	3	0	0
32	R colon	Lung	4b	1b	0
33	L colon	Liver	4b	1b	1a
34	L colon	Soft tissue	4	2	1
35	R colon	Soft tissue	4a	1a	1
36	Rectal	Liver	3	0	0
37	R colon	Liver	3	0	1a