FMISO-PET & perfusion CT at baseline & week 2 CRT as predictive markers for response in rectal cancer

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Background

- Patients with locally advanced rectal cancer are considered for neoadjuvant chemo-radiotherapy (CRT) if they have high risk operable or borderline/unresectable disease[1]
- Around 15% of patients having CRT have a complete pathological response with a similar proportion showing minimal tumour response[2]
- Hypoxia reduces response to RT and is associated with a more aggressive phenotype[3]
- This study explores the predictive value of hypoxia functional imaging using FMISO-PET and perfusion CT (pCT) in patients undergoing CRT for rectal cancer

Methods

- Patients were recruited from Churchill Hospital, Oxford University Hospitals NHS Foundation Trust, UK from October 2013 to April 2016
- Inclusion criteria were:
  - Undergoing neoadjuvant CRT for confirmed rectal adenocarcinoma
  - ≥18 years old with performance status 0-2
  - MRI demonstrating mesorectal fascia, levators or anal sphincter were involved or threatened (≤1mm) by tumour
- Imaging with FMISO-PET and pCT was done at baseline and during week 2 CRT
- FMISO SUVmax, pCT blood flow (BF) and blood volume (BV) were obtained:
  - Tumour region of interest (ROI) outlined by radiologist on contemporaneous T2W MRI
  - Rigid registration and transposition of ROI to pCT or FMISO-PET CT on Varian Eclipse
  - FMISO-PET tumour (T) and muscle (M) SUVmax obtained using PMOD software
  - GE perfusion 4.0 maps created and analysed using MIRADA DBx to obtain BV and BF

pCT

- All patients had evaluable pCT at baseline and week 2 CRT (Table 1)
- There was no relationship with response seen (Figure 1)

Figure 1: Change in median BF (a) & BV (b) from baseline to week 2 CRT
Poor (red) or good (blue) response

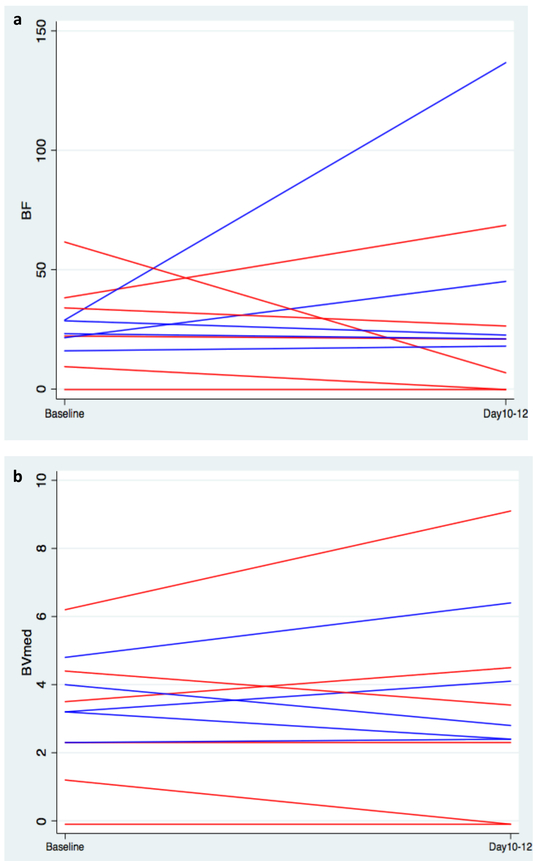

Table 1: Median BV and BF (IQR) at baseline and during chemoradiotherapy

Parameter	Baseline	Week 2 CRT
BV	3.2 (2.1)	2.8 (2.2)
BF	23.2 (18)	21 (38.3)

Table 2: Change in Tumour:Muscle (T:M) SUVmax ratios between baseline and week 2 CRT
U/E unevaluable, N/A non-applicable

#	Response	T:M SUVmax (baseline)	T:M SUVmax (on CRT)	T:M % change
1	Good	1.4	2.2	157%
2	Good	U/E	U/E	U/E
3	Poor	2.4	1.6	67%
4	Poor	2.8	2.1	75%
5	Good	U/E	1.4	U/E
6	Poor	1.6	N/A	N/A
7	Good	2.3	1.6	71%
8	Good	2.2	1.3	59%
9	Poor	2.1	1.3	62%
10	Good	N/A	N/A	N/A
11	Poor	1.1	1.3	119%

Results

Characteristics

- 11 patients with locally advanced rectal adenocarcinoma were recruited
  - Median age 67 (IQR 19)
  - 9 male (82%)
  - Stage T2 2 (18%), T3 9 (82%)
  - Stage N0 4 (36%), N1 6 (55%), N2 1 (9%)
- All patients had neoadjuvant CRT 45 Gray in 25 fractions with concurrent Capecitabine chemotherapy twice daily
- Imaging was done at median 1 (range 0-14) days before CRT and on day of fraction 10 (7-15) during CRT
- After CRT, 8 (73%) underwent total mesorectal excision, 2 (18%) active surveillance and 1 (9%) declined surgery
- Patients were classed as good (n=6) or poor (n=5) responders based on AJCC v7.0[4] tumour regression grade or response on endoscopy/MRI if no surgery

FMISO PET

- 1 patient did not undergo FMISO scanning due to tracer not being available
- 8/10 4-hour scans were evaluable at baseline and 8/9 during week 2 CRT
- In 5/7 patients with paired evaluable scans, the T:M ratio reduced however this showed no correlation with outcome (Table 2, Figure 2)
- Reasons for scans being unevaluable were (Figure 3):
  - Non-tumour uptake in the lumen due to colonic excretion of FMISO
  - Spill-in from adjacent bladder activity

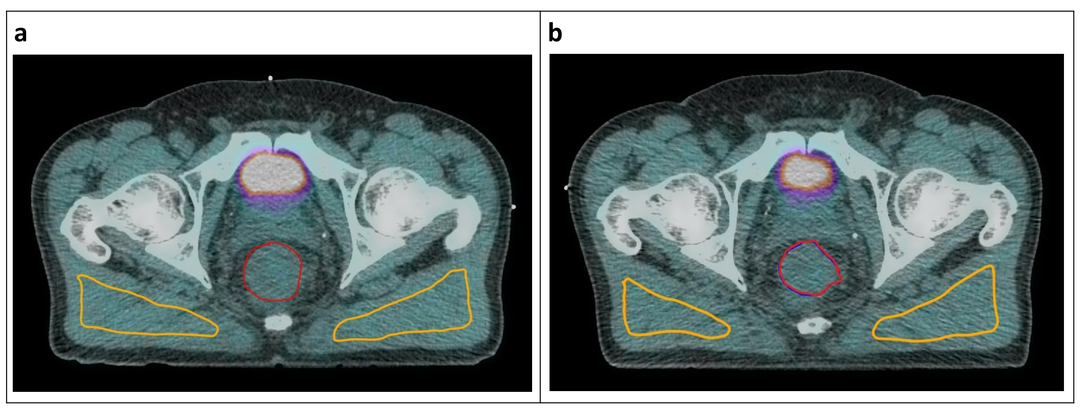

Figure 2: Patient 1 FMISO-PET at baseline (a) and week 2 CRT (b)
(Rectal tumour red, muscle orange)

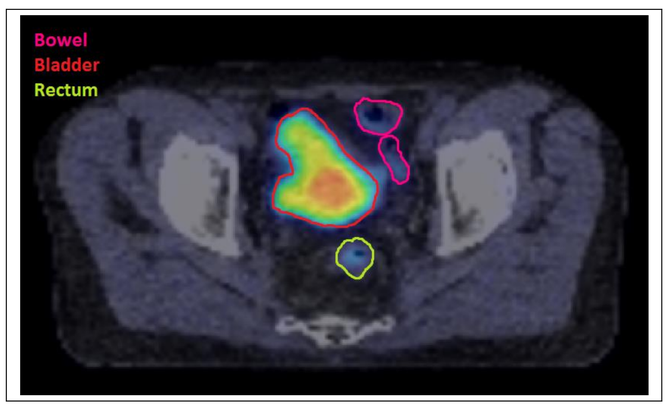

Figure 3: Example of activity seen due to FMISO excretion in bladder and bowel

Conclusions

- In this small pilot study, a reduction in FMISO uptake was not predictive of response based on tumour regression grade/clinical outcome measures
- Significant challenges in delivery and interpretation of FMISO PET scanning for rectal cancer were seen, in particular related to excretion of FMISO
- No association was seen between perfusion CT parameters and response - larger scale studies would be required to establish the value of this modality

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