10.0 APPENDIX

10.1 Response Evaluation Criteria in Solid Tumors (RECIST)[1]

Complete Response:	Disappearance of all target lesions
Partial Response	At least a 30% decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD
Progressive Disease	At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions
Stable Disease	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started

10.2 Modified Mandard Tumour Regression Grade[15]

Grade 1	Radiological complete response (no evidence of ever treated tumour)
Grade 2	Good response (dense fibrosis/ mucin; no obvious residual tumour, signifying minimal residual disease or no tumour)
Grade 3	Moderate response (>50% fibrosis or mucin and visible intermediate signal)
Grade 4	Slight response (little areas of fibrosis or mucin but mostly tumour present)
Grade 5	No response (intermediate signal intensity, same appearances as original tumour)

10.3 Central PET CT Review

A. PET/CT PROTOCOL:

1. Preparation:
• Patients to fast for at least 4 hours prior to scan. If intravenous hydration is given during this period, 0.9% normal saline should be used, NOT dextrose infusion.
• Diabetics on oral medication should ideally be given a morning appointment, asked to fast for 4 hours and should omit their medication.
• Diabetics on insulin should eat and administer their insulin as normal before 4h fast. If blood glucose level is >11mmol/l then consideration should be given to rescheduling the scan. Insulin should not be administered to lower blood glucose.
• Patients to be weighed without shoes and coats (calibrated device with QC program).
• Blood glucose to be recorded using a glucometer (calibrated device with QC program).
• Patients to drink 2-3 glasses of water prior to test to ensure hydration**.**

2. Injection:
• FDG injected via butterfly cannula under quiet conditions.
• Suggest 4.5MBq FDG per kilogram body weight (+/- 10%) under ARSAC 400MBq DRL and local centre discretion of injected activity > 400MBq for heavy patients.
• Assay FDG injectate residue, and record the net activity injected and time of injection.

3. FDG Uptake:
• Patient to remain inactive in a comfortable, warm and quiet environment during uptake time.
• Patient to empty bladder just prior to positioning on scanner bed.
• Emission scan should start at 60 +/- 5 minutes post injection.

4. Acquisition:
• Scan region to cover the base of the brain to the upper thigh.
• Use routine local protocols i.e. time/bed, 2/3D, arms up / down, CTAC etc. • Suggest scanning with arms up if possible for known body lesions only.
• Separate body and head and neck scans can be performed if locally accepted practice.
• The CT attenuation correction scan should be acquired at a maximum of 120kVp and 25mAs or using local protocols if lower.
• A transmission scan can be acquired if part of local protocols, but only CT attenuated PET scans will be used for disease evaluation.
• Patients MUST be imaged on the same PET/CT scanner when rescans are required, and uptake times should be within (+/-5 minutes) of previous scans.

5. Reconstruction Parameters:
• 3-D iterative reconstruction algorithms such as OSEM and RAMLA 3-D with CT attenuation correction using local routine parameters should be used.
.

6. Archive:
• Reconstructed CT, PET AC (CT-attenuated PET) and NAC (non-attenuated PET) data to be archived locally.

7. Quality Assurance and Control:
Under agreed QA and QC protocol – no patient scans till authorization approved.

8. PET/CT data transfer to the central laboratory:
Under agreed data transfer protocols, the following reconstructed and anonymised files should be transferred:

- CT
- PET AC
- PET NAC

A Case Report Form (CRF) should also be completed and sent with the relevant data.

B. PET/CT REPORTING AND REASSESSMENT

Baseline PET-CT will be done at 8 weeks post CRT. Reassessment PET/CT scan will be done at 16 weeks and 1 year after chemoradiotherapy treatment.

• PET/CT scans will be reviewed and scored by two named PET/CT specialists at the core lab. Visual and semiquantitative interpretation will be used. Reviewers will not be blinded to the patient's clinical status. Differences in reporting will be resolved by consensus between two PET/CT specialists at the same core lab or by a third PET/CT specialist at another participating centre where agreement cannot be reached.

The PET/CT response scans will be scored with reference to sites of presumed disease involvement on the PET/CT baseline scan. FDG-PET scan is defined as positive (score 3, 4, 5, X and Y) and negative (score 1, 2). Where PET/CT and MRI response is contradictory, biopsies should be taken to confirm or deny disease recurrence. Further treatment will be determined according to the local protocols and practice.

<u>Negative PET scan:</u>

1 no uptake
2 uptake ≤ mediastinum

NOTE if mediastinal blood pool activity is equal or greater than liver then the uptake within the lesion should be compared with liver (lesion uptake less than liver = score 2)

<u>Positive PET scan:</u>

3 uptake > mediastinum but ≤ liver4 moderately increased uptake compared to liver at any site
5 markedly increased uptake compared to liver at any site
X new areas of uptake unlikely to be related to the primary tumour **(e.g. infective / inflammatory process)**

Y new areas of uptake thought to be related to the primary tumour

Scores 1, 2 with uptake in sites abnormal on the staging scan equal or less than liver uptake will be regarded as 'negative' for disease and scores 3, 4, 5 with uptake greater than liver will be regarded as 'positive' for disease. For the purposes of treatment, patients with a score of 3 will be regarded as negative for disease. Scores 1X and 2X will also be regarded as 'negative' for colorectal carcinoma.

• A local report may also be issued but it is the score from the core lab that will be used to determine subsequent treatment for trial purposes.

C. PET/CT QC procedures

Careful quality control is essential for the success of multi-centre trials such as this. There are currently no standards for performing multi-centre trials with PET and PET/CT, though such standards are being developed by the professional organisations and NCRI PET Clinical trials Centre. The procedures below are based on those of the American College of Radiology Imaging Network.

The study cannot start and no patients are to be scanned until all of the following have been completed at site:

1. The PET/CT scan quality control document (see below) must be completed and forwarded to the core lab.
2. Initial 'start-up' scanner quality control procedures must be performed.
3. Two anonymised representative patient studies must be transferred to the core lab.
4. The data transfer and anonymization procedure must be set up and validated.
5. Written confirmation from the core lab that scanning can now start at your centre must be received.
6. Copy of ARSAC certificate must be sent to RMH GI CTU

Initial start-up QC procedures

Only centres with access to full ring dedicated 2/3-D PET/CT scanners may participate in the PET/CT arm of this study. This restriction should ensure that images acquired at all centres are of consistent quality.

The ACR-approved PET Phantom will be used for evaluating tomographic image quality for PET scanner qualification. All participating centres will be required to complete a preliminary centre qualification form, and carry out in collaboration with the core centre if required an Image Quality Phantom scan using the ACR approved Image Quality Phantom using local clinical protocols. The ACR approved phantom is a Perspex cylinder with an internal radius of 10.8 cm. The faceplate has fillable thin-walled cylinders (8, 12, 16, and 25 mm in diameter), two additional 25 mm cylinders, one for air and one for "cold" water, and a Teflon cylinder. The cylinders with be filled with 25 kBq/ml of 18F- solution, while the rest of the phantom will contain 5 kBq/ml of 18F- to simulate small regions of tracer uptake in the tumours.

The Quality of the ACR-Phantom images will be assessed visually by two nuclear medicine physicians at the core centre, and by measurement of absolute activity for

the background and the active cylinders. If significant discrepancies are observed, for example due to the use of widely differing reconstruction parameters, these will be resolved prior to the start of the study.
A qualified local physicist could carry out this scan, however, if required a member of the core lab team could perform this scan.

Representative Patient Studies
Two anonymised patient studies (CT attenuation corrected PET, CT and non-attenuation corrected PET) acquired using the proposed study protocol should be transferred to the core lab.

Data Format and Archiving
All studies to be transferred to the core lab (CT attenuation corrected PET, non-attenuation corrected PET, and CT) must be in DICOM format. BMP files, jpeg files, screen saves and hard copies are not acceptable. Image data transferred through a PACS system will not be accepted, as many PACS systems convert DICOM images to another format and then reconvert them back to DICOM when exporting to a CD or FTP. Howevere, data could be recorded directly to a CD using the PET scanner's workstation or other multimodality image viewing, and archiving systems like Nuclear Diagnostics (HERMES Medical Solutions) and Link Medical (NMpacs) could be used to transfer data after initial testing and validation by the core lab. Raw data must be archived according to local protocol, and at least until the images have been accepted by the core lab. For full details please refer to section E – data transfer.

Data transfer and anonymisation procedure
All patient identifying information must be removed from the images prior to transfer. A procedure for naming, anonymising and transferring studies from the scanning site must be established. This will vary between sites. This can be validated when transferring the test phantom and patient data as above.

Routine scanner QC procedures
A documented scanner quality assurance program must be in place with records kept, covering daily, monthly, quarterly and annual QC testing. Sample results of the QC procedures together with details of their frequency should be submitted to the core lab for every PET/CT scanner being qualified for use in this trial. The routine CT QC must include a water filled phantom scanned on a weekly basis, to measure image noise and CT number as described in IPEM (Institute of Physics and Engineering in Medicine) Report 91.

Additional scanner QC required during the trial
SUV is used as a primary response end point, therefore accurate and consistent estimation of Standard Uptake Values for all patient scans and between all participating centres is required. This will be achieved via a rigorous and regular testing of SUV accuracy and consistency of all participating scanners. All participating centres are required to perform an SUV validation scan on a monthly basis at least, and phantom scan data and results are sent to the core centre using a Phantom Data Transmittal Form. SUV validation scans are carried out using the local manufacturer-approved SUV phantom (F-18 or Ge-68). The average SUV for a large ROI placed at the centre of the phantom must be 1.0 ± 10% and on visual inspection the image should show no artefacts. The relevant sections of the patient data sheet must be completed to confirm the results of this test. All phantom scans received by the core centre will be reviewed to check consistent scanner performance and accurate SUV measurements. All SUV validation scans should be carried out by local suitably qualified staff.

Furthermore, as this study uses SUVs defined in terms of patient weight, the scales used to weigh the patients must be accurate to within 10% of a standard weight of 70 kg. This must be demonstrated as part of the initial setup via appropriate scales calibration certificates or appropriate testing of the accuracy of the scales.

Confirmation that study can start at your site
When the core centre is satisfied that all the above has been completed satisfactorily, a letter will be forwarded to both the participating PET centre and RMH GI CTU to confirm that the centre can now participate in the trial. No subjects should be scanned before this has been received.

Contact
For enquiries relating to the scanning protocol, please contact the following at the core lab:

Name:	Dr. Sue Chua
Core Lab Centre:	Nuclear Medicine and PET Department The Royal Marsden Hospital Downs Road Sutton SM2 5PT
Phone No:	0208 661 3544
Email Adress:	sue.chua@rmh.nhs.uk

Name:	Dr. Gary Cook
Core Lab Centre:	Nuclear Medicine and PET Department The Royal Marsden Hospital Downs Road Sutton SM2 5PT
Phone No:	0208 661 3921
Email Adress:	gary.cook@rmh.nhs.uk

For enquiries relating to the quality control and data transfer only, please contact the following at the core lab:

Name:	Dr. Salem Sassi
Core Lab Centre:	Joint Department of Physics The Royal Marsden Hospital Downs Road Sutton SM2 5PT
Phone No:	0208 661 3727
Email Adress:	salem.sassi@icr.ac.uk

Name:	Dr. Jonathan Gear
Core Lab Centre:	Joint Department of Physics The Royal Marsden Hospital Downs Road Sutton SM2 5PT
Phone No:	0208 661 1394
Email Adress:	jonathan.gear@icr.ac.uk

For all other enquiries please contact the trial team at RMH CTC

D. PET-CT SCAN QUALITY CONTROL DOCUMENT

Please complete this document and return to the above individuals (names and contacts as above) before any patient from the trial undergoes a PET/CT scan.

Contacts at scanning site –

Person responsible for performing the scanning procedures (and a deputy to cover leave)

Name of Primary Contact:	
Telephone:	
Email:	
Name of Deputy Contact:	
Telephone:	
Email:	

Person responsible for ensuring adherence to QC procedures (and a deputy to cover leave)

Name of Primary Contact:	
Telephone:	
Email:	
Name of Deputy Contact:	
Telephone:	
Email:	

Person responsible for anonymisation and data transfer (and a deputy to cover leave)

Name of Primary Contact:	
Telephone:	
Email:	
Name of Deputy Contact:	
Telephone:	
Email:	

Scanner technical specification

Please confirm that you have a –

Full Ring PET/CT Camera	YES	NO

Please state –

Manufacturer and Model :	
Date of installation :	
Axial field of view :	
Sensitivity in cps/MBq/ml for uniform 20cm cylinder:	

Quality Control Procedures

Is a documented quality QA program in place	YES	NO

Setup and Normalisation

The frequency at which the PM tubes of the PET scanner are set-up is:	
The frequency at which normalization is carried out on the PET scanner is :	

Daily and Weekly PET and CT Checks

CT tube warm up and air calibration are carried out on a daily basis	YES	NO
Manufacturer's recommended daily PET QC test carried out	YES	NO
Please give details of Manufacturer's recommended daily PET QC test, and any further daily QC tests carried out :		
CT number and noise are measured on a weekly basis (described in IPEM Report 91)	YES	NO

Monthly/Annual Quality Control

Sensitivity of the PET scanner checked on at least an annual basis	YES	NO
Annual CT checks are carried out by CT experts on an annual basis(described in IPEM Report 91)	YES	NO
PET-CT scanner alignment is checked on at least an annual basis	YES	NO

Additional Procedures to be Undertaken as Part Of This Study

Scan of a uniform $^{18}F/^{68}Ge$ phantom will be carried out to check image quality and confirm that SUV measures 1.0 ± 10% on a monthly basis.	YES	NO
QC of the weighing scales will be carried out at least annually	YES	NO
If any of the procedures described in this document cannot be carried out for whatever reason the Trial Physicists from the core lab will be contacted immediately and no further studies will be undertaken by your centre until the issues have been resolved	YES	NO

Data Acquisition and Reconstruction

Please supply the following information for the protocol to be used in this study, this will be the protocol used for all data acquired at your centre as part of this trial –

Half body emission scan duration per bed position (give time in minutes)	
Acquisition mode (specify 2D or 3D)	
Slice overlap	

CT details for half body attenuation correction –

mAs :		kVp:		pitch :		slice thickness (mm):	

Emission scan reconstruction parameters –

Matrix size (e.g. 128 * 128 * 31)	
Voxel size (e.g. 2.0 * 2.0 * 2.0 mm3)	
Reconstruction algorithm(e.g. OSEM 3D, RAMLA 3D)	
Smoothing filter and cut-off if used (e.g. Hanning, 0.5 Nyquist)	
Iterative reconstruction algorithm parameters (number of iterations, subsets)	

Signed by person responsible for ensuring adherence to quality control procedures

Name:	
Date:	

PHANTOM SCAN EVALUATION
(to be completed by Core Lab)

PET Centre :	
Scanner Manufacturer and Model :	
QC tests performed by :	
Date :	

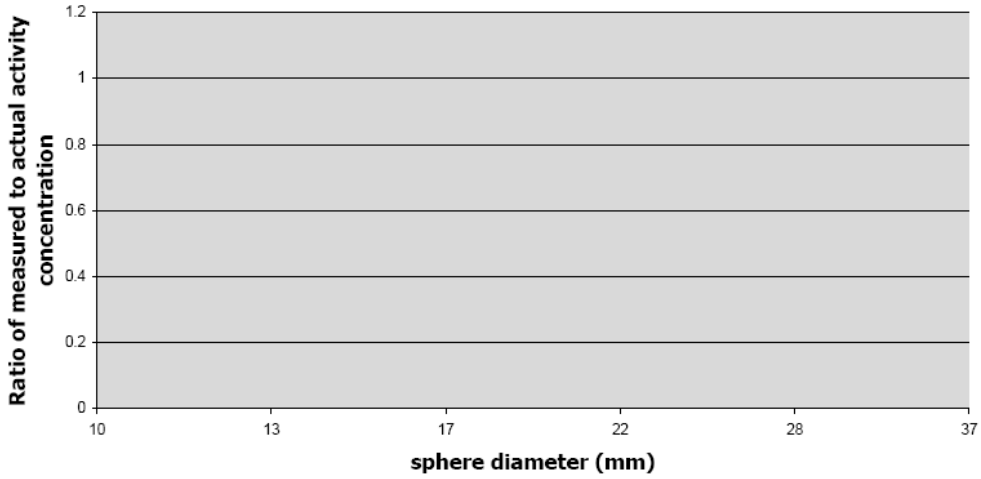
Qualitative Analysis

Image Quality	Acceptable	Not Acceptable
PET/CT alignment on core centre reporting system	Acceptable	Not Acceptable
Comments		

Cylinder activity concentration at scan start time :		kBq/ml
Background activity concentration at scan start time :		kBq/ml

	Activity Concentration		
	Measured (M)	Actual (A)	Ratio
Sphere Diameter(mm)	kBq/ml	kBq/ml	M/A
25			
16			
12			
8			

A recovery curve should be generated from the tabulated data:



Average SUV for a large ROI positioned over the background:_____ (1 ± 0.1)

Recovery Curve	Acceptable	Not Acceptable

TEST PATIENT DATA FOR PET/CT SCAN - PATIENT 1

PET-CT Scan acquired at (PET Centre) :	

Patient's initials :	
Date of PET-CT scan :	

Time of administration of activity (hour:min)	
Activity at time of administration (MBq)	
Patient height (cm)	
Patient weight (kg)	
Patient fasting state (time last ate)	
Patient blood glucose	
Scanner sensitivity in units of Bq/ml(voxel value)	
Daily quality control result for the day of the scan	

	START TIME	NO. OF BED POSITION	DURATION PER BED POSITION	TOTAL SCAN POSITION
HALF BODY EMISSION SCAN				

Test data review (to be completed by Core Lab)

Comments:

APPROVED	DISAPPROVED

NAME DATE

NAME DATE

TEST PATIENT DATA FOR PET/CT SCAN - PATIENT 2

PET-CT Scan acquired at (PET Centre) :	
Patient's initials :	

Date of PET-CT scan :	

Time of administration of activity (hour:min)	
Activity at time of administration (MBq)	
Patient height (cm)	
Patient weight (kg)	
Patient fasting state (time last ate)	
Patient blood glucose	
Scanner sensitivity in units of Bq/ml(voxel value)	
Daily quality control result for the day of the scan	

	START TIME	NO. OF BED POSITION	DURATION PER BED POSITION	TOTAL SCAN POSITION
HALF BODY EMISSION SCAN				

Test data review (to be completed by Core Lab)

Comments:

APPROVED	DISAPPROVED

NAME DATE

NAME DATE

NOTIFICATION TO PET SCANNING FACILITY OF APPROVAL TO SCAN PATIENTS IN TRIAL

From:	
To:	PET Scanning Facility

Fax Number:	
To	RMH Trials Unit
Fax Number:	020 8661 3750

Approved for trial

QC procedures	YES	NO
Scan acquisition and reconstruction parameters	YES	NO
Phantom data and patient test data	YES	NO
Data transfer	YES	NO

Name Date

Patient Test Data	YES	No

Name 1 Date

Name 2 Date

The above named Centre has complied with the requirements for PET/CT scanning and is a recognised scanning facility in the trial. The Centre undertakes to notify the Core Lab immediately of any deviations in QC and scan acquisition or reconstruction parameters from those agreed.

D. DATA TRANSFER

Baseline PET-CT scan data will be reviewed centrally once the patient has been registered into the trial.

Data should be saved on an approved data storage device.. The following files are required:

- CT attenuation corrected half body images (skull base to mid thigh)
- Non-attenuation corrected half body images
- Half body CT scan
- PET/CT report from local imaging team

All image files must be in DICOM format. It is highly recommended that CDs be created directly from the acquisition PET/CT workstation rather than from a secondary PACs system or file library. Specifically, image files that have been converted to savescreens and then reconverted back into DICOM format are NOT acceptable.

A PET/CT acquisition form must be completed and sent with the data CD.

Images and acquisition forms must be sent by post to:
The Deferral of Surgery Trial Coordinator
GI and Lymphoma Unit
Department of Medicine
The Royal Marsden NHS Foundation Trust
Downs Road
Sutton
Surrey SM2 5PT

It is strongly recommended that scans be sent by registered post (recorded or special delivery). These can be tracked on the Royal Mail website.

RMH CTU will forward the scan data to the PET central review team. The PET central review team will review the scan and will fax a report to the site study team and to RMH CTU.

Following review, scan data will be returned to RMH CTU to be archived.

E. ACQUISITION FORM

Timing and Deferral of Rectal Surgery Following a Continued Response to Pre-operative Chemoradiotherapy

ACQUISITION DATA FOR PET-CT SCAN
(To be completed by PET scanning facility)

PET/CT scan acquired at:		PET Centre
Patient's initials:		
Patient's trial number:		
Referring consultant:		
Consultant telephone number:		
Consultant fax number:		
Hospital address:		
Date of PET/CT scan:		
Study timepoint (circle as applicable)	8 weeks / 16 weeks / 1 year	

Time of administration of activity (hour:min)	
Activity at time of administration (MBq)	
Site of tracer administration and state left or right	

Patient height (cm)	
Patient weight (kg)	
Patient fasting state (time last ate)	
Patient blood glucose	
Scanner sensitivity in units of Bq/ml (voxel value)	
Daily quality control result for the day of scan	
Any deviations from the previously forwarded protocol?	
If yes, specify:	

	START TIME	NO. OF BED POSITIONS	DURATION PER BED POSITION	TOTAL SCAN DURATION
HALF BODY SCAN				

10.4 MRI methods & data sheet

Method

Indications and patient preparation The examination should be performed in those patients with histologically proven rectal carcinoma who present for disease staging. Ensuring that the patient is comfortable and pain free will ensure a good quality examination free from unwanted motion artifact. Patients need to be fully informed about the length of time of the scans, be positioned comfortably within the scanner and pain-free. There is no role for purgative bowel preparation or enemas. Small bowel movement is not a problem in our experience therefore anti-peristaltic agents are not indicated. The patient is placed supine on the table and the flexible 4-element phased array body/pelvic coil is placed firmly around the pelvis to ensure good compression and to minimise the possibility of motion. A full bladder is unnecessary and is uncomfortable with the compression from the body coil. The referring surgeon should indicate the tumour position (in terms of height above the anal verge) and any history of past pelvic pathology and surgery. The imaging must be performed before the multidisciplinary meeting to aid in the preoperative decision making process.

Hardware

Magnet

A 1.0T/1.5T system can be used. All of the images presented here have been produced with a 1.5T machine. The main consequence of using a 1.0T magnet is the longer image acquisition times. Equally good images can be produced on these magnets.

Phased array coils:

These coils gain the advantages of the surface coil by obtaining higher signal but with greater coverage than a single surface coil and improved homogeneity.

Sequences recommended in the local staging of rectal cancer:

The initial sequences performed are the localisation images, in the coronal and sagittal planes to image the tumour and plan the high resolution images that are performed axial to the rectum.

- The first series is the sagittal T2W-FSE, which enables identification of the primary tumour
- The second series - large field of view axial sections of the whole pelvis from the iliac crest to the symphysis pubis

Sequence 3:

While the second series is being acquired, the high-resolution images can be planned. The sagittal T2 weighted images obtained are used to plan T2-weighted thin-section axial images through the rectal cancer and adjacent peri-rectal tissues. It is critical that these images are performed perpendicular to the long-axis of the rectum (figure 1).

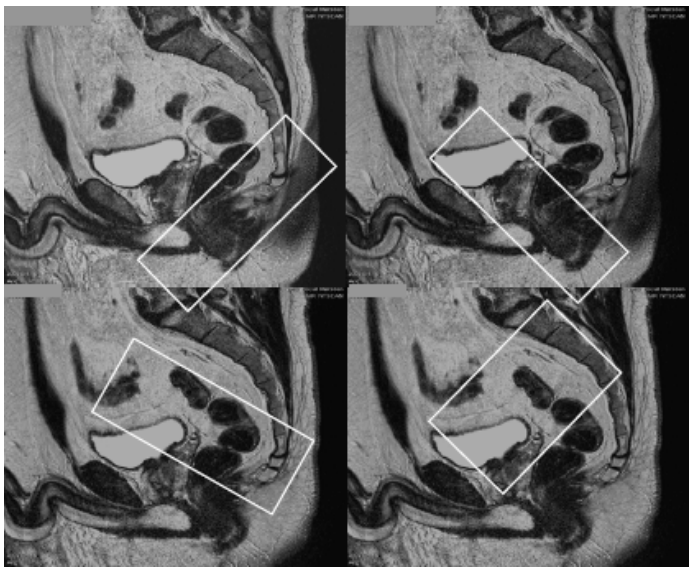


Figure 1

The images are obtained by using a 16cm field of view and 3mm section thickness.

Sequence 4:

The rapid change in calibre of the rectal lumen at the level of the anorectal junction limits the usefulness of oblique axial imaging alone. At this level axial images may not show the rectal wall in its entirety and clear delineation between the outer edge of the rectal wall and the levator muscle may not be possible. This can potentially lead to overstaging. It is therefore useful to utilise a high spatial resolution coronal imaging sequence which will show the levator, the sphincter complex, the intersphincteric plane and the relationship to the rectal wall most optimally (figure 1).

Potential factors that may impair the quality of images

Coil Positioning.

In order to prevent poor signal to noise from the anorectal junction (figure 2),

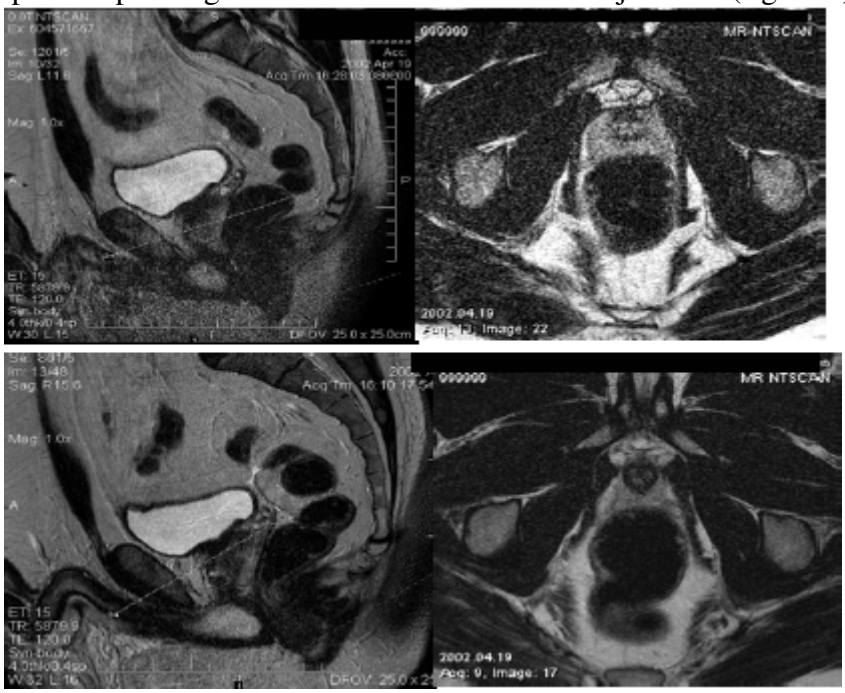


Figure 2

it is important that the phased array coil is centred optimally to ensure adequate coverage of the rectum, mesorectum and anal sphincter complex.

Thus there should be adequate coverage from the level of the sacral promontory to below the symphysis pubis (figure 3).

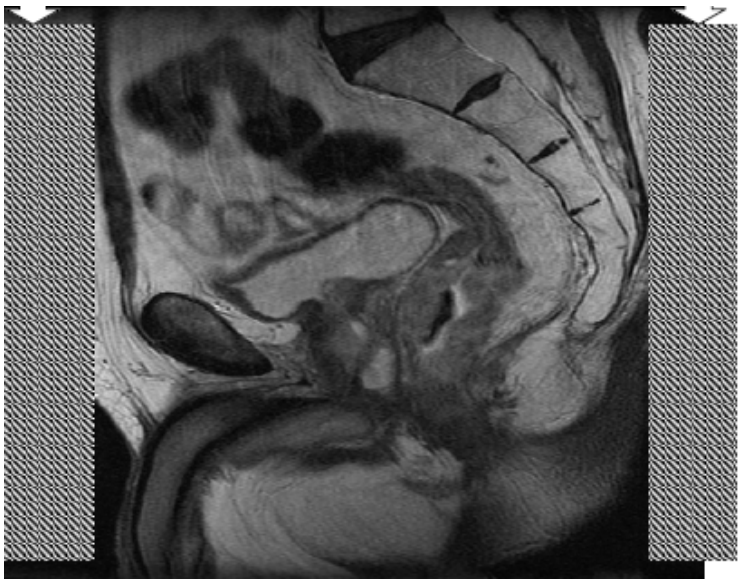


Figure 3

Choice of sequences

T1 weighted imaging

Although the availability of short TR/TE volume imaging can provide images of high spatial resolution, images obtained fail to show adequate contrast to depict either tumour or the layers of the bowel wall (figure 4).

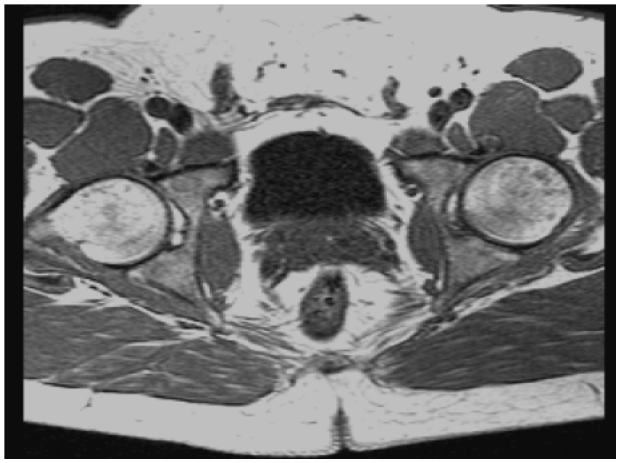


Figure 4

Fat saturation and contrast enhancement.

Contrast enhancement has not been shown to be an effective method for the local staging of rectal cancer. A contrast-enhanced technique requires the high signal from surrounding perirectal fat on T1 weighted images to be suppressed to

permit visualisation of high signal enhancement of tumour. This results in a further reduction in signal to noise ratio and potential overstaging of tumours due to enhancement of adjacent non-tumour tissue (figure 5).

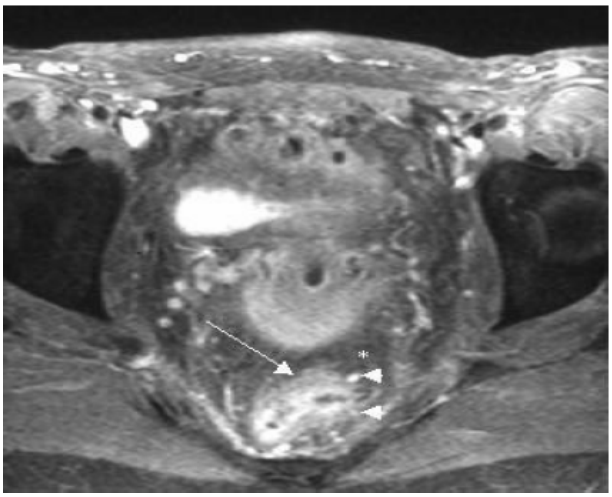


Figure 5

T2 Weighted Fast spin-echo (T2 FSE)

T2 weighted images of the rectal wall and pararectal tissues result in visualisation of individual bowel wall layers and tumour returns a brighter signal than the muscle coat but low signal intensity than perirectal fat and thus superior depiction of tumour when compared with T1 weighted images (figure 6)

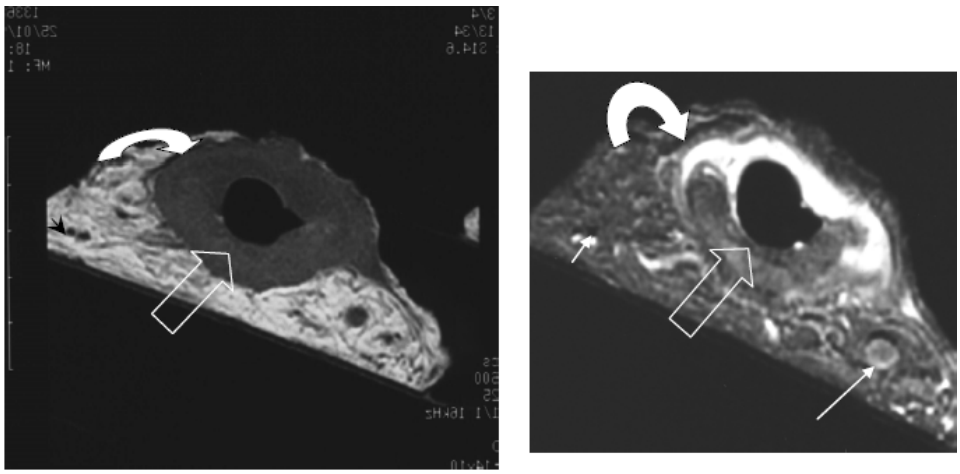


Figure 6

Thus T1, fat saturated or STIR imaging of the rectum and perirectal tissues offers no additional staging information and should not be used.

Cross-talk

This varies with machines and patients and is manifested on the images obtained as loss of signal and unexpected loss of detail (figure 7).

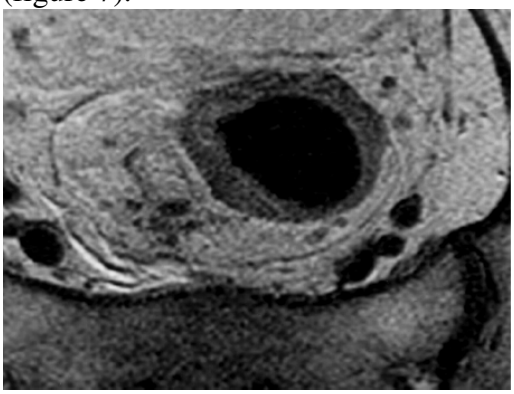


Figure 7

This is overcome by interleaving slices during the high resolution acquisition or increasing the slice gap.

Tumour not seen on initial sagittal sequences

On occasion, lack of clinical detail or the presence of a small tumour prevents the tumour being seen on the sagittal images. In these instances, tumour may only be visible on the high resolution images. In order to ensure that the tumour has not been missed it will be necessary to perform high resolution scans along the entire length of the rectum (as shown in figure 2).

Patient unable to tolerate long scan.

Some patients (<5%),either due to co-existing medical conditions or claustrophobia, find the scan impossible to tolerate, some of the sequences may be omitted. A combination of patient discomfort, excessive motion of the anterior abdominal wall may result in motion artefact. This is seen as horizontal bands across the image (figure 8).

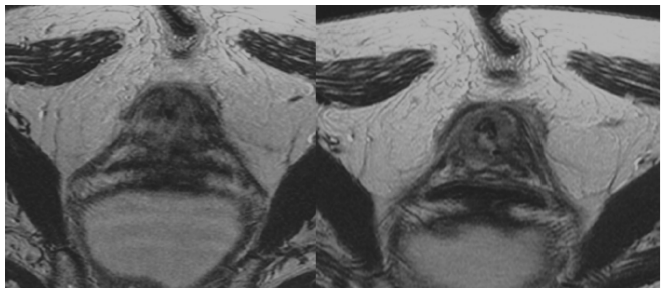


Figure 8

Of all of the sequences the oblique high resolution scans are the most important. The sagittal views can be shortened by altering the parameters; the large field of view axials are performed last and may even be omitted if the patient is in considerable discomfort.

Patient MRI datasheet

Radiologist Date:

Study Code:

Patient Name:

Date of Birth:

Sex:	M	F
Image quality ok:	Yes	No
Tumour covered:	Yes	No
Nodal territory covered:	Yes	No
Correct planes:	Yes	No
Radiotherapy:	Yes	No
Previous MRI	Yes: date / /	No

MRI T-stage:

- T1 Submucosa
- T2 muscularis
- T3a : <1mm
- T3b : 1-5mm
- T3c : 5-15mm
- T3d : >15mm
- T4a Into adjacent organs
- T4b perforation of visceral peritoneum

Extramural venous invasion: **Yes** **No**

If yes, score: 1 2 3 4 5
(seeEMVI scoring sheet supplement)

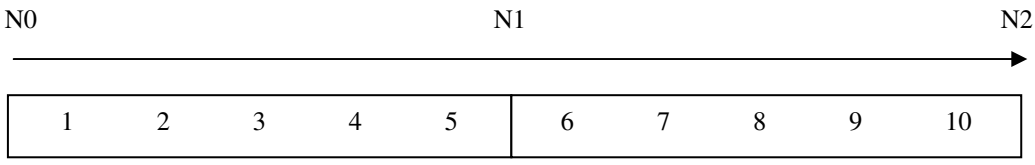
Do involved veins threaten mesorectal fascia?
Yes **No**
(i.e. are they ≤ 1mm from the fascia)

Mesorectal Lymph Node Morphology

High resolution

No nodes visible
Nodes visible – all high intensity
1-3 nodes visible
(showing no more than 1 criterion for malignancy)
1-3 nodes visible
(with both criteria for malignancy)
4 or more nodes visible with both criteria for definite tumour deposits

Overall impression of nodal status



Yes No
Do any nodes lie within 1mm of the CRM

Confidence of score

Evidence of Pelvic Sidewall Lymph Nodes: **Yes** **No**
(if yes, please circle all that apply below)

Site of node: HYPOGASTRIC/ INTERNAL ILIAC/ OBTURATOR/ EXTERNAL ILIAC/ COMMON ILIAC,/ INGUINAL

Node features: UNIFORM SIGNAL INTENISTY/ HETEROGENEOUS/ SMOOTH / IRREGULAR,

Benign/Malignant

Tumour height above levator origin?
If yes choose one of the following:

Confined to muscle coat
Extending beyond muscle coat
Extending to <1mm of MR fascia
Extending to or beyond MR Fascia

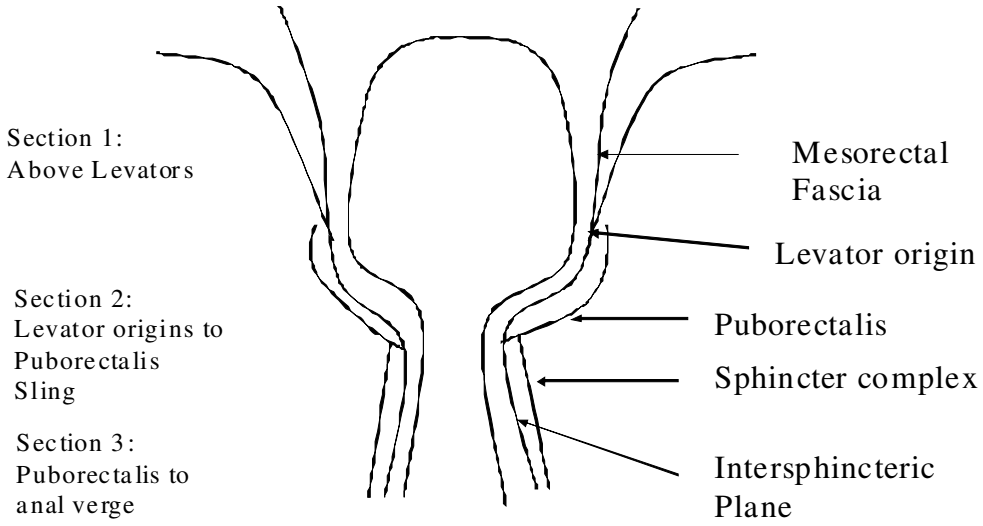
Tumour height between levator and puborectalis sling?
If yes choose one of the following:

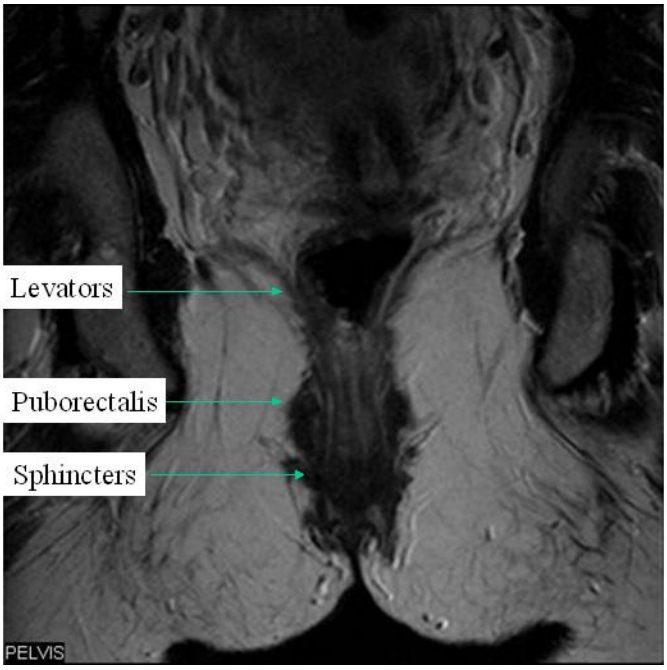
Confined to muscle coat
Extending beyond muscle coat
Extending to <1mm of levator muscle
Extending into or beyond levator muscle

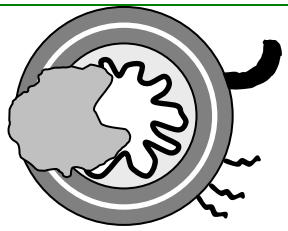
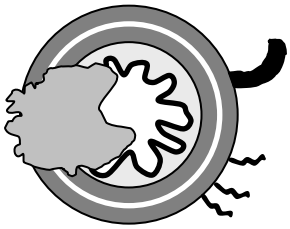
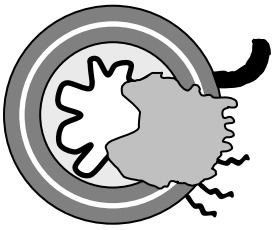
Tumour at or below puborectalis sling?

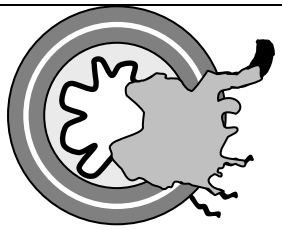
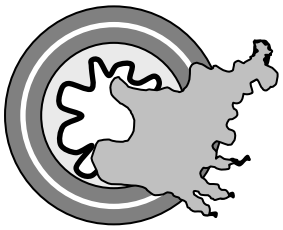
Into submucosal layer/part thickness of muscularis propria
Full thickness of muscularis propria
Into intersphincteric plane
Into External sphincter
Beyond External sphincter into ischiorectal tissue

Draw on Diagram minimum planes required to clear tumour
Distance from outer edge of muscularis propria/internal sphincter required to achieve adequate radial clearance at deepest margin of tumour (mm)





MRI-EMVI score	Imaging features	Illustration
0	The pattern of tumour extension through the muscle coat is not nodular, and there are no vessels adjacent to areas of tumour penetration.	
1	Minimal extramural stranding / nodular extension seen, but not in the vicinity of any vascular structures.	
2	Stranding demonstrated in the vicinity of extramural vessels, but these vessels are of normal calibre, and there is no definite tumour signal seen within the vessel.	

3	Intermediate signal intensity apparent within vessels, although the contour and calibre of these vessels is only slightly expanded	
4	Obvious irregular vessel contour or nodular expansion of vessel by definite tumour signal.	

FOR ANY POST RX MRI RADIOLOGICAL TUMOUR REGRESSION GRADE

Which best describes the tumour regression on MRI:

Grade 5	No response (intermediate signal intensity, same appearances as original tumour)
Grade 4	Slight response (little areas of fibrosis or mucin but mostly tumour)
Grade 3	Moderate response (>50% fibrosis or mucin, and visible intermediate signal)
Grade 2	Good response (dense fibrosis; no obvious residual tumour, signifying minimal residual disease or no tumour)
Grade 1	Radiological complete response (rCR) (no evidence of ever treated tumour.

10.5 Follow-Up Schedule

Timeline From completion of CRT	Toxicity Scales	DRE	CEA	Scans	Endoscopy
4 weeks	Lent Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	MRI	
8 weeks		DRE	CEA	MRI, FDG-PET	
12 weeks	Lent-Soma, EORTC	DRE	CEA	MRI,	Flex Sig †
16 weeks		DRE	CEA	MRI/FDG-PET	
6 month	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	MRI	Flex Sig
9 month	Lent-Soma, EORTC	DRE	CEA	MRI	Flex Sig
12 month (1 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	CT, MRI, FDG-PET	colonoscopy
15 month	Lent-Soma, EORTC	DRE	CEA		
18 month	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	MRI	Flex Sig
21 month	Lent-Soma, EORTC	DRE	CEA		
24 month (2 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	CT, MRI	Flex Sig
30 month	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA		
36 month (3 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	CT, MRI	Flex Sig
42 month	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA		
48 month (4 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	MRI	Flex Sig
54 month	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA		
60 month (5 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	MRI	colonoscopy
72 month (6 yr)	Lent-Soma, EORTC, MIBDQ,	DRE	CEA	MRI	Flex Sig

	Vaizey				
84 month (7 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA	MRI	Flex Sig
96 month (8 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA		
108 month (9 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA		
120month(10 yr)	Lent-Soma, EORTC, MIBDQ, Vaizey	DRE	CEA		colonoscopy

DRE refers to “digital rectal examination”. Flex Sig refers to “Flexible Sigmoidoscopy”. CEA refers to “CarcinoEmbryonic Antigen”.

† The nature of this first endoscopy is at the discretion of the Surgeon. An Examination under Anesthetic at this first assessment may be chosen.

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Patient Trial Number _____

10.6 LENT-SOMA

Site	Method		Grade 0-4 (blank if not assessed)
SKIN	**Subjective**	**Scaliness**	
		Sensation	
	Objective	**Oedema**	
		Alopecia	
		Pigmentation	
		Ulcer	
		Telangiectasia	
		Fibrosis	
		Atrophy	
	Measurable	**Sensation**	
		Ulcer	
		Oedema	
		Fibrosis	
BONE	**Subjective**	**Pain (S)**	
		Function (S)	
		Joint movement (S)	
	Objective	**Fracture (O)**	
		Mucosa soft tissue (O)	
		Skin over bone (O)	
		Joint movement (O)	
	Measurable	**Pain (M)**	
		Function (M)	
		Joint movement (M)	
BLADDER URETHRA	**Subjective**	**Dsyuria (S)**	
		Frequency (S)	
		Haematuria (S)	
		Incontinence (S)	
		Decreased stream (S)	
	Objective	**Haematuria (O)**	
		Endoscopy (O)	
		Maximum volume (O)	
		Residual volume (O)	
	Measurable	**Dsyuria (M)**	
		Frequency (M)	
		Haematuria (M)	
		Incontinence (M)	
		Decreased stream (M)	
RECTUM	**Subjective**	**Stool Frequency (S)**	
		Sphincter control (S)	

Site	Method		Grade 0-4 (blank if not assessed)
		Pain (S)	
		Tenesmus (S)	
		Mucosal loss	
	Objective	Bleeding (O)	
		Stricture (O)	
		Ulceration (O)	
	Measurable	Pain (M)	
		Tenes / Stool freq (M)	
		Bleeding (M)	
		Stricture (M)	
		Ulceration (M)	
		Sphincter control (M)	
SMALL INTESTINE COLON	Subjective	Stool Frequency (S)	
		Stool consistency (S)	
		Pain (S)	
		Constipation (S)	
	Objective	Melena (O)	
		Wt loss from RT (O)	
		Stricture (O)	
		Ulceration (O)	
	Measurable	Pain (M)	
		Stool consist/freq (M)	
		Bleeding (M)	
		Stricture (M)	
		Ulceration (M)	
MALE SEXUAL	Subjective	Erectile function (S)	
		Dryness (S)	
		Desire (S)	
		Satisfaction (S)	
	Objective	Frequency (O)	
		Orgasm (O)	
	Measurable	Impotence (M)	
		Psychosocial (A)	
FEMALE SEXUAL	Subjective	Dyspareunia (S)	
		Dryness (S)	
		Desire (S)	
		Satisfaction (S)	
	Objective	Vaginal stenosis/length (O)	
		Synechiae (O)	
		Frequency (O)	
		Orgasm (O)	

Site	Method		Grade 0-4 (blank if not assessed)
	Measurable	**Dryness (M)**	
		Stenosis/synechiae (M)	
		Dyspareunia (M)	
		Psychosocial (A)	
		vaginal measurement (A)	
VULVA	**Subjective**	**Dryness (S)**	
		Prurutis (S)	
		Pain (S)	
	Objective	**Pigmentation (O)**	
		Alopecia (O)	
		Atrophy (O)	
		Appearance (O)	
		Ulceration/necrosis (O)	
		Fibrosis (O)	
		Oedema (O)	
		Introital stenosis (O)	
		Serous transudate (O)	
	Measurable	**Pruritis/atrophy (M)**	
		Pain (M)	
		Ulceration (M)	
		Introital stenosis (M)	
VAGINA	**Subjective**	**Dyspareunia (S)**	
		Dryness (S)	
		Bleeding (S)	
		Pain (S)	
	Objective	**Stenosis/length (O)**	
		Dryness (O)	
		Ulceration (O)	
		Atrophy (O)	
		Appearance (O)	
		Synechiae (O)	
		Bleeding (O)	
	Measurable	**Dyspareunia/pain (M)**	
		Atrophy (M)	
		Bleeding (M)	
		Stenosis (M)	
		Dryness (M)	
		Ulceration (M)	
VESSELS	**Subjective**	**Arterial (S)**	

Site	Method		Grade 0-4 (blank if not assessed)
		Venous (S)	
	Objective	**Arterial (O)**	
		Venous (O)	
	Measurable	**Arterial (M)**	
		Venous (M)	
		Doppler ultrasound (A)	

Form completed by

Name_____Date_____

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10.7 EORTC QOL ***Date*** **Patient Trial Number:**

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

	Not at All	**A Little**	**Quite a Bit**	**Very Much**
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

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For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

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10.8 Vaizey

Date: *dd___mm___yy___* Patient Trial Number_____

TheVaizey Incontinence Questionnaire

	Never	*Rarely*	*Sometimes*	*Weekly*	*Daily*
Incontinence for solid stool	0	1	2	3	4
Incontinence for liquid stool	0	1	2	3	4
Incontinence for gas	0	1	2	3	4
Alteration in lifestyle	0	1	2	3	4

	No	*Yes*
Need to wear a pad or plug	0	2
Taking constipating medicines	0	2
Lack of ability to defer defecation for 15 minutes	0	4

Never, no episodes in the past four weeks;
Rarely, 1 episode in the past four weeks;
Sometimes, >1 episode in the past four weeks but <1 a week;
Weekly, 1 or more episodes a week but <1 a day;
Daily, 1 or more episodes a day.

Add one score from each row: minimum score = 0 = perfect continence;
maximum score = 24 = totally incontinent.

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10.9 MIBDQ Date_____Patient Trial Number_____

In the last 2 weeks please tell us how often you have:	More than ever before	Extremely frequently	Very frequently	Moderate increase in frequency	Some increase in frequency	Slight increase in frequency	Not at all/ normal
1 Had your bowel open?							
2 Felt tired and worn out?							
3 Felt frustrated, impatient or restless?							
4 Been unable to do what you want because of your bowels?							
5 Had loose bowel movements?							
6 Worried about your energy levels?							
7 Worried about having to have something done about your bowels?							
8 You had to cancel an engagement because of your bowels?							
9 Been troubled by pain in your bottom?							
10 Felt generally unwell?							

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In the last 2 weeks please tell us how often you have:	More than ever before	Extremely frequently	Very frequently	Moderate increase in frequency	Some increase in frequency	Slight increase in frequency	Not at all/ normal
11 Worried about not being able to find a lavatory?							
12 Been prevented doing leisure or sports by your bowels?							
13 Been troubled by pain in your tummy or bottom?							
14 Been waking at night or having difficulty sleeping?							
15 Been depressed or discouraged?							
16 Not gone somewhere because there is no lavatory nearby?							
17 Passed large amounts of gas?							
18 Worried about getting to the weight you would like?							
19 Worried about your illness?							
20 Been troubled by bloating?							

In the last 2 weeks please tell us how often you have:	More than ever before	Extremely frequently	Very frequently	Moderate increase in frequency	Some increase in frequency	Slight increase in frequency	Not at all/ normal
21 Been relaxed and free of tension?							
22 Had a problem with bleeding from yourbottom?							
23 Been embarrassed about your bowels?							
24 Felt like you need to have your bowels open but nothing happens?							
25 Felt tearful and upset?							
26 Been troubled by accidental soiling?							
27 Felt angry as a result of your bowel problems?							
28 Felt limited in sexual activity because of yourbowels?							
29 Felt disgusted about your bowel problems?							
30 Felt irritable?							

In the last 2 weeks please tell us how often you have:	More than ever before	Extremely frequently	Very frequently	Moderate increase in frequency	Some increase in frequency	Slight increase in frequency	Not at all/ normal
31Experienced lack of understanding from others?							
32Felt satisfied, happy or pleased with your life?							