Test your assessment of Rectal tumour response using Tumour Regression Grading (TRG) Systems

Learning objective

- Understand the MRI features of treatment response in rectal cancer described in different tumour regression grading (TRG) systems

- Improve confidence in recognising features of treatment response and residual or recurrence rectal tumour following chemoradiotherapy

Background

- Neoadjuvant chemoradiotherapy is the standard of care for locally advanced rectal cancers

- Post-treatment MRI has the potential to modify subsequent management:
  - Define surgical approach. For example, permit sphincter-sparing surgery in low rectal tumours with favourable response
  - Support decision to defer surgery with watch-and-wait approach

Tumour response grading systems

- A current limitation of MRI is the significant learning curve associated with image evaluation[1]
- Recognition of the imaging features of treatment response and residual disease is essential to identify good responders (for which watch-and-wait approach may be appropriate) and poor responders (for who additional systemic chemotherapy may be indicated)
- The same imaging features are also important for the diagnosis of disease relapse during a watch-and-wait programme.

Rectal tumour response: T2WI MRI features

- Successful treatment with chemoradiotherapy is characterized by:
  - Overall decrease in the size of the primary tumour
  - Intermediate T2 signal replaced by low signal fibrosis
  - A small minority of tumours may develop a mucinous response following chemoradiation with increased T2 signal. These mucin lakes generally contain no or rare isolated tumour cells and therefore mucinous transformation is generally considered a good prognostic sign (unlike primary mucinous tumours, which have an overall poorer prognosis)[2]
- Tumour response can be objectively assessed using tumour regression grading systems

Published mrTRG systems

- Use of MRI TRG (mrTRG) is not routine in many centres and so far has not shown good agreement with pathological TRG.
- However, diagnosis of sustained treatment response is an important component of any watch-and-wait approach.
- We seek to increase confidence in assessing rectal MRI following treatment of rectal tumours with chemoradiotherapy by considering these scoring systems.
- Grading systems are broadly based on the proportion of fibrosis evident at the site of primary tumour. Two examples systems published in the literature are shown on the following slide.

Patel (2012)[3]

Based on high resolution T2WI

GRADE	RESPONSE	DESCRIPTION
1	Complete radiological response	No evidence of treated tumour
2	Good response	Dense hypointense fibrosis. Minimal residual tumour
3	Moderate response	~50% fibrosis/mucin and intermediate signal representing residual tumour
4	Slight response	Minimal fibrosis/mucinous degeneration, mostly tumour
5	No response	Tumour has the same appearance as baseline

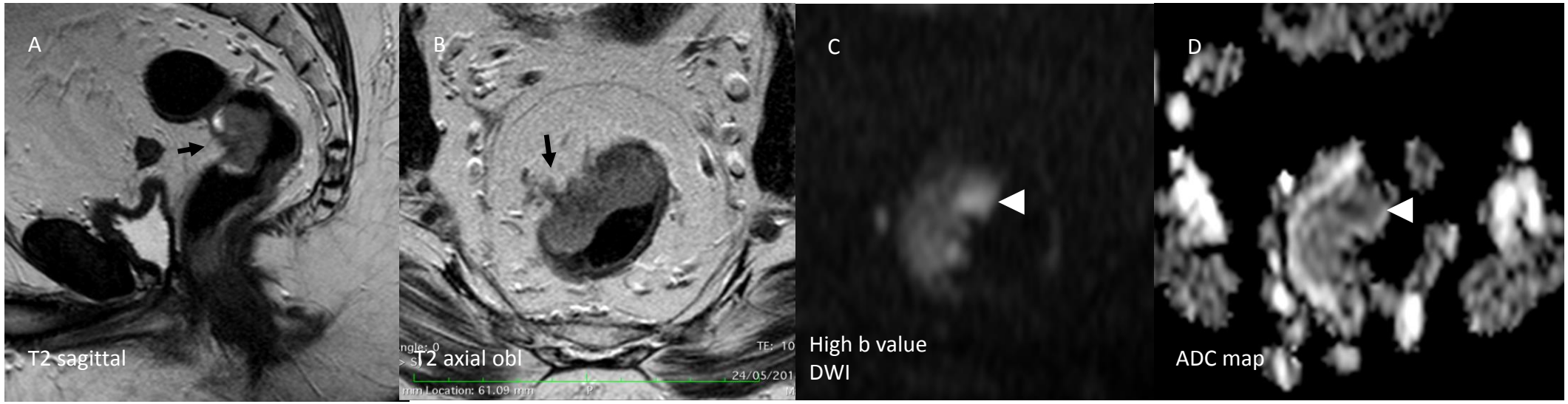
Lee (2016)[4]

(Based on high resolution T2WI and high b value DWI)

GRADE	RESPONSE	DESCRIPTION
0	Complete regression	No tumour signal intensity on T2WI or DWI
1	Intermediate regression	Dominant fibrosis outgrowing residual viable tumour; regressed area >50% (DWI read side-by-side to complement T2WI)
2	Poor regression	Dominant residual viable tumour with obvious fibrosis; regressed area <=50% (DWI read side-by-side to complement T2WI)

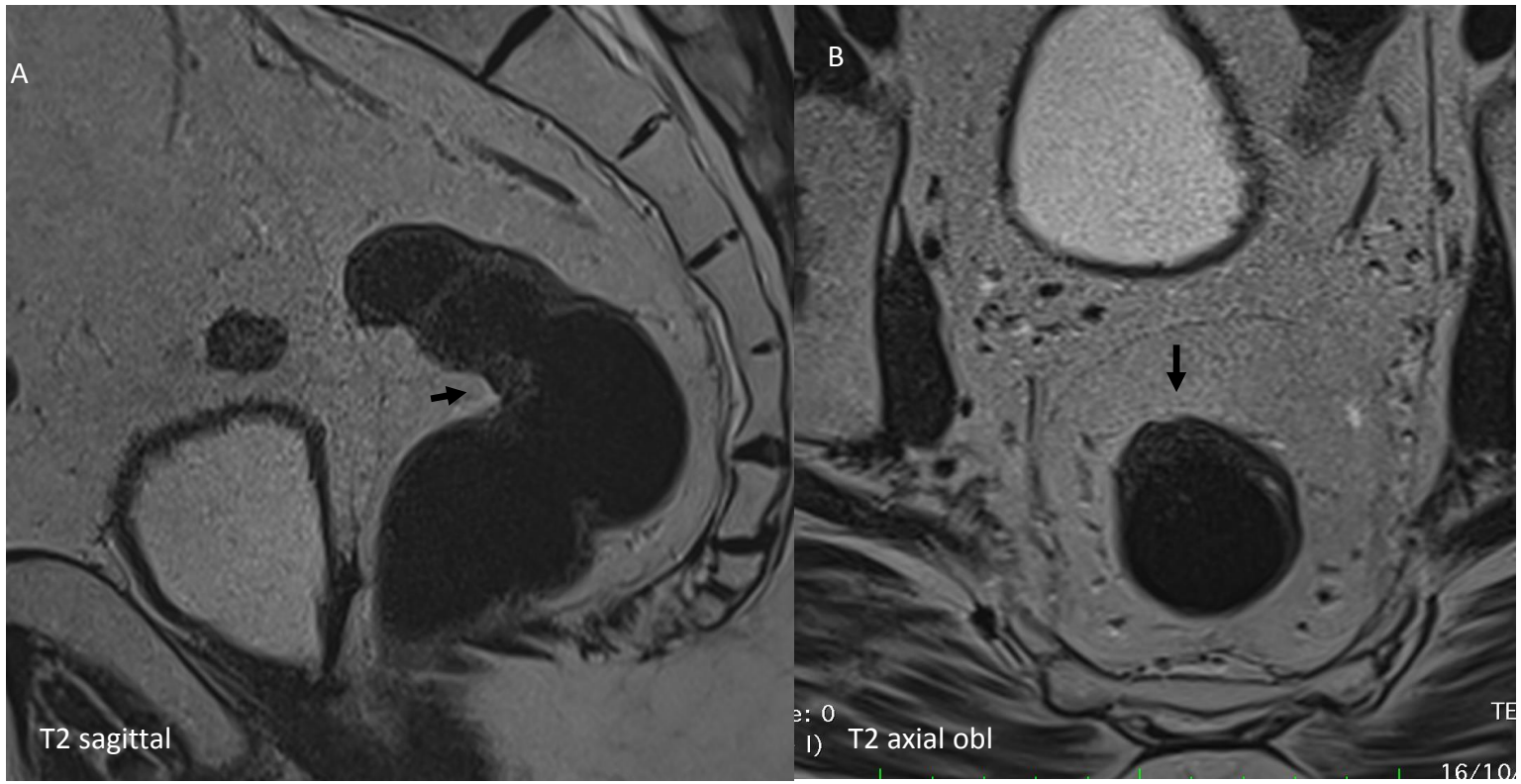
Case 1

Baseline MRI



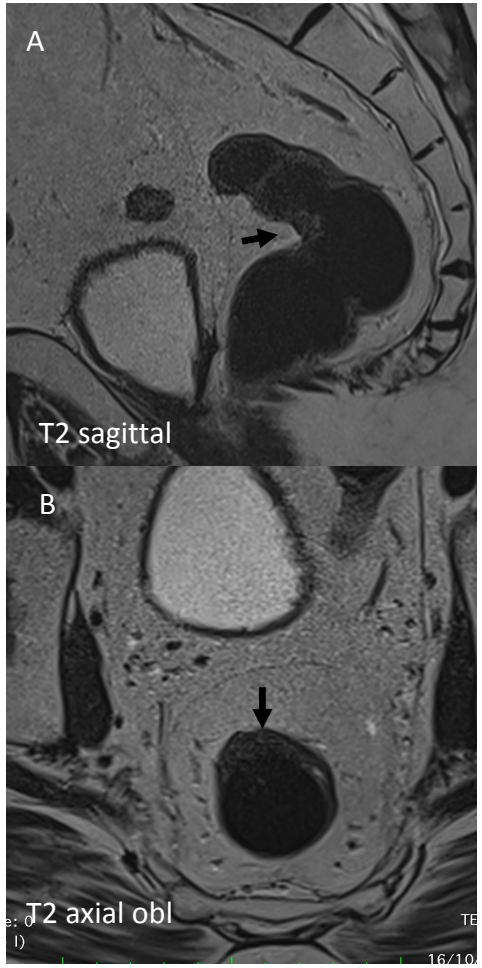
Discussion:
Baseline MRI shows semi-annular midrectal tumour (black arrow, A) with characteristic intermediate signal on T2WI and a leading edge at the 10 o ‘clock position (B), extending through the muscularis propria with evidence of extramural vascular invasion (EMVI) (black arrow). Circumferential resection margin (CRM) is clear. There is evidence of restricted diffusion (arrowheads in C and D).

Case 1 – post chemoradiation



How would you assess response to treatment?

Case 1 – post chemoradiation



- No intermediate tumour signal is seen on T2WI (black arrows in A and B)
- Very minimal low signal fibrosis (black arrows in A and B)
- This would be characterized as TRG 1 or complete regression

- The patient underwent examination under anaesthesia (EUA) and biopsy for equivocal endoscopic findings.
- There was no evidence of high grade dysplasia or invasive neoplasia

- The patient continued to be managed on a watch-and-wait approach

Watch-and-wait approach

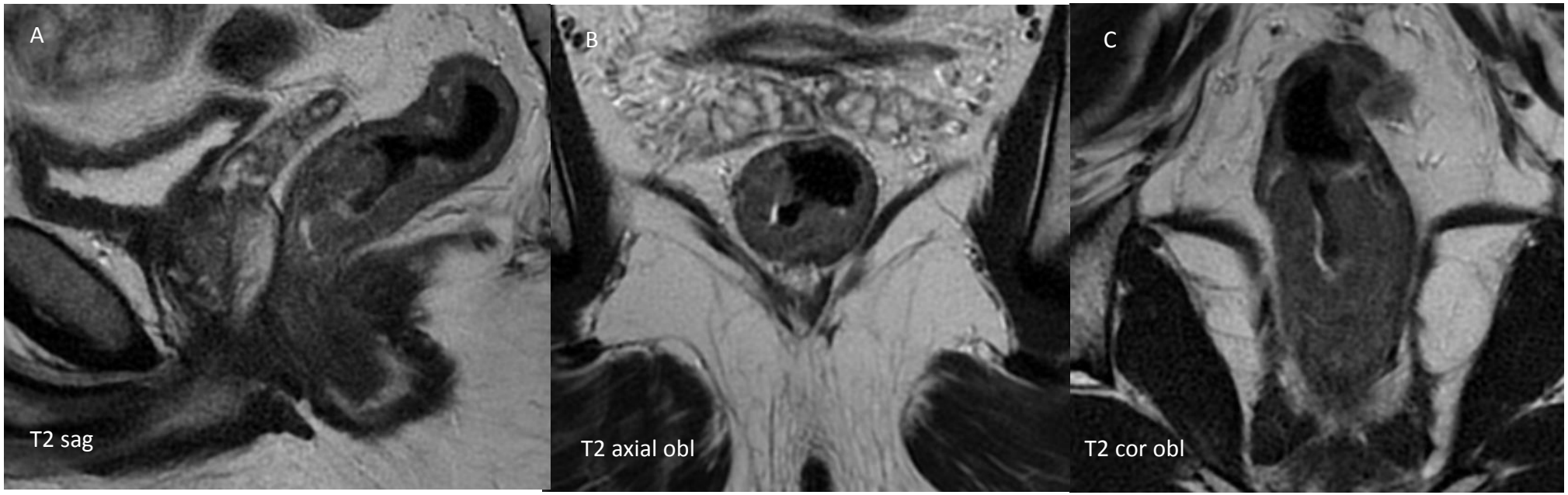
- Following chemoradiotherapy, many patients (up to 30%) experience a complete clinical and radiological response(Smith BMJ).
- A systematic review showed no difference in overall survival has between patients who received immediate surgery versus the “watch-and-wait” group (in which salvage surgery was possible in 83.8%) (Kong JC, 2017).
- Clinical review and endoscopy are the gold standard for diagnosing complete response, however MRI plays an important supportive role.
- Patients with a poor CRT response (mrTRG4&5) have a 5-year overall survival of 27% versus 72% (p=0.001) for a good CRT response (mrTRG1-3)[5].

Example Watch-and-Wait approach[6]

Years 1-2	Years 3-5	After 5 years
Clinical review every 3 months with digital rectal examination (DRE) and flexible sigmoidoscopy	If complete response maintained, DRE and flexible sigmoidoscopy reduced to every 6 months then annually	Annual DRE, flexible sigmoidoscopy and CEA blood test
Pelvic MRI every 4-6 months	**Last MRI is at 36 months** (relapse rate very low after this)	**MRI** or CT based on clinical suspicion
Carcinoembryonic antigen (CEA) blood test every 4 months	CEA blood test every 6 months	
CT Thorax abdomen and pelvis every 6 months	One further CT Thorax abdomen and pelvis at 36 months	
Colonoscopy as per NICE surveillance guidelines		

Suspicion or confirmation of tumour regrowth at any stage should prompt surgical referral and full workup for radical surgery[6]

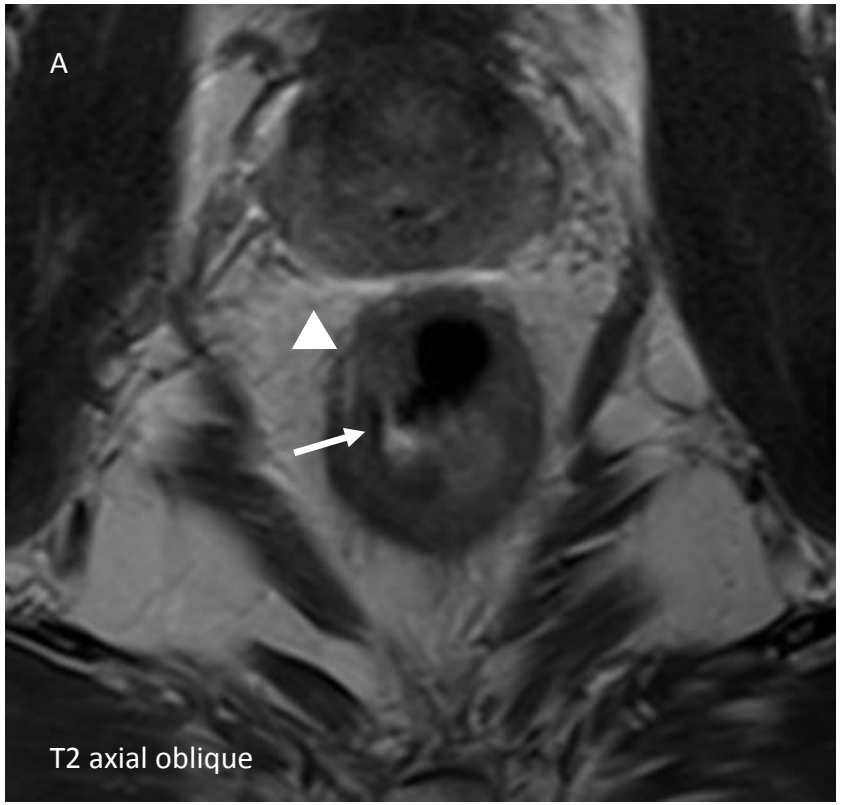
Case 2 -Baseline MRI

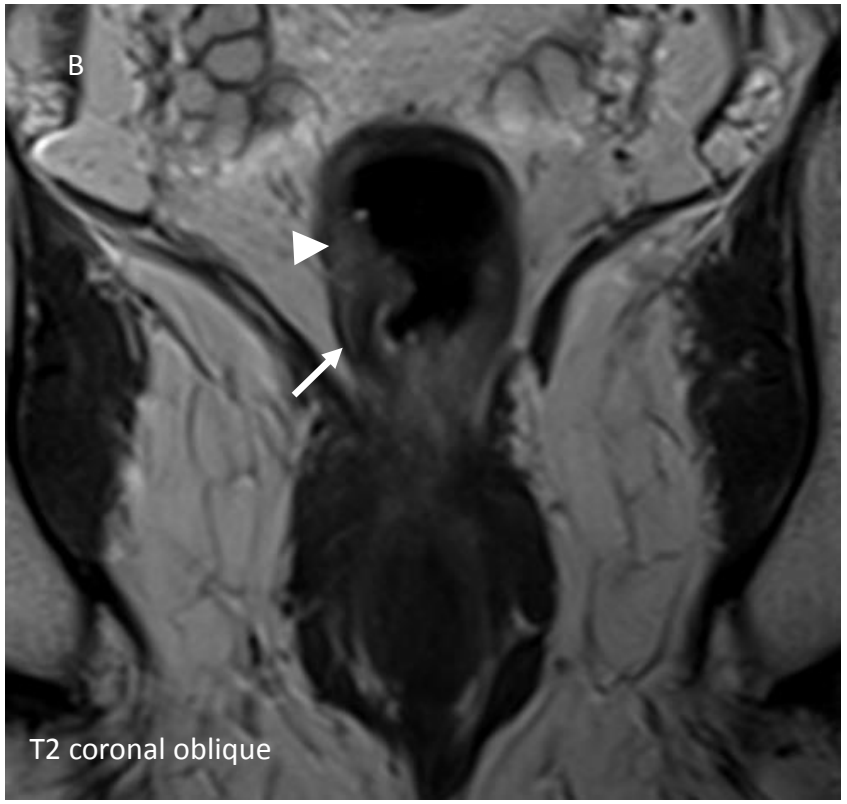


Discussion:

There is a semi –annular tumour involving the mid and lower rectum of homogenous intermediate signal on T2WI. The leading edge is at 8-10 o'clock. There is no extension beyond the muscularis propria. No EMVI is present and the intersphincteric plane and CRM are clear. mrT2 N0.

Case 2 - 6 months post-chemoradiation





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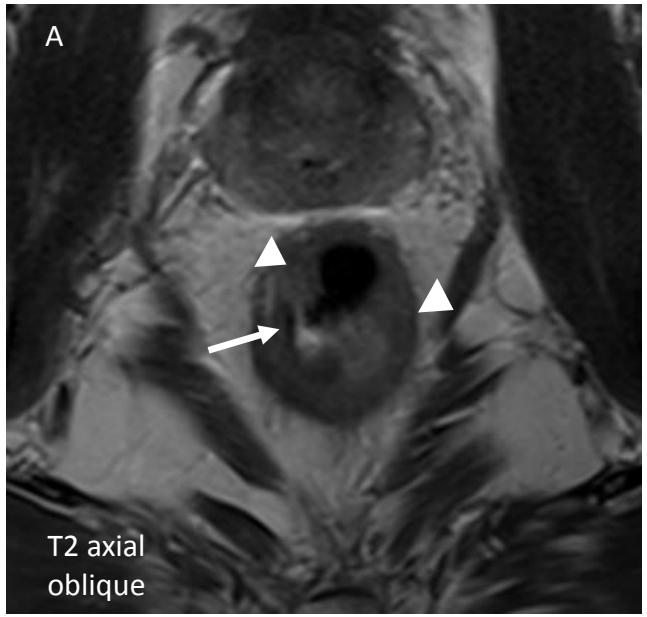
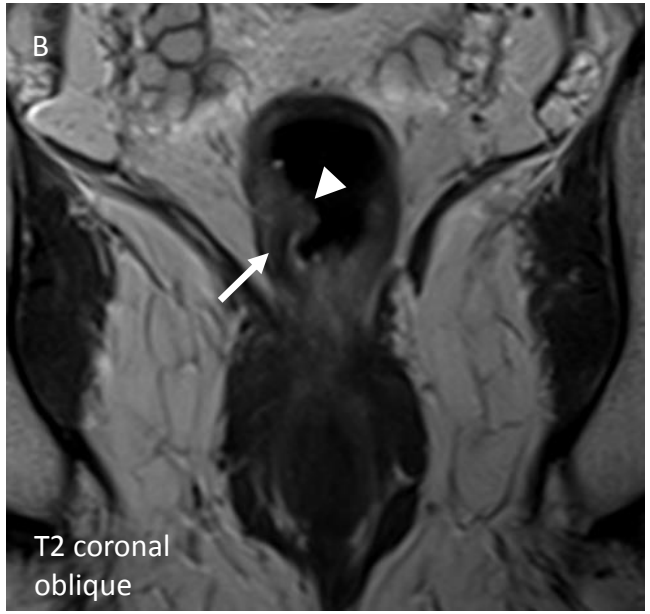
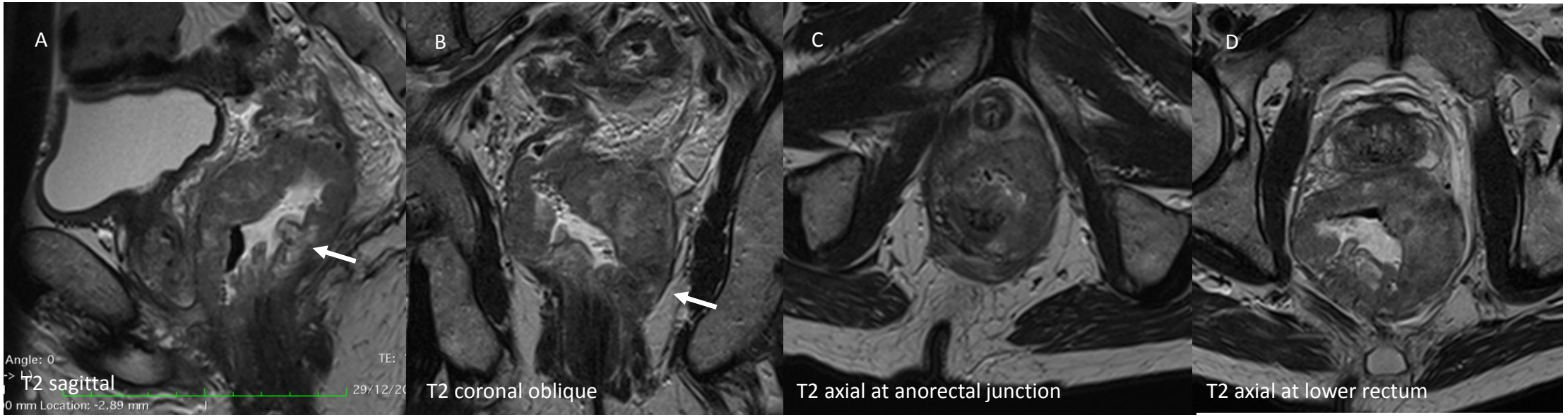
Case 2 - 6 months post-chemoradiation





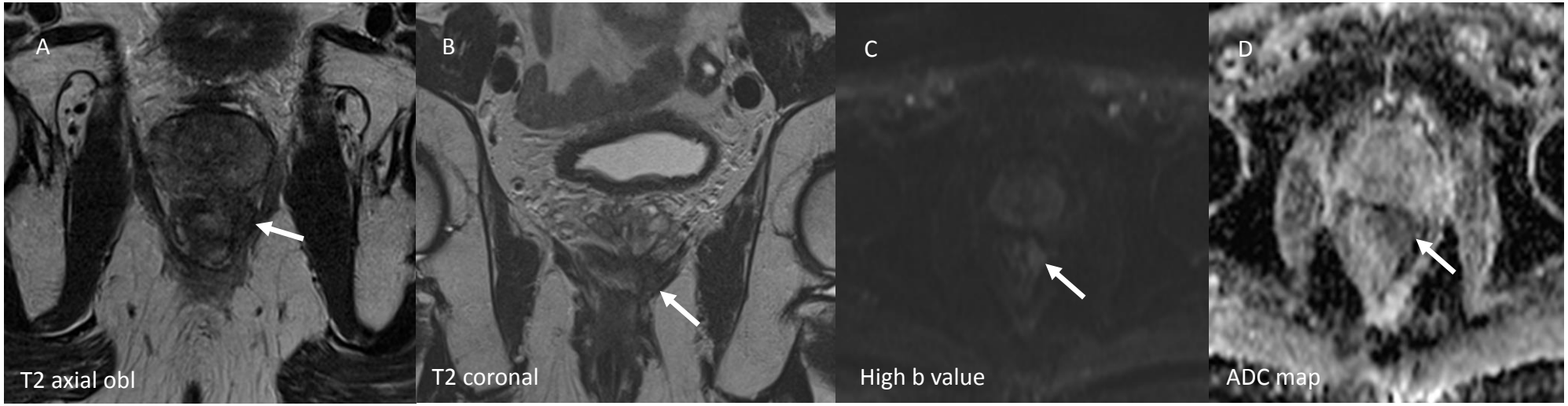
- High resolution T2-weighted sequence axial and coronal to the lower rectum show low signal fibrotic band (arrows in A and B) at the site of lower rectal tumour shown on baseline imaging. However, intermediate signal tumour persists (arrowheads in A and B).
- This would be characterized as TRG 3 (Patel, 2012), or intermediate regression (Lee, 2016).
- EUA and biopsies showed adenocarcinoma, Laparoscopic abdominoperineal resection was performed.
- Residual moderately differentiated adenocarcinoma, % of Tumour Present: 50% ypT2 ypN0, R0

Case 3 Baseline MRI



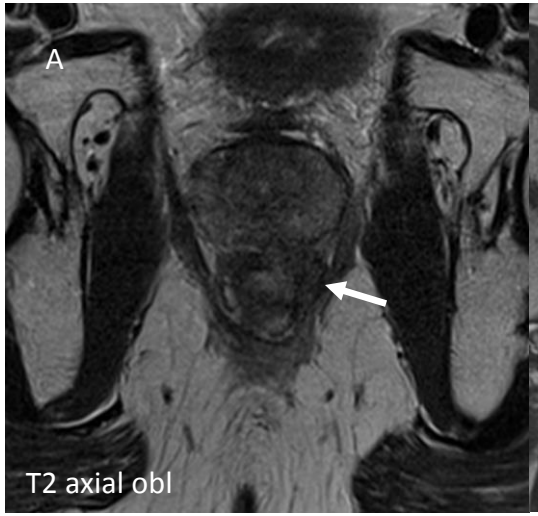
Discussion:
There is a large annual tumour involving the mid and lower rectum invading into the left levator muscle (white arrow in B) with intermediate signal and areas of high signal on T2WI representing mucin (white arrow in A).

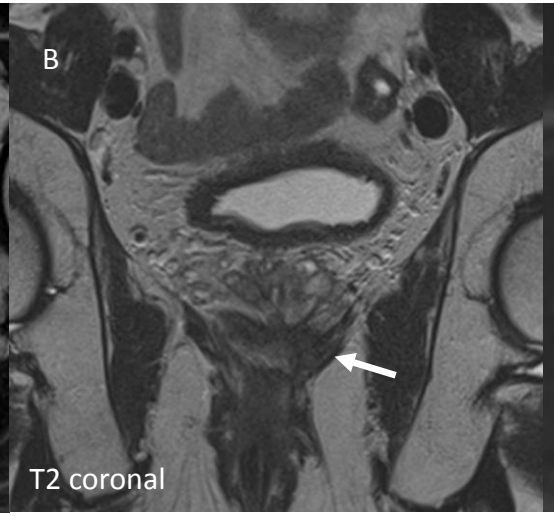
Case 3 post chemoradiation

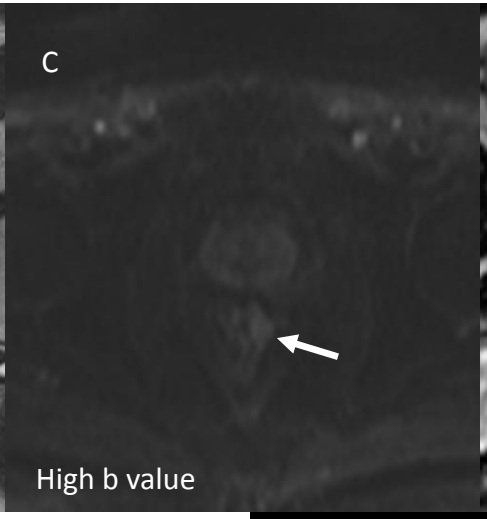


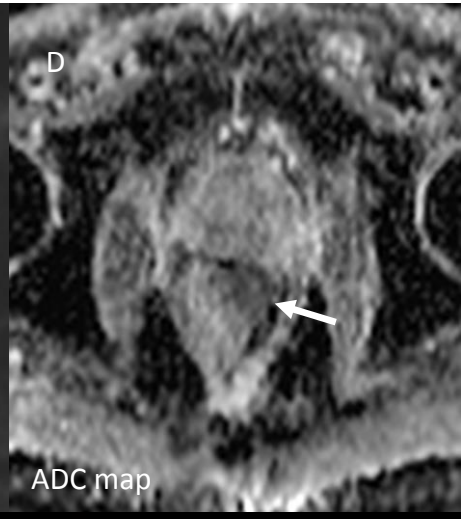
How would you assess response to treatment?

Case 3 post chemoradiation

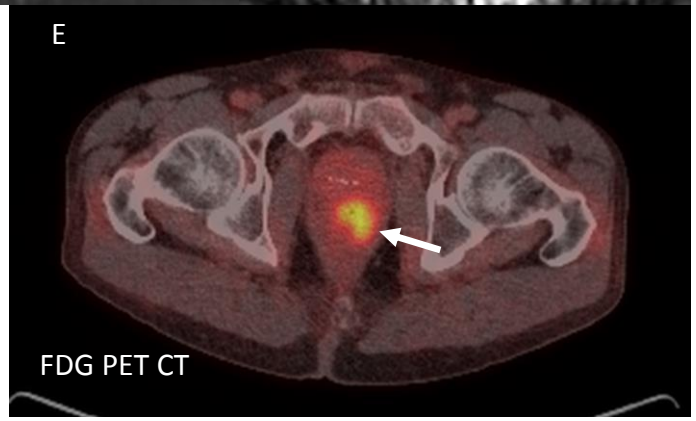








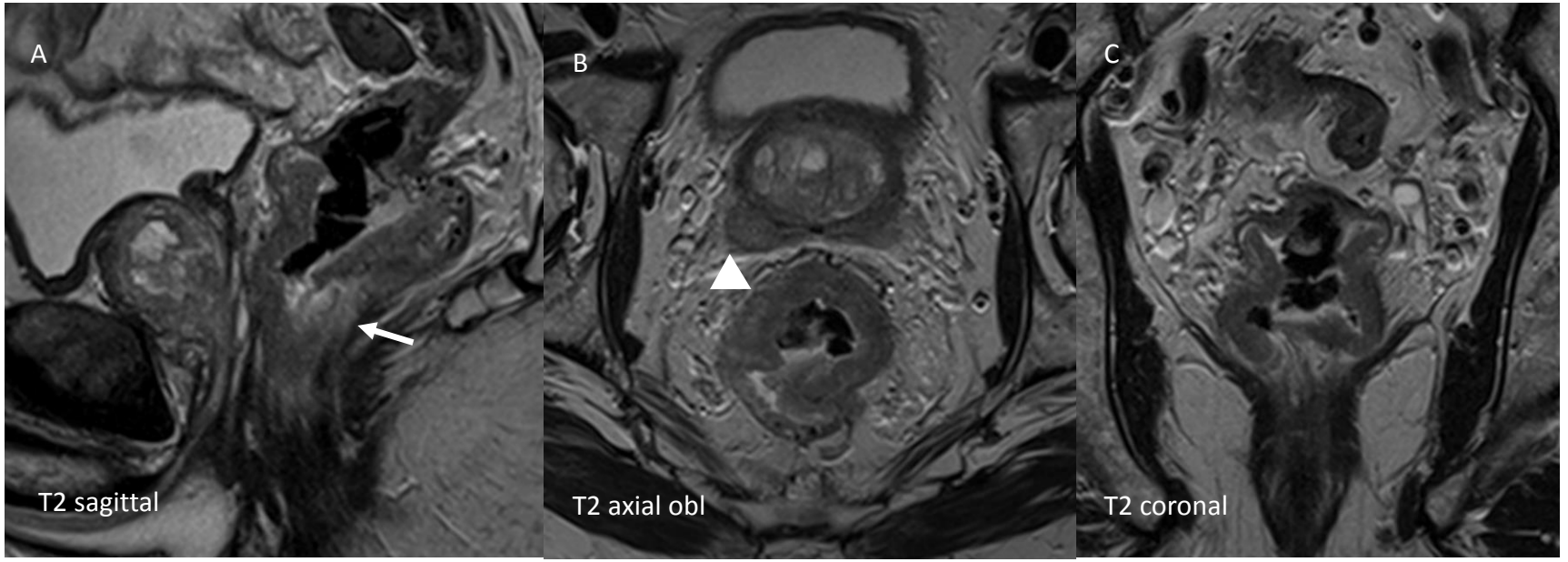
- There has been excellent response with significant decrease in the overall size of the tumour. There is predominant low signal fibrosis (e.g. white arrow heads in A). An ill-defined area of T2 signal change at the left levator muscle (white arrow in A and B) corresponds to focal restricted diffusion (white arrows in C and D)
- This would be characterized as TRG 2 (Patel) or intermediate response (Lee)
- An FDG PET-CT performed at a later date confirmed progressive residual tumour at this site (white arrow in E)



Rectal Tumour response: Diffusion-weighted Imaging

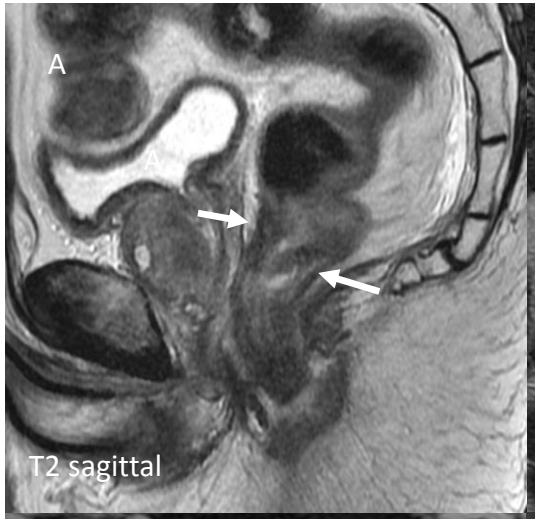
- In highly cellular tissues, such as tumours, the diffusivity of water molecules is reduced and therefore high signal is maintained when diffusion-sensitizing gradients are applied to a T2 weighted sequence
- In the context of post-treatment MRI, high signal on diffusion weighted sequences is suggestive of residual tumour
- However there are potential pitfalls:
  - T2 “shine through” artefact results high signal on high b value sequence due to intrinsic high T2 signal of the tissue. This is mitigated by careful review of ADC map, which reveals low signal if there is true restriction of diffusion.
  - T2 “dark-through” artefact refers to low signal on ADC due to fibrosis. This may be mitigated by careful review of high b value sequence, which reveals high signal if there is true restriction of diffusion.
  - Susceptibility artefacts due to gas in the rectal lumen can produce false high signal[2]

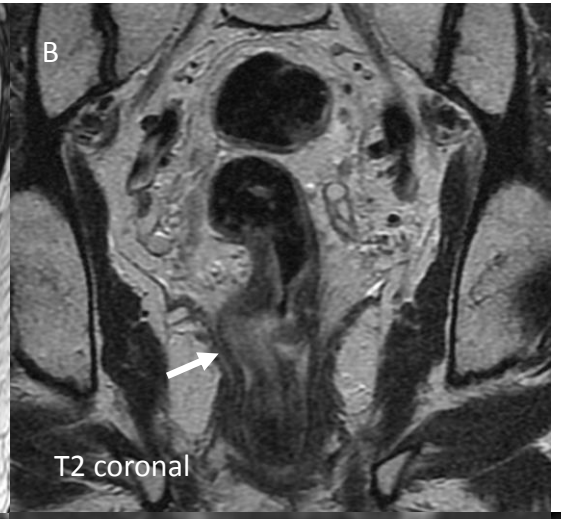
Case 4 Baseline

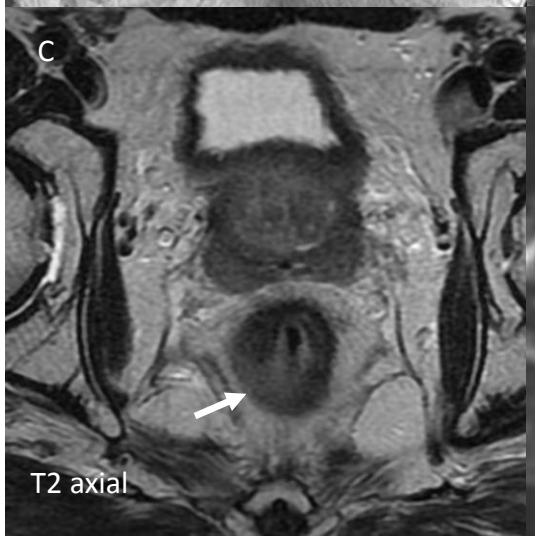


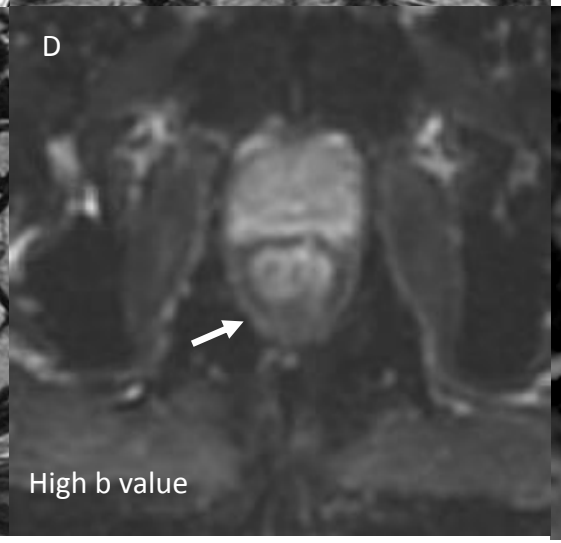
Discussion:
MRI shows a semi-annualar mid and lower rectal tumour with intermediate and high (mucinous) signal (white arrow in A) on T2WI and extension beyond the muscularis propria. The CRM is unsafe (<1mm at 11 o’ clock position, arrow head in B). T3b.

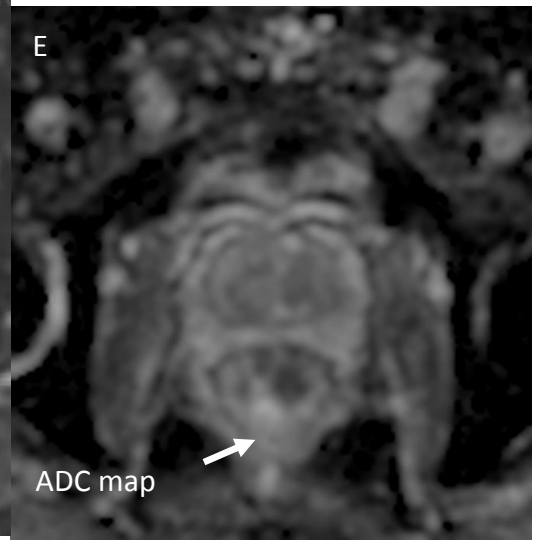
Case 4 post chemoradiation





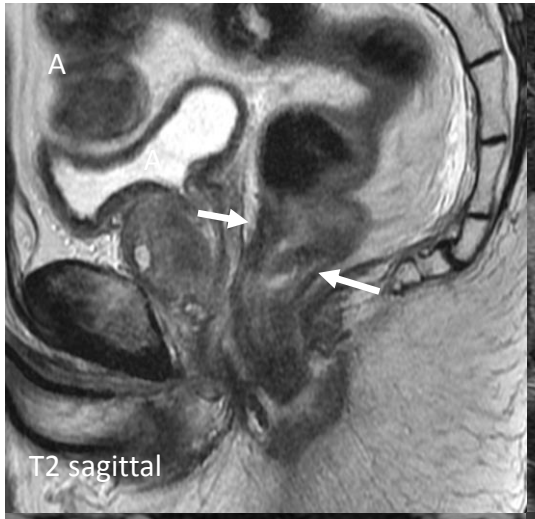


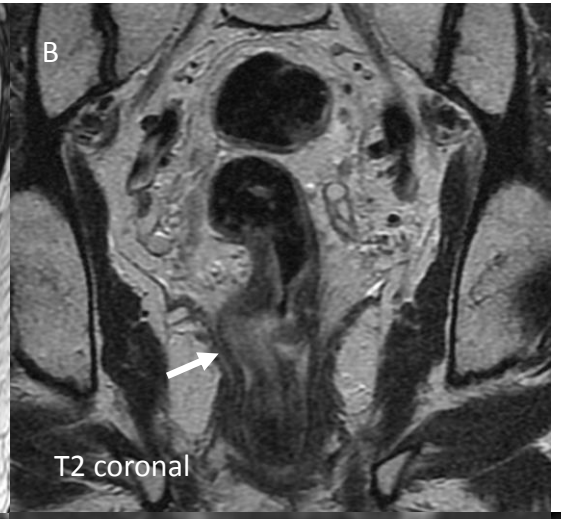


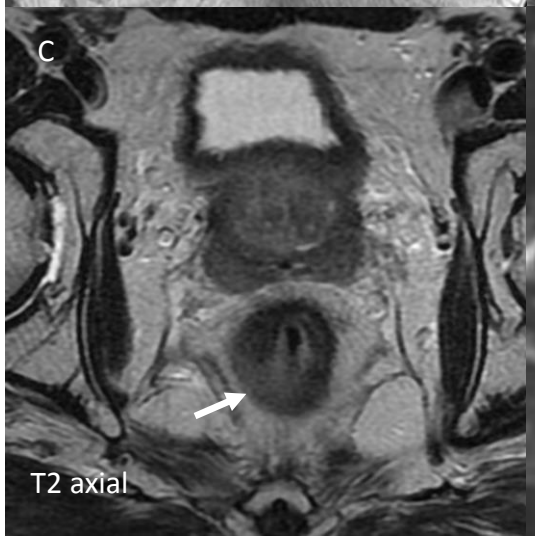


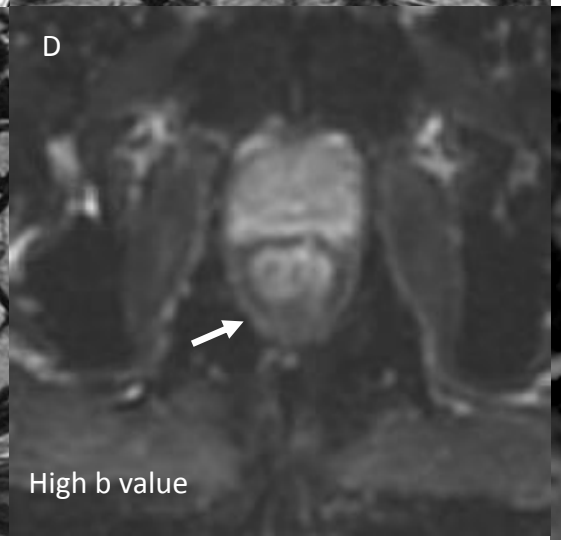
How would you assess response to treatment?

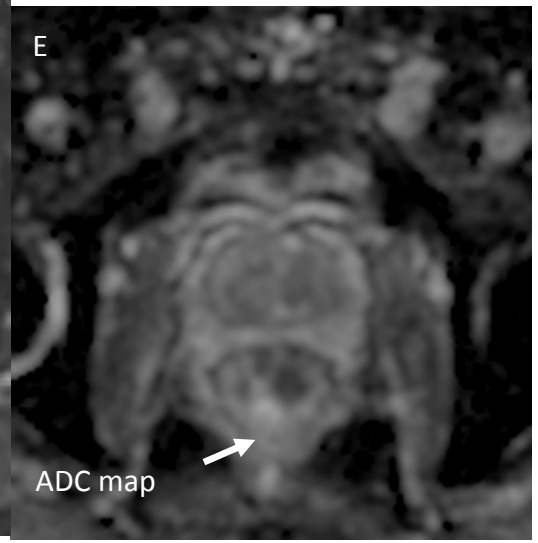
Case 4 post chemoradiation





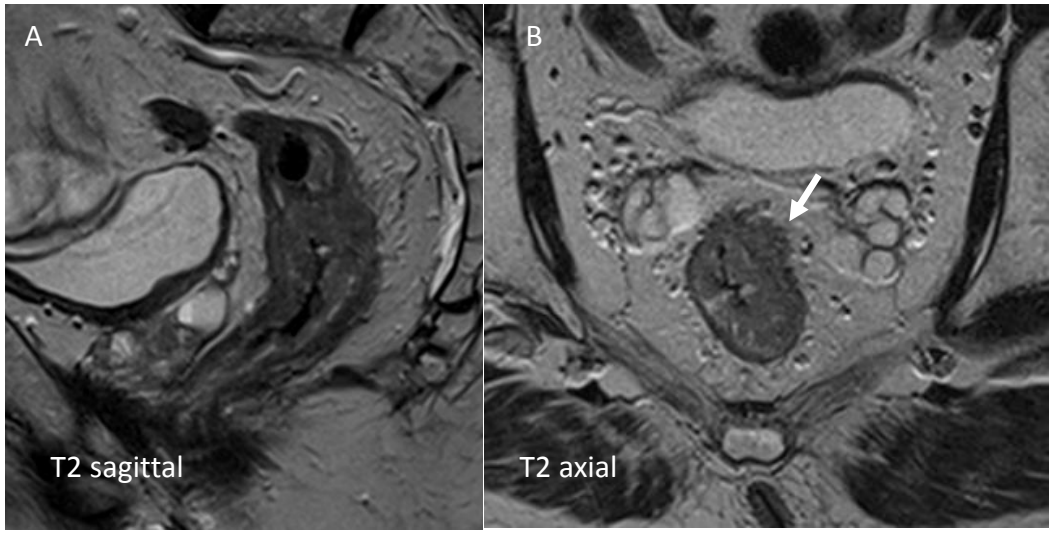






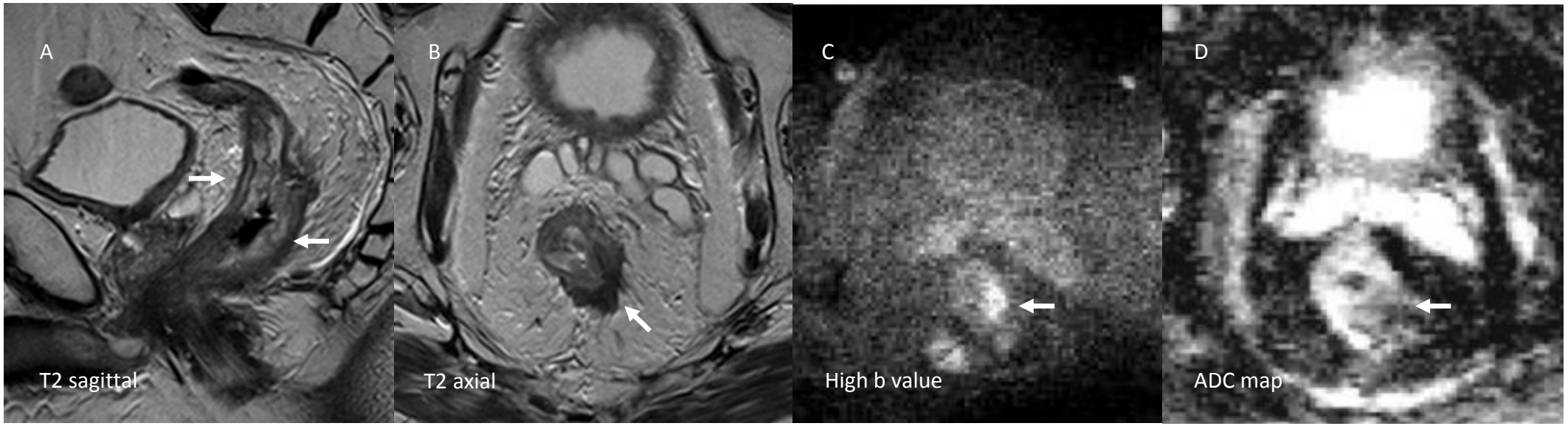
- Low signal fibrosis predominates (white arrows in A)
- High signal posteriorly (white arrows in B and C), shows high signal on both high b value sequence and ADC map (white arrows in D and E), in keeping with T2-shine through.
- This would be characterized at TRG2 with “pseudotumour” appearance posteriorly
- Abdominopelvic resection revealed T2a tumour

Case 5 Baseline



- Annular mid and lower rectal tumour with leading edge at 11-2 o'clock (arrow in B), where tumour extends through the muscularis propria.
- The CRM is involved anteriorly
- T4a

Case 5 post chemoradiation



How would you assess response to treatment?

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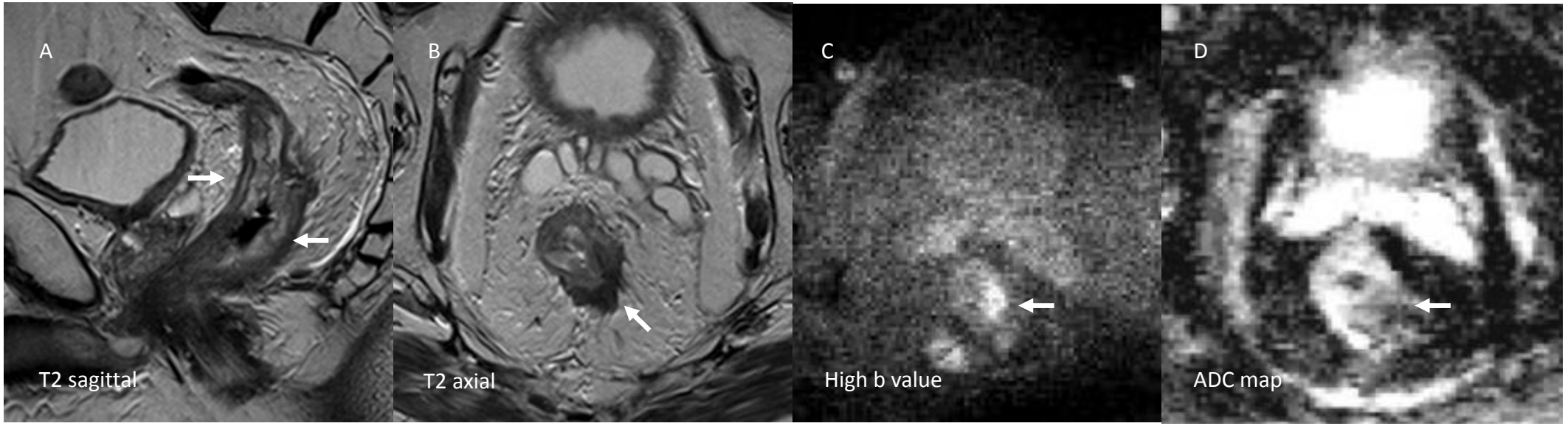

- High signal within the tumour following treatment suggests mucinous transformation (arrows in A)
- Intermediate and high signal tumour predominates with low signal fibrosis (arrows in B) comprising less than 50%
- There is evidence of restricted diffusion (arrows in C and D)
- Appearances represent mrTRG 4 (Patel) or poor regression (Lee)

Concluding remarks

- mrTRG for rectal cancer are not in routine clinical use in many centres
- There is currently insufficient evidence to support their use in guiding management, though the ongoing TRIGGER trial seeks to address this
- Despite this, an appreciation of imaging features of treatment response and residual or recurrent disease within a treatment field is desirable in the era of the “watch-and-wait approach”, in which MRI plays an adjuvant role to clinical and endoscopic assessment.

References

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