



Anal squamous cell carcinoma - What are the differences in MRI evaluation when compared to low rectal adenocarcinoma?

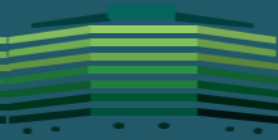
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We have no conflict of interest to declare

Learning objectives

- Although less common than low rectal adenocarcinoma (LRA), anal squamous cell carcinoma (ASCC) is also a major cause of morbimortality and must be treated in reference centers with multidisciplinary team decisions. The radiologist has a pivotal role as imaging evaluation with pelvic MRI supports decisions when it comes to the management of both lesions.
- By showing illustrative cases from our archives, this poster will present relevant information about ASCC which the radiologist must be aware of. We will compare and enlighten the differences between ASCC and LRA, which is the main differential diagnosis
- Teaching points:
 - Describe etiopathogenesis, lymphatic pathways and imaging findings in pelvic MRI
 - Imaging staging criteria
 - Management approaches

Background and Epidemiology



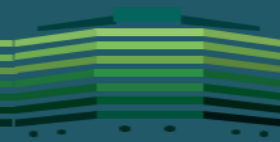
ASCC

- Anal cancer is much less common than colorectal cancer, representing only 8,300 new cases per year and about 1,280 deaths (data estimated for 2019)
- Risk factors: HPV infection, HIV infection, multiple sex partners, anal intercourse, immunosuppression, smoking
- The prevention includes HPV vaccination, condom use, treating HIV infection and avoidance of smoking

Colorectal adenocarcinoma

- Colorectal cancer has remained the third most common cancer in the United States, with an estimated 44,180 new cases of rectal cancer, and 51,020 deaths by colorectal cancer in 2019¹
- Risk factors: overweight, sedentary lifestyle, processed meat intake, alcohol use, inherited syndromes^{2 3}
- The prevention includes physical activity, avoidance of alcohol intake and red meat in excess and screening tests when indicated

Epidemiology



Risk Factors for Low Rectal low rectal adenocarcinoma (LRA) and anal squamous cell carcinoma (ASCC)

ASCC	LRA
Immunosuppression (particularly human immunodeficiency virus - HIV)	>50 years
Cervical and Vulvar cancer	Obesity
Anal intercourse	Smoking
HPV (16 and 18)	Physical inactivity
Smoking	Consumption of red or processed meat
Multiparity	Alcohol consumption
	Associated hereditary syndromes (nonpolyposis disorders such as Lynch syndrome; several polyposis disorders, including familial adenomatous polyposis)

Anatomy and Histology of the Anorectum

- The rectum measures approximately 15 cm in length and is usually divided by the distance from the anal verge in high, medium and low rectum, this last located less than 5,0 cm from the anal verge
- The dentate line divides the low rectum (with columnar crypt-forming epithelium) and the anal canal (with anal squamous mucosa). It is seen macroscopically, but it is not seen in imaging
- Anatomical anal canal extends from the level of the dentate line to the anal margin
- For surgical purposes, the anal canal may be regarded as that portion of the terminal intestine which extends from the anorectal ring-to the the anal margin.
 - The surgical anal canal is longer than its anatomical counterpart

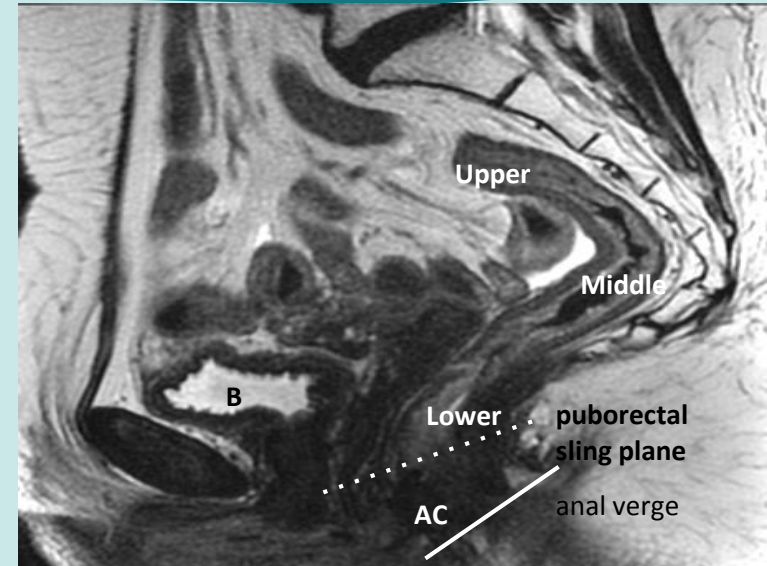


Fig 1. MRI sagittal plane T2-weighted imaging showing the rectal segments and the canal anal. The anal verge is the lowermost portion of the anal canal continuous (line). Puborectal sling (the upper portion of the puborectal muscle) delimit the uppermost portion of the canal anal (dotted line). AC: Anal Canal.

Anatomy and Histology of the Anorectum

- The anal sphincter comprises two components:
 - **internal sphincter** - smooth muscle ; distal continuation of the inner circular muscular layer of the rectum
 - **external sphincter complex** - skeletal muscle; composed of several muscular parts, including the inferior confluence of the levator ani muscle and the puborectalis sling

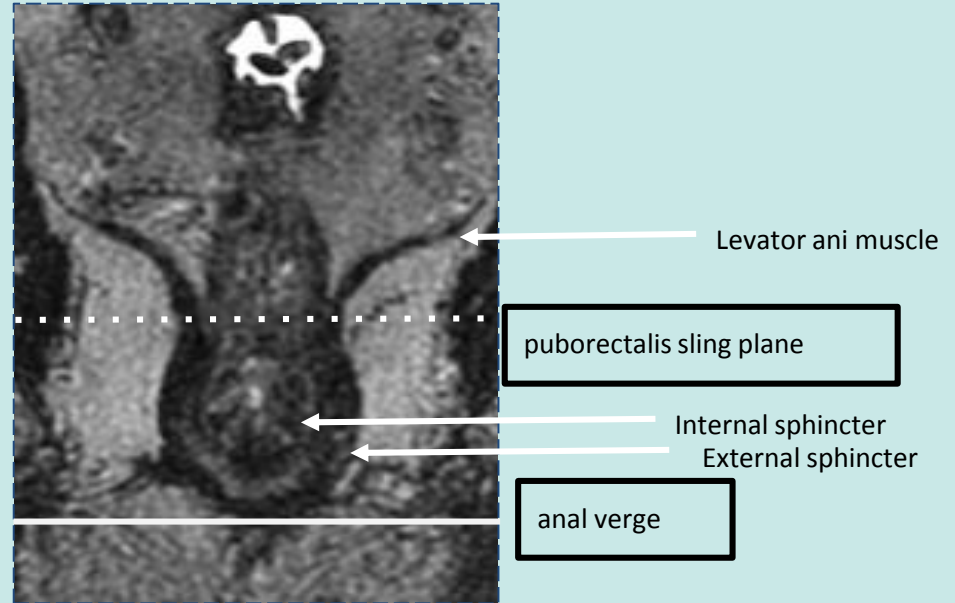


Fig 2. Coronal T2-weighted MRI imaging shows the anatomy of the anal canal. The puborectalis sling (the upper portion of the puborectalis muscle) delimits the uppermost portion of the anal canal (dotted line). The anal verge is the lowermost portion of the anal canal (line).

Anatomy and Histology of the Anorectum

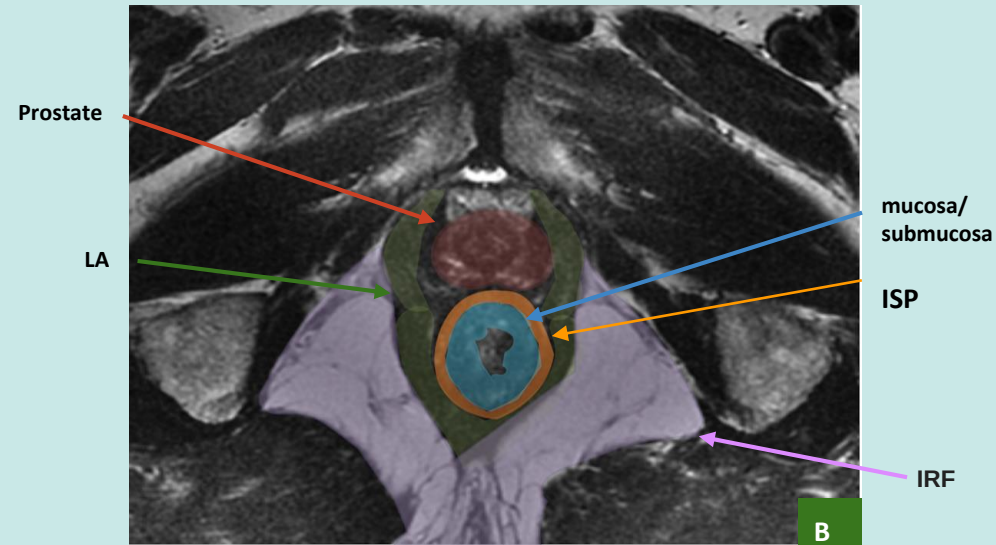
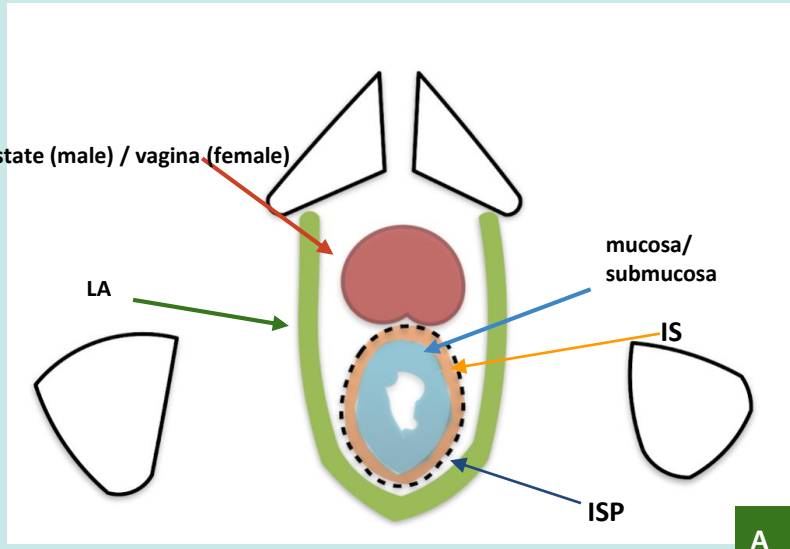


Fig 3. Schematic (A) and axial T2WI in a male patient (B) showing the anatomy of the anal canal .
LA: Levator ani muscle, IS: Internal sphincter, IAF: ischioanal fossa, ISP: Intersphincteric plane

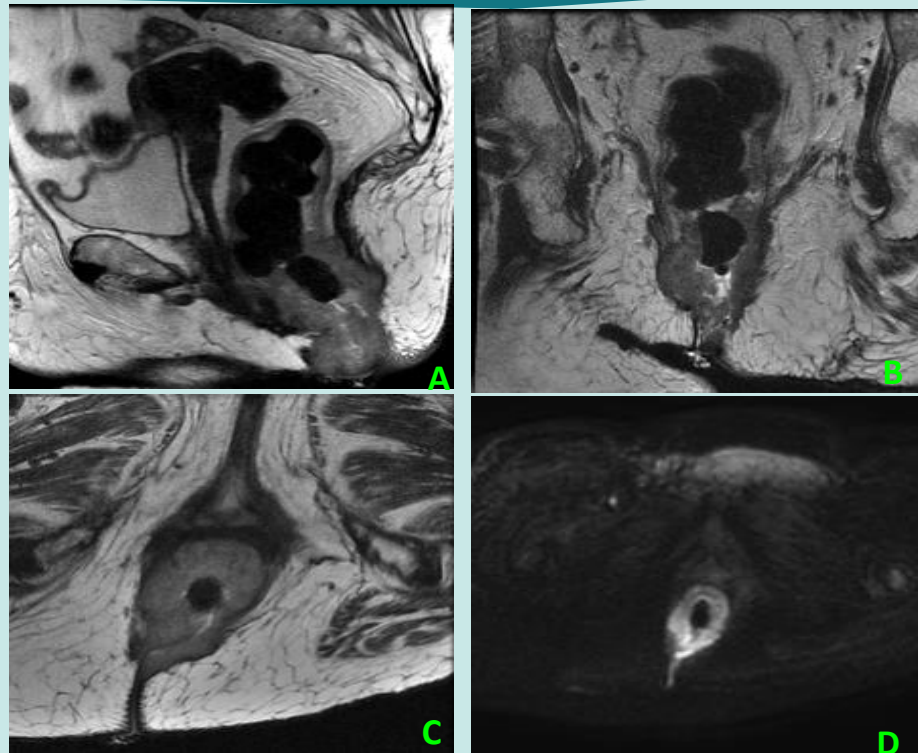
Imaging Evaluation of an Anorectal Lesion

- In cases where histopathological data is unavailable when MRI is performed, the radiologist may misdiagnose an anorectal lesion, taking LRA for ASCC.
- Therefore, the radiologist should know the pathologic diagnosis when reading the MRI in order to correctly stage the lesion. The adequate staging aids proper treatment decisions
- Some features might help differentiation between ASCC and LRA. T2 intermediate signal intensity, a larger distance from the anal verge to the distal edge of the lesion and the absence of anal sphincter invasion are more frequent findings among LRA. Necrotic signal intensity, invasion of the anal verge and lack of the raised-rolled-edge pattern are more common in ASCC.

Imaging Evaluation of an Anorectal Lesion

- MRI is used to locally stage since better tissue contrast is provided when compared to CT.
- T2WI is capable of detecting and staging the primary lesion
- The lesion must be evaluated in sagittal, lesion-axial and coronal axis (the latter provides the best lesion-sphincter complex assessment)
- Other sequences like DWI may aid lesion detection

Fig 4. T2W sagittal (A), coronal (B) and axial (C) images showing the primary ASCC lesion of the anal canal. (D) On DWI and ADC map, lesion shows restricted diffusion.



Imaging Evaluation - T staging

- ASCC: T staging is based on the primary lesion longest diameter, measured in any sequence
 - T1: $\leq 2,0$ cm
 - T2: $2,0$ cm $<$ lesion $<$ $5,0$ cm
 - T3: $> 5,0$ cm
- T staging in LRA is related to the depth of invasion, with particular attention to tumor extension through the rectal wall layers (submucosa, muscularis propria and mesorectal fat)
 - Endorectal ultrasound better evaluates initial rectal lesions, differentiating submucosal and muscularis propria invasion (T1 vs T2)
 - In MRI, high-spatial-resolution T2-weighted sequences are particularly useful for the evaluation of tumor depth because it allows good visualization of rectal layers
- In LRA, the mesorectal fascia is an important landmark because it represents the potential surgical margin in total mesorectal excision.
 - MRI report must describe the distance between the tumor and the mesorectal fascia. The presence of tumor within 1mm of the mesorectal fascia is a risk factor for local recurrence

Imaging Evaluation - T staging

Sphincter complex invasion

- In ASCC, the external sphincter invasion makes no difference in T staging
- In LRA, external sphincter invasion means T4 visceral
 - In MRI report, it is also important to report the distance between the tumor and the upper border of the intersphincteric plane (upper margin of the puborectalis muscle). Standardized surgical procedures are chosen according to the relationship between the lesion and the external sphincter or the elevator ani complex

Imaging Evaluation - T staging

		T staging
	ASCC	LRA
T1	The tumour measures 2cm or less	The tumor has grown into the submucosa
T2	The tumour is larger than 2cm but smaller than 5cm	The tumor has grown into the muscularis propria
T3	The tumour is larger than 5cm	The tumor extends to mesorectal fat.
T4	The cancer is any size but it is growing into the surrounding organs, such as the urethra, prostate, vagina or bladder	T4a: The tumor has grown into the surface of the peritoneum. T4b: The tumor has grown into other organs or structures (anal external sphincter)

T criteria: Size

T criteria: Depth of invasion

Imaging Evaluation - T staging (ASCC)

T1

The tumour measures 2cm or less

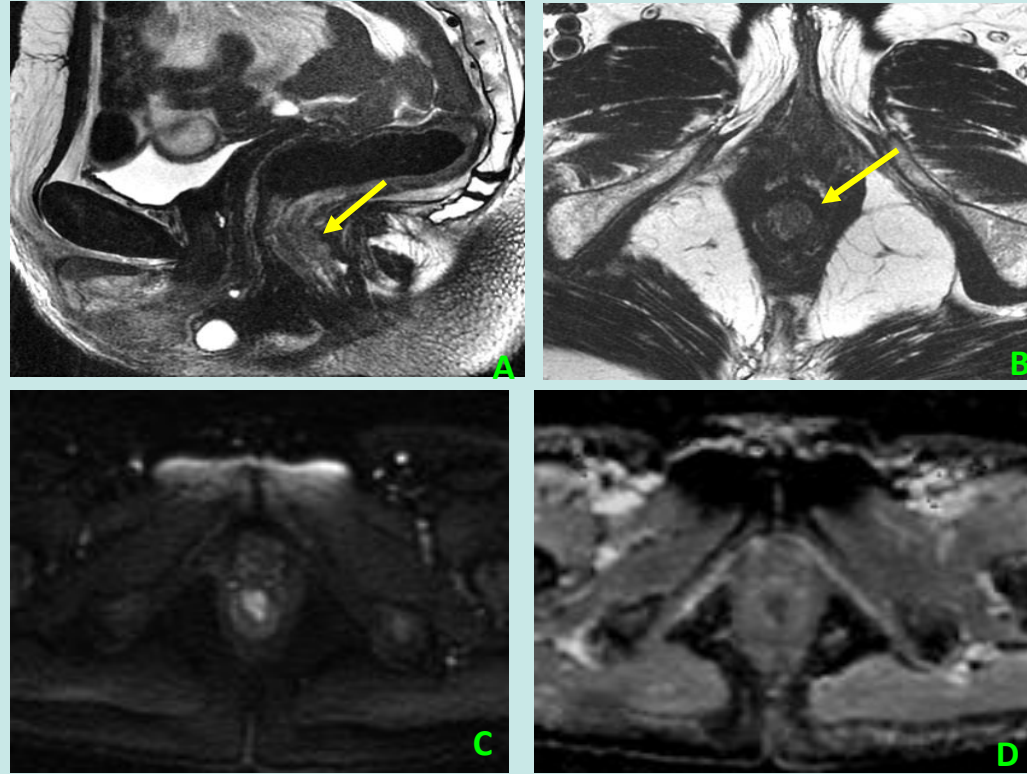


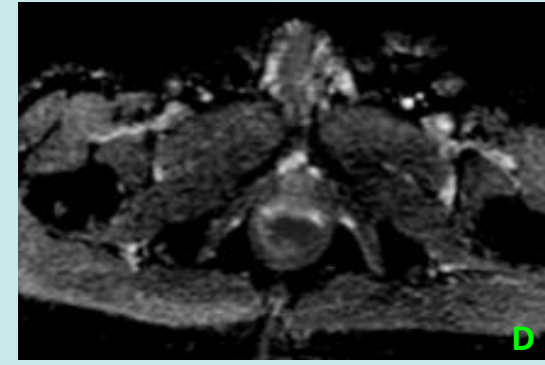
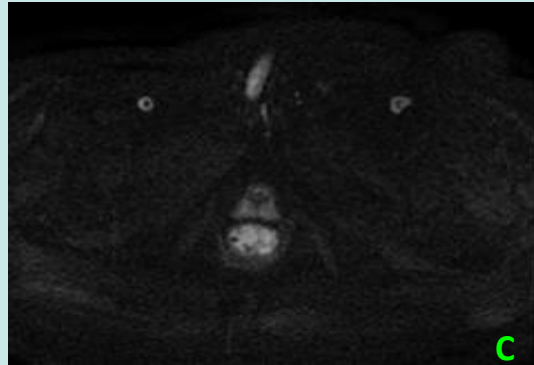
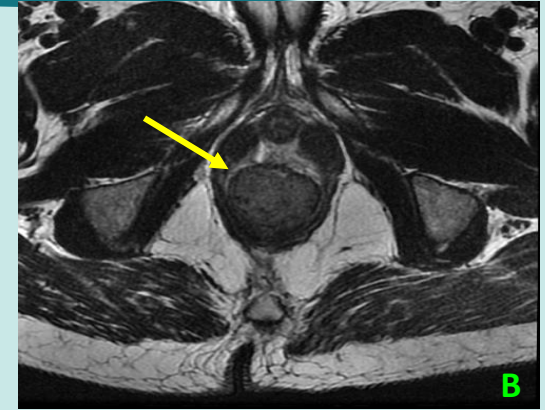
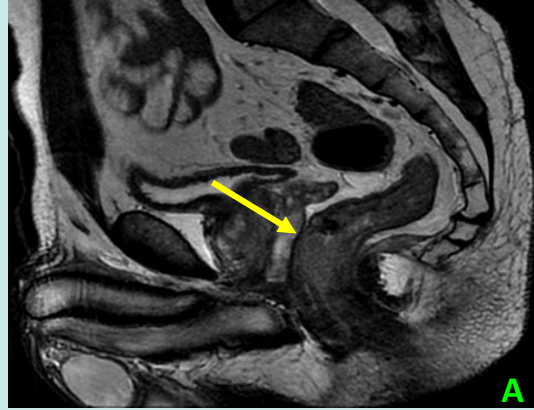
Fig 5. T2W sagittal and axial images showing the primary lesion of the anal canal measuring less than 2.0 cm on the largest axis. **(A, B)** locally extensive lesion with intermediate signal intensity on T2 (yellow arrow). **(C, D)** On DWI and ADC map, the lesion shows restricted diffusion.

Imaging Evaluation - T staging (ASCC)

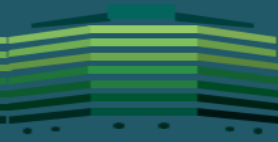
T2

The tumour is larger than 2cm but smaller than 5cm

Fig 6. T2W sagittal and axial images showing the primary lesion of the anal canal measuring larger than 2.0 cm on the largest axis. **(A, B)** locally extensive lesion with intermediate signal intensity on T2 (yellow arrow). **(C, D)** On DWI and ADC map, the lesion shows restricted diffusion.



Imaging Evaluation - T staging (ASCC)



T3

The tumour is larger than 5cm

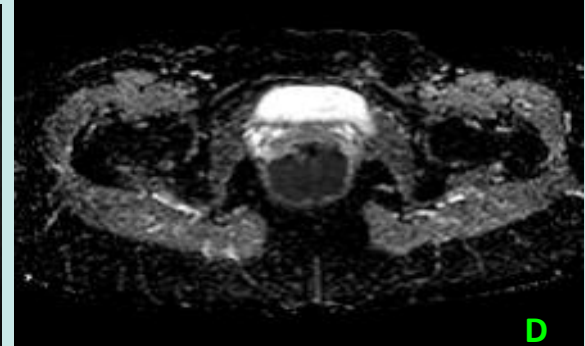
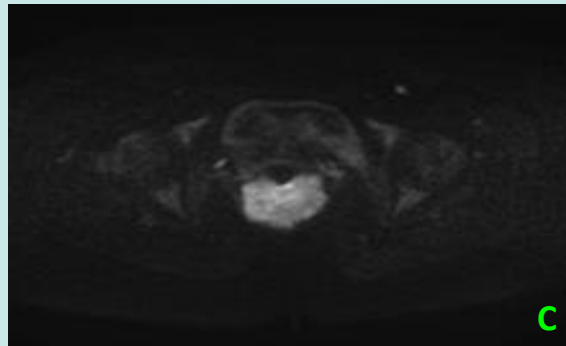
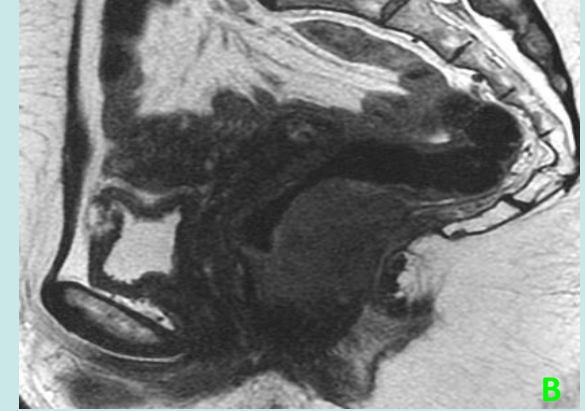
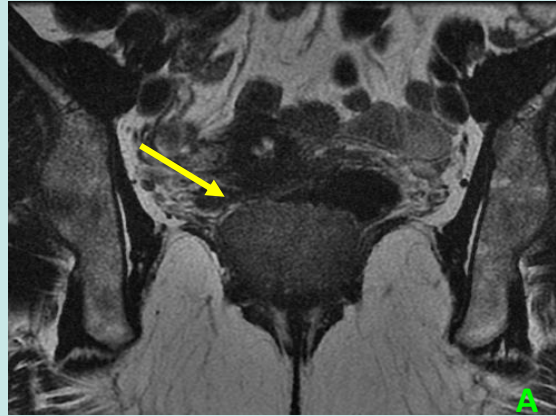
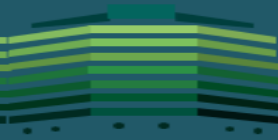


Fig 7. Coronal and sagittal **T2W** images showing lesion larger than 5 cm in the anal canal. **(A, B)** locally extensive lesion with intermediate signal intensity on T2 (yellow arrow). **(C, D)** On DWI and ADC map, the lesion shows restricted diffusion.

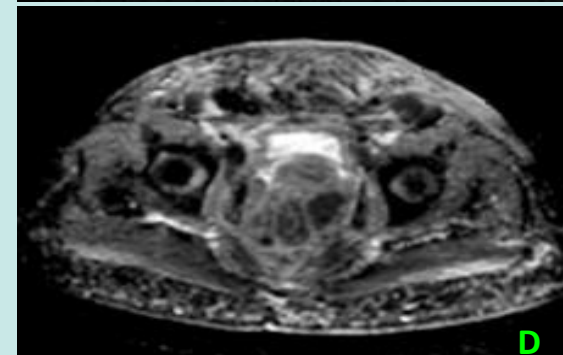
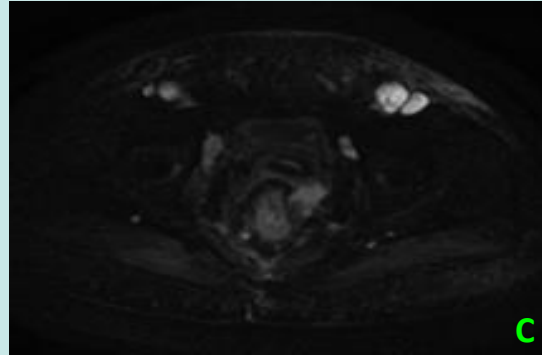
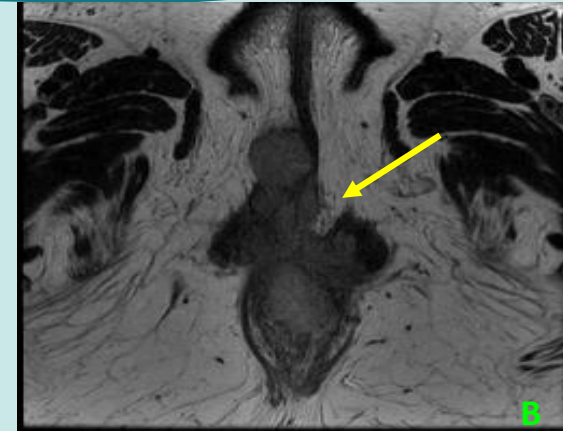
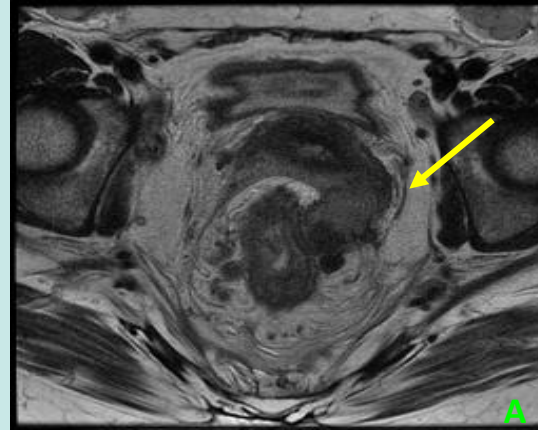
Imaging Evaluation - T staging (ASCC)



T4

The cancer is any size but it is growing into the surrounding organs, such as the urethra, prostate, vagina or bladder

Fig 8. MRI axial plane T2-weighted MRI imaging showing lesion of the anal canal, invading the uterus. **(A, B)** extensive lesion with intermediate signal intensity on T2 invading the uterus and the perineum (yellow arrow). **(C, D)** On DWI and ADC map, the lesion shows restricted diffusion.



Imaging Evaluation - T staging - LRA

T4a (peritoneal)

T4b (visceral)

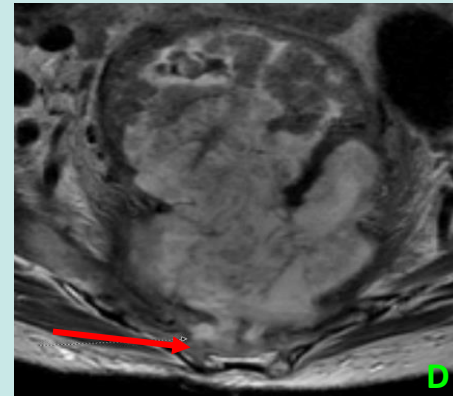
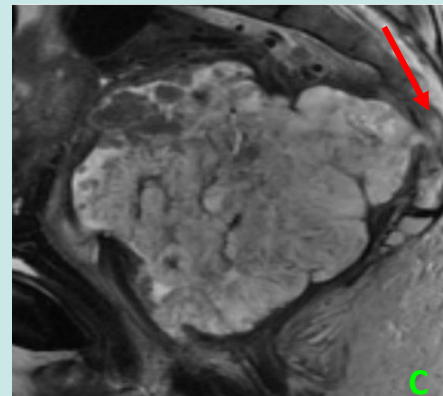
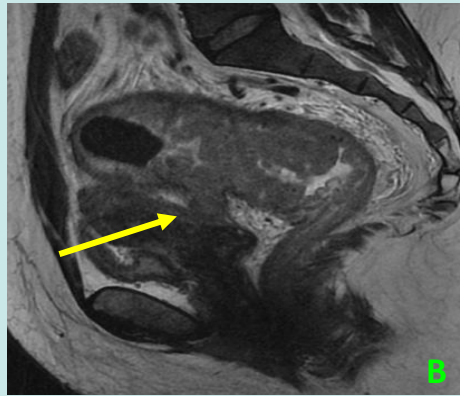
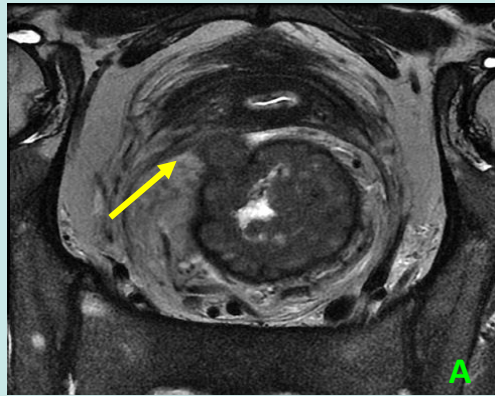


Fig 9. MRI axial of the lesion and sagittal plane T2-weighted MRI imaging showing T4 low rectal adenocarcinoma (LRA). **(A, B)** the lesion extends to the peritoneal surface (yellow arrow). Another case of T4 showing extension of the lesion beyond the own muscular layer, being emphasized infiltration of the bone marrow sacral in the level of S5 (red arrow), forming a visceral T4 **(C, D)**.

Lymphatic spread / N staging

Regional node sites:

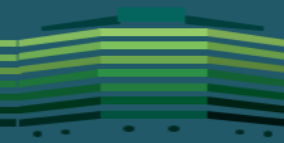
- Rectal adenocarcinoma: inferior mesenteric, superior rectal, middle rectal, mesorectal and internal iliac
- ASCC: mesorectal, internal iliac, and inguinal

Imaging has limited accuracy for nodal staging

Imaging findings related to nodal involvement in MRI according to 2016 ESGAR consensus meeting recommendations for Rectal Cancer

- Mucinous signal for LRA (high T2 signal)
- Enlarged size (based on short axis measure)
- Morphologic features:
 - Round shape (rather than usual oval shape)
 - Heterogeneous signal
 - Irregular border
- However, in ASCC, most patients are not submitted to surgery. So, the lack of surgical specimens makes the histological confirmation of radiological findings of nodal status virtually impossible

Lymphatic spread / N staging

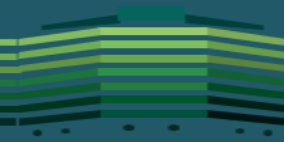


N staging		
ISSUE	ASCC	LRA
N stage	Based on locations of positive regional nodes	Based on number of positive regional nodes regardless of which regional lymph node stations are affected
Stations considered regional	Mesorectal (inferior rectal), internal iliac, and inguinal.	inferior mesenteric, superior rectal, middle rectal, mesorectal (inferior rectal), and internal iliac.
Not considered regional nodes	Common iliac or retroperitoneal adenopathy	inguinal and femoral nodes

Lymphatic spread / N staging

N staging	
ASCC	LRA
N0: no regional nodal metastasis	N0: no regional nodal metastasis
N1: mesorectal nodes	N1: 1-3 positive regional nodes
N2: unilateral inguinal and/or internal iliac nodes	N2: 4 or more positive regional nodes
N3: internal iliac and mesorectal nodes and/or bilateral internal iliac and/or bilateral inguinal nodes	N1C: tumor deposit within the mesorectal fat

Lymphatic spread / N staging – Inguinal nodes



- In patients with rectal adenocarcinoma, inguinal nodes are considered nonregional, and classified as M1 disease
 - The exception to this rule is LRA extending to the anal canal: inguinal nodes may be treated with curative intent
- In ASCC, inguinal nodes are considered regional - included in the initial radiation field
 - boost radiation dose if gross nodal disease
- In some studies, FDG PET/CT had higher sensitivity compared to MRI and contrast-enhanced CT for detection of abnormal lymph nodes and could help nodal staging both in ASCC and LRA
 - Again, the lack of surgical specimens in ASCC makes the histological confirmation of radiological findings of nodal status virtually impossible, limiting PET's accuracy calculation

Imaging Evaluation - N staging

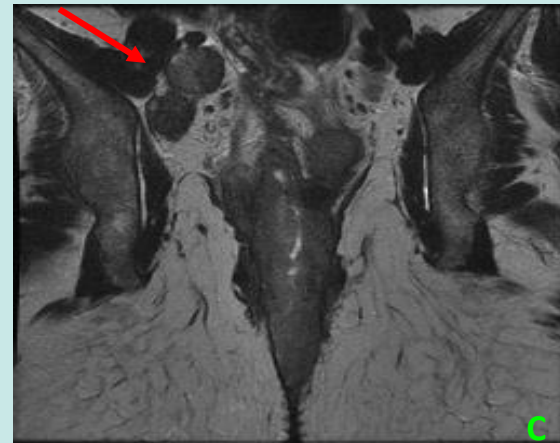
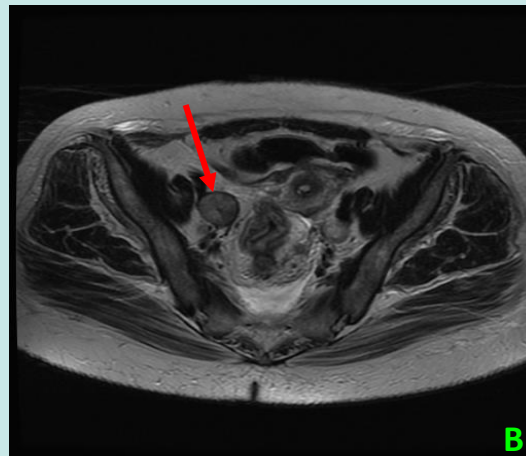
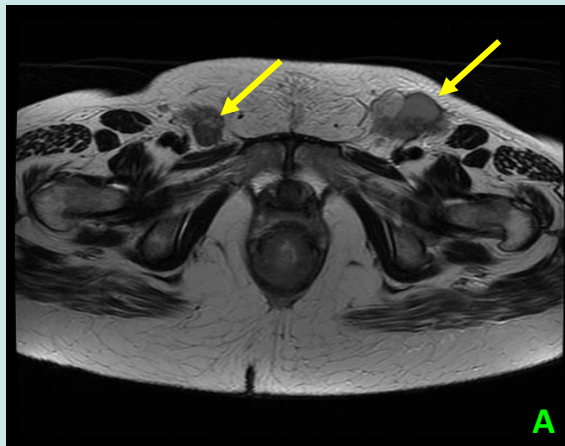
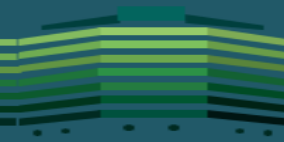
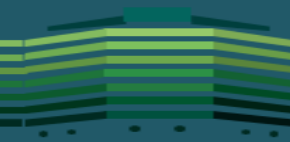


Fig 10. MRI axial and coronal plane T2-weighted MRI imaging showing lymph node metastasis. **(A)** bilateral inguinal nodes (yellow arrow) and **(B, C)** internal iliac (red arrow).

Imaging Evaluation - M staging



M staging	
ASCC	LRA
M0: no distant metastasis	M0: no evidence of metastases
M1: distant metastasis (e.g. liver and lungs, non regional positive nodes)	M1a: distant metastases confined to one organ (e.g. liver, lung, ovary, non-regional node)
	M1b: distant metastases confined to more than one organ or to the peritoneum

Imaging Evaluation - M staging (ASCC)

M1

Non-regional nodes and distant metastasis

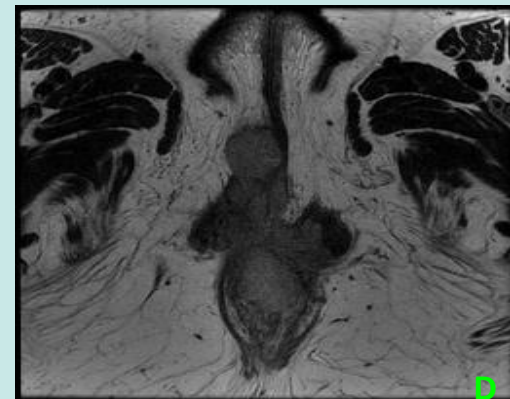
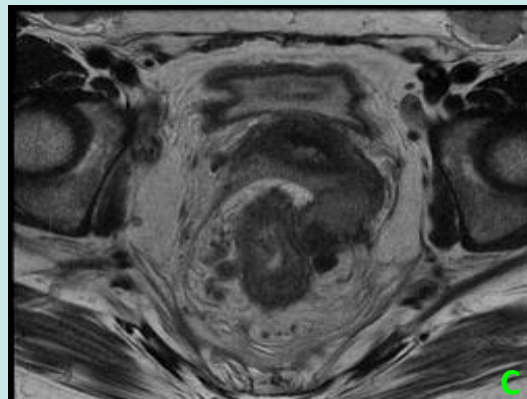
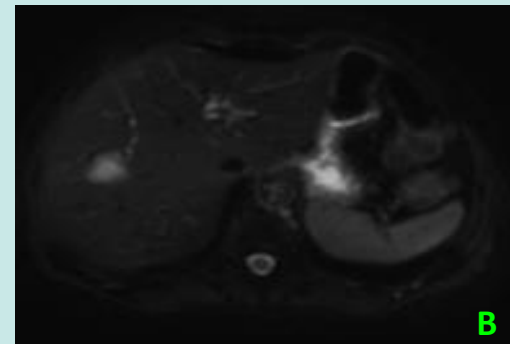
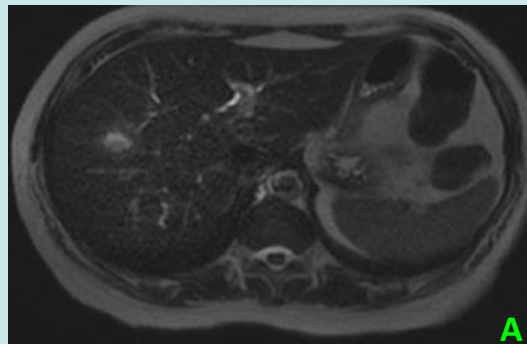
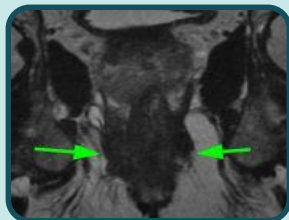


Fig 11. MRI axial images of the liver in the sequence T2 (A) and diffusion (C) showing an anal canal metastatic lesion (M1). (B, D) shows the T4 lesion of the anal canal.

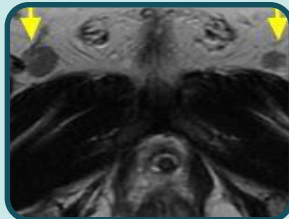
ASCC x LRA - Staging

ANAL SQUAMOUS CELL CARCINOMA



Invasion of the
external sphincter

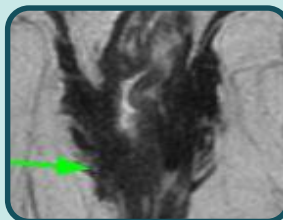
DO NOT MEAN T4



Suspicious Inguinal
nodes are considered
regional

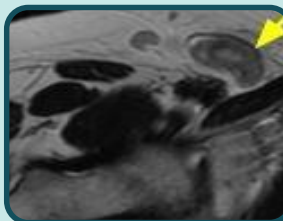
N+

LOW RECTAL ADENOCARCINOMA



Invasion of the
external sphincter

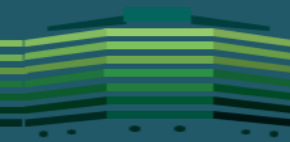
MEAN T4



Suspicious Inguinal
nodes are
considered non
regional

M1

Treatment Management



ASCC

- Curative radiation therapy and chemotherapy is the standard of care
- the gold standard for locally advanced disease is the Nigro scheme (Mitomycin, infusional 5-Fluorouracil and radiotherapy with 50,4 Gy) With the limited availability of Mitomycin, the alternative treatment is based on the ACT-II trial (Cisplatin, infusional 5-Fluorouracil and radiotherapy with 50,4 – 54 Gy)
- The standard radiation field should include the pelvis, anus, perineum, and inguinal nodes
- MRI is performed 6 weeks after the end of radiotherapy to assess treatment response
- Longer intervals of reassessment
- Abdominal-perineal resection used only for salvage in patients with persistent disease.

LRA

Often includes trimodality curative therapy (chemotherapy, radiation, and surgery) depending on clinical staging (CS) and reference center.

- Surgical resection without neoadjuvant treatment for initial cases, when the lower limit lies more than 1,0 cm from the anorectal junction
- Neoadjuvant chemoradiation followed by surgical resection in locally advanced lesions, lesions with lower limit less than 1,0 cm from the anorectal junction or positive nodal in some reference centers
- MRI is performed 6 weeks after the end of radiotherapy to assess treatment response

After neoadjuvant chemo-RT, patients with clinically complete response may be able to be followed closely with clinical, radiologic, and endoscopic examinations without surgery (Watch and wait regimen)

Chemoradiation Treatment

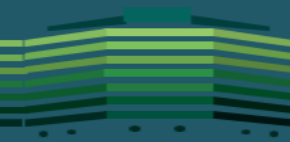
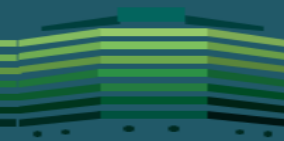


Fig 12. 55-years-old male patient, HIV +, the biopsy was consistent with ASCC. **(A, B)** locally extensive lesion with intermediate signal intensity on T2, measuring 4,0 cm (yellow arrow). **(C, D)** On DWI and ADC map, lesion shows restricted diffusion. **(E)** There were suspicious mesorectal lymph nodes (green arrows). MRI pre-treatment staging: T2N1. The patient was treated with curative chemoradiation therapy (CRT) and post-treatment MRI (8 weeks after the end of radioterapy), showed no evidence of residual tumor, with a fibrotic scar at the previous lesion location as shown on T2 **(F,G)**, DWI **(H)** and ADC map **(I)**. Significant size reduction of suspicious lymph nodes **(J)**.

Remember...



Key distinctions between ASCC e LRA		
Issue	ASCC	LRA
Histology	Squamous cell carcinoma	Adenocarcinoma
T staging	Based on size	Based on depth of invasion
Definition of regional nodes	Mesorectal (inferior rectal) and internal iliac; discrepant sites: inguinal and femoral.	Mesorectal (inferior rectal) and internal iliac; discrepant sites; inferior mesenteric, superior rectal, middle rectal.
N staging	Based on location of nodes	Based on number of nodes
Nodal station in radiation field (beyond primary field)	Inguinal	Mesorectal and internal iliac; external iliac nodes are added when tumor invades the anterior pelvic structures (T4).
Inclusion of radiation therapy	Standard for all anal canal cancers, any T2 or higher anal margin cancer	T3 or higher or N + disease

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Thank you!