Computed Tomography vs Magnetic Resonance Imaging in the evaluation of intra- and extra-peritoneal rectal cancer

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Aims and objectives

The discrimination between intra- and extraperitoneal rectal cancer has important implications for both oncologic and surgical grounds, since these different tumors have to be treated in different ways and since they present different risks of local recurrence and different prognosis [**1**]: tumors located above the peritoneal reflection have to be considered as colon cancers, since they share the same clinical course, while locally advanced (>T3a or N+) extraperitoneal rectal tumors take advantage of combined chemoradiation preferentially administered before surgery (i.e. neoadjuvant chemoradiation) [**2, 3**].

Recent studies dealt with the role of MRI in directly showing the relationship between the peritoneal reflection and the tumor on high-resolution images [**4, 5**], thus providing an accurate preoperative identification of tumor's location and a tailored treatment planning. However, patients with rectal cancer routinely undergo a contrast-enhanced CT scan of chest and abdomen looking for distant metastasis: in this scenario, a direct visualization of the peritoneal reflection (and consequently of the location of tumors) may be possible on CT images as well as on MR images. The purpose of our study was to compare the diagnostic performance of CT with that of MRI to determine the extra- or intraperitoneal location of rectal cancers, using surgical exploration as reference standard.

Methods and materials

Inclusion of patients

This was a retrospective, single-center, institutional review board approved study. Patients were included by performing a search in our single-institution radiology database looking for patients with a recent diagnosis of rectal carcinoma (any T and N stage) scheduled for surgery (i.e. anterior resection or total mesorectal excision - TME -), with or without neoadjuvant therapy, between January 2012 and December 2013. In this time interval, we included all patients who both underwent thin-section rectal MRI for local tumor staging and contrast-enhanced CT for distant metastases staging before surgery. Surgical exploration was used as reference standard to assess the exact position of the inferior margin of tumors with respect to the APR. Exclusion criteria were represented by general contraindications to MRI (e.g. claustrophobia, pacemaker, ferromagnetic metal fragments or implanted medical devices). Renal insufficiency (GFR <30ml/min) was considered an exclusion criteria for CT but not for rectal MRI, since the latter is commonly performed without intravenous injection of paramagnetic contrast media.

MRI and CT protocols

High-spatial-resolution pelvic MRI examinations were performed with a 1.5T MRI scanner (Signa™ HDxt, GE Healthcare, Milwaukee, WI) and a pelvic phased-array coil, according to a standardized protocol [**4, 6**]. The following parameters were applied for two-dimensional T2-weighted fast-recovery fast spin echo (FSE) sequences: repetition time (TR)/ echo time (TE) 4000-6000/80-160, echo-train length 24-49, flip angle 90°, bandwidth 50 kHz, field-of-view (FOV) 18-36 cm, matrix 256×256, number of excitations 4-6. FSE T2-weighted sequences (slice thickness 4 mm, interslice gap 0.4 mm) with a large field of view were first oriented in the three orthogonal planes (sagittal, axial, and coronal), without fat saturation, enabling identification of the primary tumor. High-resolution oblique axial and coronal scans (slice thickness 3-3.5 mm, interslice gap 0.3 mm) were further oriented perpendicular and parallel to the long axis of the tumor, in order to avoid misinterpretation due to partial volume effects. In the case of low rectal cancers, high-spatial-resolution coronal images were performed to optimally show the levator muscles, the sphincter complex, as well as the intersphincteric plane. A Diffusion-Weighted Imaging (DWI) sequence (b 1000 s/m^2, TR 7100, TE 60-90, bandwidth 250 kHz, FOV 40×40, slice thickness 4.0 mm, interslice gap 0.4 mm, matrix 128×128, number of excitations 6) was acquired in the axial plane for aiding the identification of the inferior edge of tumors. Patients did not receive bowel preparation or spasmolytic agents. Intravenous paramagnetic contrast medium was not administered.

CT examinations were performed with a 64-slice CT scanner (LightSpeed VCT, GE Healthcare, Milwaukee, WI). Contrast-enhancement was produced by i.v. injection of

iodinated contrast medium with an iodine concentration ranging between 350 and 370mg/mL (iobitridol, Xenetix 350, Guerbet, or iopamidol, Iopamiro 370, Bracco). The iodine load was 1.5 mg per kg of body weight. The flow rate was set at 3.2-3mL/s with an automatic injector and CT acquisition was started in the portal phase 45s after contrast media bolus detection in the upper abdominal aorta, using a bolus-tracking software. In some cases a CT with water enema (CT-WE) was performed, using a previously described technique [**7**]. Large bowel cleansing was obtained with a low fiber diet for 3 days before the CT-WE, and oral administration of 2000 mL of an isotonic non-absorbable electrolyte solution containing poly- ethylene glycol (Isocolan, Bracco, Milan, Italy) was given the afternoon before examination. At the time of examination, large bowel lumen was distended by the trans-rectal introduction of 1500-2000mL of tap water with the patient placed on the CT table. To reduce abdominal discomfort of patients and to avoid motion artifacts during the CT acquisition, bowel hypotonia was obtained by the intravenous injection of 2 mL hyoscine-N-butylbromide 20 mg/mL (Buscopan, Boehringer Ingelheim). CT images were acquired with the patient in supine position. Bowel wall enhancement was produced with the same technique described for conventional CT examinations.

Image analysis

All MRI and CT studies were reviewed in consensus on a dedicated workstation (ADW 4.6, GE Medical Systems, Milwaukee, WI) by two abdominal radiologists (MR and FP) with 5 and 10 years of experience in abdominal imaging, respectively, blinded to the location of the masses. They had to define the extra- or intra-peritoneal location of tumor's inferior edge with respect to the APR. This anatomical structure was defined according to Brown et al. [**8, 9**]. On MR midsagittal images the APR was identified as a thin hypointense linear structure coursing along the superior aspect of bladder (men) or uterus (women) to reach its attachment onto the anterior rectal wall (**Figure 1B**), as previously described [**4, 5**]. On FSE T2-weighted axial images, the peritoneum attaches in a V-shaped manner onto the anterior rectal wall, an appearance that has been defined as "seagull" sign [**8**]. DWI axial sequences were helpful to confirm the level of the inferior edge of tumors [**10**]. On CT images the APR was identified as a thin slightly hyperdense linear structure, surrounded by hypodense fat tissue, coursing as previously described on MR images (**Figure 1A**). Curved planar reformations were helpful to identify the correct location of the APR (**Figure 2A**). The two readers defined the quality of identification of the APR according to a 4-point confidence scale: 0, not visible; 1, poor; 2, good; 3, excellent. The distance from the inferior edge of tumors to the anal verge was measured in millimeters by means of an electronic digital caliper both on MRI and the CT images (**Figure 2B**). This measurement required two or more interconnecting straight lines for an approximate total length on MR images and the use of multi-planar reconstructed images on CT examinations. The distance between the anal verge and the APR was registered too (**Figure 2B**).

Standard of reference

We used surgical exploration as reference standard to assess the exact position of the inferior margin of tumors with respect to the APR: as previously described [**4, 11**], the limit between intra- and extra-peritoneal rectum has been defined intra-operatively as the site where the peritoneal serosa leaves the lateral walls of rectum merging inferiorly toward the midline to cover the anterior surface (i.e. APR) [**4**].

Statistical analysis

Categorical variables were expressed as number and percentage, while continuous variables as mean and standard deviation. The normal distribution of MRI and CT measurements was assessed by means of the D'Agostino-Pearson test. Mann-Whitney test was used to assess the presence of a significant difference between MRI and CT measurements, while their degree of correlation was assessed by the Spearman's rank test. The diagnostic performance of MRI and CT in determining the extra- vs intra-peritoneal location of rectal cancers was calculated using tables with positive cases corresponding to the extra-peritoneal location and negative cases to the intra-peritoneal location. Sensitivity, specificity, disease prevalence, as well as positive and negative predictive values were calculated.

Images for this section:

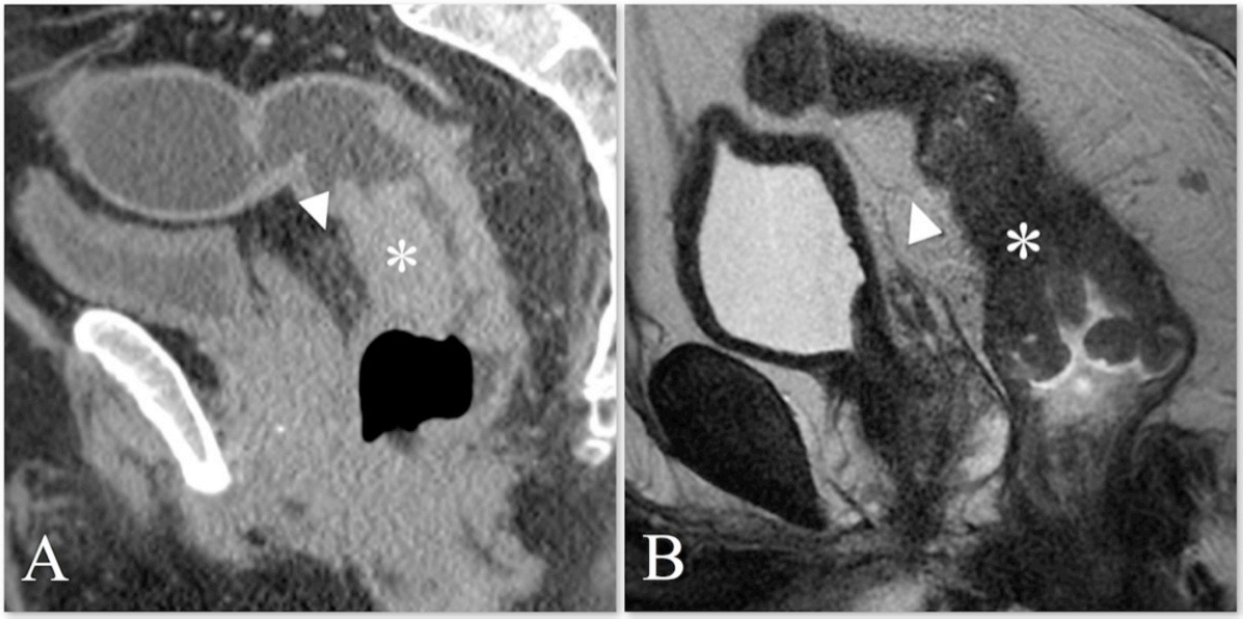

Fig. 1: CT with water enema and rectal MRI of a 68-years old man with locally advanced rectal cancer (T3c, N2, M0). Sagittal reconstructed CT image (A) and sagittal T2-weighted MR image (B) showing the location of the peritoneal reflection (arrowhead), appearing as a linear hyperdense/hypointense linear structure, with respect to the tumor (*). It is important to notice that the confidence of detection of the APR is much higher using MR images compared to CT images.

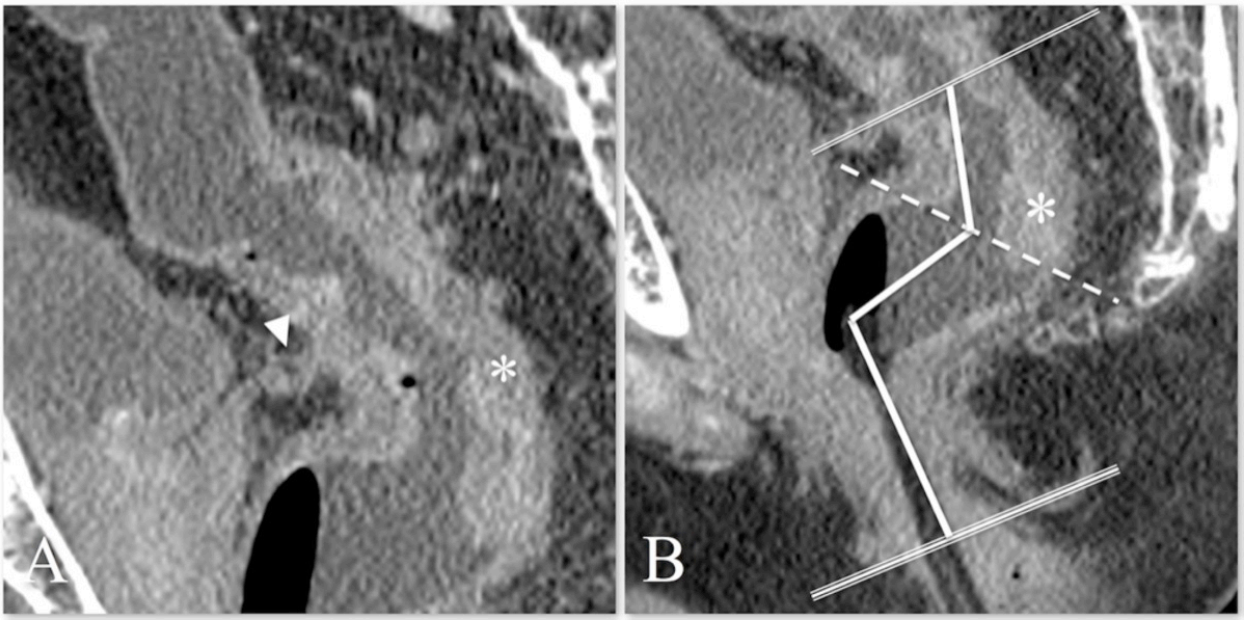

Fig. 2: CT with water enema of a 73-years old male patient with locally advanced rectal cancer (T3c, N2, M0). In this case, the use of a curved planar reformation (A) was helpful to identify the correct location of the APR (arrowhead) and its relationship with the rectal tumor (*). On sagittal reconstructed image (B) we can see the evaluation of the distance from the inferior edge of the tumor (dotted line) to the anal verge (triple line) by means of two interconnecting lines measured with an electronic digital caliper. Using the same modalities, the distance between the anal verge and the APR (double line) was registered too.

Results

Patients' characteristics

38 patients were included: 24 (63%) men and 14 (37%) women with a mean age of 68.8±9.4 years (range: 55-83 years). Mean height and weight of male patients were 172.2±9.8 cm and 73.6±8.8 kg, respectively, and mean BMI was 23.8±3.3. Mean height and weight of female patients were 164.3±9.2 cm and 64.1±9.7 kg, respectively, and mean BMI was 24.0±2.9. 2 patients had a stage I (T1/2, N0, M0) rectal cancer, 7 patients had a stage II (T3 or T4, N0, M0) rectal cancer, and 29 patients presented a stage III (T1/2, T3, T4, N1 or N2, M0) tumor. The prevalence of extra-peritoneal cancers was 35/38 (92%), while that of intra-peritoneal cancers was 3/38 (8%).

Image analysis and diagnostic performance

The APR was appreciable in all (100%) MRI examinations and in 36/38 (94.7%) patients on CT images: reviewing MR images, the quality of individuation of the APR was defined excellent by the two readers in 14/38 (36.8%) MRI examinations, good in 22/38 (57.9%) and poor in 2/38 (5.3%) cases; reviewing CT images, the quality of individuation of the APR was defined excellent by the two readers in 6/38 (15.8%) examinations, good in 19/38 (50%) cases, poor in 11/38 (28.9%) cases and, as previously reported, not visible in 2/38 (5.3%) cases (**Table 1**).

On MR images the mean distance from the APR to the anal verge was 100.8±20.5 mm (range 73-133) for males and 95.9±15.7 mm (range 70-121) for females (p=0.4426, t-test for independent samples); on CT examinations the mean distance from the APR to the anal verge was 102.2±13.1 mm (range 81-124) for males and 97.5±12.5 mm (range 78-115) for females (p=0.4579, t-test for independent samples). Mean distances from the APR to the anal verge for all patients were 98.97±18.8 mm at MR and 100.6±12.9 mm at CT (p=0.6653, t-test for independent samples) (**Table 2**).

MR, as previously described [**4**], was characterized by an excellent diagnostic performance: sensitivity 100% (95% CI: 89.62% to 100.00%), specificity 75% (95% CI: 20.34% to 95.88%), positive predictive value 97.14% (95% CI: 85.03% to 99.52%), negative predictive value 100% (95% CI: 30.48% to 100.00%). Diagnostic performance of CT, excluding 2 patients without visualization of APR, resulted as follows: sensitivity 100% (95% CI: 89.32% to 100.00%), specificity 60% (95% CI: 15.40% to 93.51%), positive predictive value 94.29% (95% CI: 80.81% to 99.13%), negative predictive value 100% (95% CI: 30.48% to 100.00%) (**Table 3**).

The mean distance from the inferior edge of tumors to the anal verge was 62.3±21.2 mm at MR and 62.5±20.1 mm at CT (p=0.8181 Mann-Whitney test for independent samples)

(**Table 2**). The two measurements were strongly correlated (Spearman's coefficient of rank correlation (rho): 0.995; p<0.0001).

Images for this section:

	MR	CT
Excellent	14/38 (36.8%)	6/38 (15.8%)
Good	22/38 (57.9%)	19/38 (50%)
Poor	2/38 (5.3%)	11/38 (28.9%)
Not visible	-	2/38 (5.3%)

Table 1: Quality of detection of the APR on MR and CT examinations.

	MR	CT	*P-value*
Mean distance between APR and anal verge	98.97±18.8 mm	100.6±12.9 mm	0.6653
Mean distance between inferior edge of tumor and anal verge	62.3±21.2 mm	62.5±20.1 mm	0.8181

Table 2: Mean distances between APR and anal verge and between inferior edge of tumors and anal verge, with statistical significance.

	MR	CT*
Sensitivity	100%	100%
Specificity	75%	60%
PPV	97.14%	94.29%
NPV	100%	100%

Table 3: Diagnostic performance of MR and CT in evaluation of intra- or extra-peritoneal location of rectal cancers. *CT values were computed excluding the 2 patients in whom the APR was not detected.

Conclusion

Recent studies have already discussed how the position of rectal tumors with respect to the APR has important treatment implications, since extra- and intra-peritoneal cancers present different systemic spread [**1, 4, 12, 13**]: as a consequence, an accurate preoperative identification of the APR may address extra-peritoneal tumors to neoadjuvant therapy [**13**], since choosing the optimal treatment for each patient is crucial in relation to the risk of under- or overtreatment. Rigid rectoscopy may provide a measurement of the distance from the inferior edge of tumors to the anal verge, and several trials on pre-operative radiation have considered patients using different cut-off measures, varying in a range of 12-16 cm from the anal verge [**14-16**], with a consistent risk of overtreatment. Paparo et al. recently found that a cut-off measure <10 cm is sufficient to reach a 100% sensitivity in detecting extra-peritoneal cancers, preserving an acceptable specificity [**4**], results confirmed by the Dutch TME trial, which showed no beneficial effect of radiation therapy for cancers above 10 cm from the anal verge [**14**].

If the greatest limitation of endoscopy is represented by the lack of an optimal cut-off measure to distinguish extra- from intra-peritoneal tumors, due to the great variability of APR location, MRI recently showed its ability to overcome this limitation, providing a clear preoperative visualization of APR in addition to the loco-regional staging [**4, 5**]. Other imaging modalities showed great potentiality in the evaluation of local and systemic involvement of rectal cancer, such as FDG-PET and FDG-PET/CT, especially with respect to clinical management and neoadjuvant treatment planning of locally advanced rectal cancer [**17, 18**]; however, also CT and CT-WE may provide important informations about the loco-regional features of rectal cancers, while they are commonly used as the initial staging modality because of their wide availability and their ability to evaluate distant metastasis [**19**]: in this scenario, we decided to verify if the APR could be detected on CT and CT-WE as well as on MR images, allowing an accurate discrimination between intra- and extra-peritoneal rectal cancers. As seen on MR images, the APR is a thin hypointense/hyperdense linear structure running from the tip of the seminal vesicles in men or from the utero-cervical angle in women to its attachment on the anterior rectal wall [**4, 5**]. If motion artifacts are the main causes that may prevent the visualization of the APR on MR images, beam hardening artifacts due to the presence of metallic hip prosthesis represent a major limitation for the detection of the APR and of tumor location on CT images (**Figure 3**).

In our study, the diagnostic performances of MRI and CT in distinguishing extra- vs intra-peritoneal tumors were comparable, but in 2 cases CT did not allow the visualization of the APR, while it was detected in all MR examinations. However, when compared to MR imaging, the intrinsic inferior spatial and contrast resolution of CT can be partially balanced out by the employment of post-processing techniques, as usually happens for emergency finalities (e.g. bowel obstruction) [**20**]: in particular, the use of CT curved planar reformations to obtain a straight representation of the rectum helped us in the

evaluation of the level at which the different structures involved are localized (**Figure 2A**). Nevertheless, the use of these tools does not always compensate for the intrinsic limitation of CT in local evaluation: in fact, we were not able to identify the location of the APR in two patients, one because of the presence of beam hardening artifacts, the other one because of the poor quality of visualization. Furthermore, it is important to notice that despite we expected a better diagnostic performance of CT-WE compared to conventional CT, because of bowel distention that should allow an easier and more accurate measurement of the distances between the anal verge and the APR and the tumors' inferior edge respectively, we did not detect significant differences between the two techniques.

Limitations of our study are mainly represented by the low prevalence of intra-peritoneal cancers, but this percentage, despite the low number of patients included in the current study, is coherent with our previous results and with the common clinical practice [**4, 5**]. All examinations were performed before surgery and/or neoadjuvant chemoradiation, so potential tumor's shrinkage did not influenced our results. We have already pointed out that a minor methodological limitation is represented by the use of the anal verge as landmark for the lower part of the external sphincter on MR and CT images, possibly leading to clinical and anatomical discrepancies; however the excellent correlation between MRI and rigid rectoscopy [**4**] and between CT and MRI measurements pushed us to consider the anal verge as a reliable marker at cross-sectional imaging.

The results of our study further confirm the great clinical value of MRI in determining the extra- vs intra-peritoneal location of rectal cancers by the direct visualization of APR in a preoperative setting; CT and CT-WE showed as well to have the possibility to play a potential supporting role in the evaluation of rectal cancer, but it appears unlikely that CT could currently replace MRI in local staging. Furthermore, MRI and CT measurements of the distance between the tumor's inferior edge and the anal verge demonstrated a strong correlation.

Images for this section:

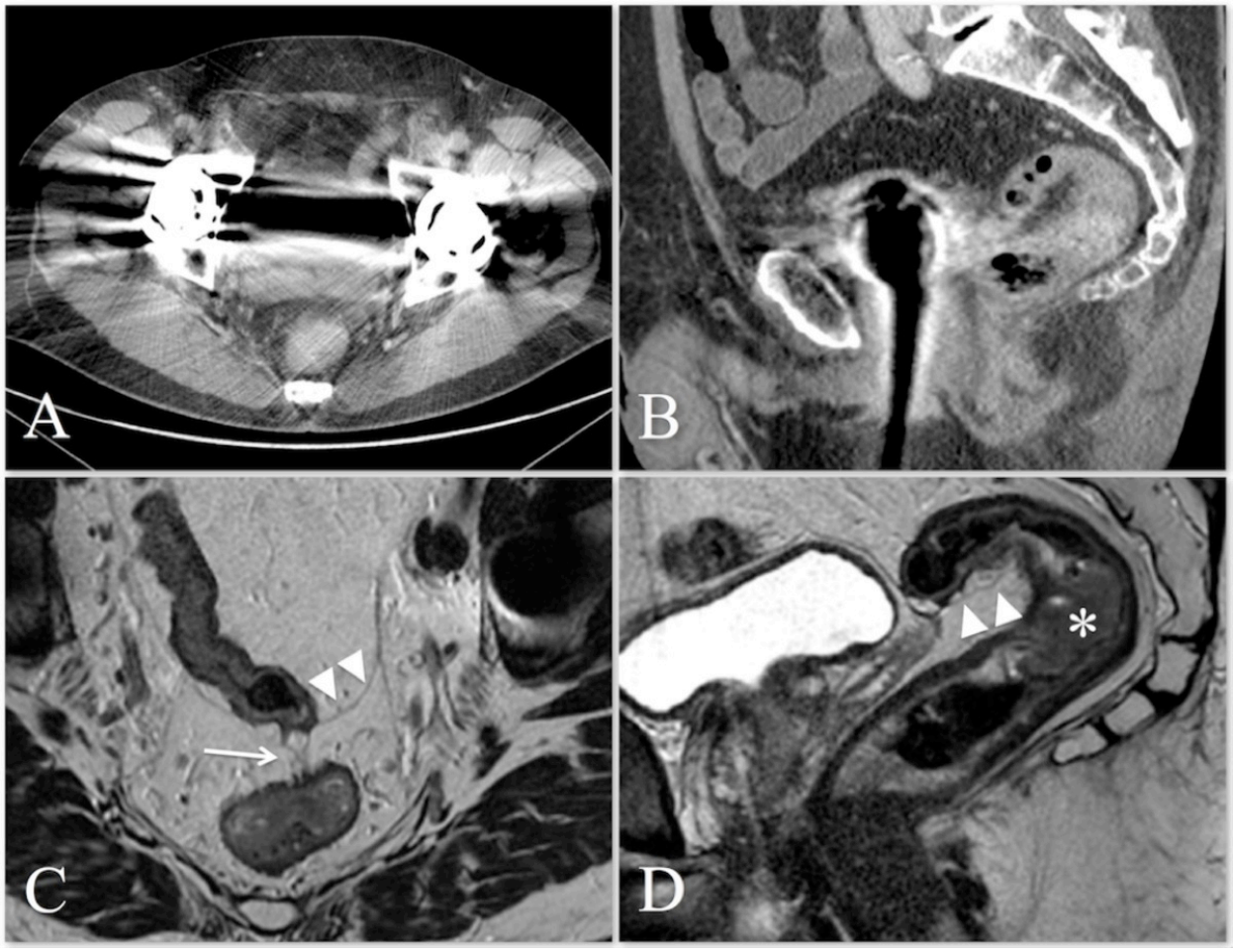

Fig. 3: Abdominal CT (A, B) and rectal MR (C, D) of a 69-years old man with rectal cancer (T3a, N2, M0). Axial (A) and sagittal reformatted (B) CT images show the presence of severe beam hardening artifacts due to the presence of a bilateral hip prosthesis, not allowing a proper visualization of the pelvic region. On the other hand, MRI can provide a precise depiction of the peritoneal reflection (arrowheads), appearing as a hypointense linear structure, and of its attachment on the anterior wall of the rectum (arrow in C) both on axial (C) and sagittal (D) T2-weighted images: in this patient, the inferior edge of the tumor (* on D) is located under the APR.

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