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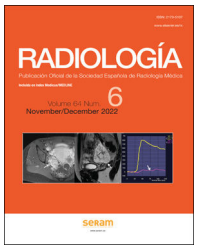

UPDATE IN RADIOLOGY

Clinical applications of bladder magnetic resonance imaging: Beyond the VI-RADS® classification

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Abstract Bladder cancer is a cause for serious concern due to its high prevalence and the considerable challenges it poses in terms of morbidity, costs, and mortality. In recent years, magnetic resonance imaging (MRI) of the bladder has proved to be a useful tool with a significant impact on both local staging and the assessment of neoadjuvant treatment responses. This article reviews the main anatomical, histological and radiological characteristics of bladder neoplasms, describes bladder MRI, explains the VI-RADS® classification—which should only be used to classify malignant lesions and in studies undertaken principally to evaluate the probability of tumour infiltration in the muscular layer—and specifies how this technique can optimise the clinical management of patients with bladder neoplasms.

PALABRAS CLAVE
Cáncer de vejiga;
Resonancia magnética;
VIRADS®;
Cáncer de vejiga no músculoinvasivo;
Neoplasias de vejiga músculo infiltrantes

Aplicaciones clínicas de la resonancia magnética de vejiga: más allá de la clasificación VIRADS®

Resumen El cáncer de vejiga es una enfermedad de gran relevancia debido a su alta prevalencia y su importante morbilidad, coste y mortalidad. En los últimos años, la resonancia magnética (RM) de vejiga ha demostrado ser una herramienta útil con gran impacto tanto en la estadificación local como en la valoración de respuesta a los tratamientos neoadyuvantes. El objetivo de este trabajo es repasar las principales características anatómicas, histológicas y radiológicas de las neoplasias de vejiga, presentar la RM de vejiga, explicar la clasificación VIRADS®,

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que debe ser utilizada únicamente en lesiones malignas y cuya principal finalidad es evaluar la probabilidad de infiltración tumoral en la capa muscular, y describir cómo esta técnica puede optimizar el manejo clínico de los pacientes con neoplasias vesicales.

Introduction

Bladder cancer is the ninth most common cancer in both sexes worldwide, with more than 600,000 new cases diagnosed each year as of 2020.[1,2] Urothelial carcinoma is the most common histological subtype, accounting for around 90% of bladder tumours.[3] The management of this type of tumour depends on local staging, with invasion of the muscle layer being the most relevant factor. With this in mind, bladder tumours are classified into 2 groups: superficial or non-muscle-invasive bladder tumours (NMIBT) and muscle-invasive bladder tumours (MIBT). This is of great relevance as there are large differences in the treatment, prognosis and survival of patients.[4]

Although significant advances in the treatment of bladder neoplasms have been made in recent years, these have not been reflected in patient prognosis, which has not changed significantly over the last 30 years.[5] For this reason, there is great interest in improving both the local staging process and the assessment of neoadjuvant treatments (NT) in MIBT. In this regard, the introduction of magnetic resonance imaging (MRI) and the development of the Vesical Imaging Reporting and Data System (VIRADS®) classification and its variants[6,7] are bringing about a radical change in the management of these tumours, which has led the European Association of Urology to recommend bladder MRI prior to transurethral resection (TUR)[8], provided this technique is available.

The aim of this work is to introduce bladder MRI, explain the VIRADS® classification and describe how this technique can optimise the clinical management of patients with bladder neoplasms.

Normal bladder anatomy

The bladder is an extraperitoneal, hollow organ. It is located in the pelvis, behind the symphysis pubis and in front of the uterus in women and the rectum in men.

The bladder wall is composed of three main layers. From internal to external, these are the mucosa, the muscularis propria and the perivesical fat. The mucosa, in turn, is composed of superficial urothelium and subepithelial connective tissue of variable thickness called the lamina propria, which contains a thin muscle layer (muscularis mucosae). This thin muscle layer incorporates prominent vascular structures and is not always present. In cases where it is absent, the prominent vessels described can be used as a locator for the muscularis mucosae.[9] This finding is relevant for staging bladder tumours. The remaining connective tissue located between the muscularis mucosae and the muscularis propria of the bladder is called the submucosa.[10]

The muscularis propria is of variable thickness and is composed of abundant smooth muscle fibres with different orientations. In the outermost region of the muscle layer, fat foci can be observed which continue into the perivesical fat layer.[11]

MRI is an imaging technique with excellent contrast resolution. This technique can differentiate, in different sequences, the superficial (mucosal) layer from the muscle layer, given their different histological composition. In T2-weighted sequences the muscle layer is hypointense, while the superficial layer (urothelium and lamina propria) is not usually differentiated if there is no associated disease. In diffusion with high b-values (800—1000) and apparent diffusion coefficient (ADC), the muscle layer shows a slight homogeneous and intermediate signal, while the superficial layer is not identified. In the early phases of a dynamic contrast-enhanced (DCE) MRI study (about 30 s after contrast injection), the superficial layer shows an early, intense and homogeneous enhancement, while the muscle layer shows a later and less intense enhancement[10] (Fig. 1).

The superficial layer can be distinguished in T2-weighted sequence, diffusion and ADC when it is thickened by inflammatory disease or other causes. In these cases, it will be seen as a hyperintense layer in T2, hypointense in diffusion and with high ADC values.

Bladder neoplasm: morphological and histological features

Bladder tumours can mainly present three different behaviours: exophytic lesions (endoluminal growth), endophytic lesions (intramural growth) and flat or non-mass effect lesions. Within the exophytic lesions, two different morphologies can be distinguished: sessile and polypoid.[12] Polypoid lesions (Fig. 2) show intravesical growth and a lesional stalk with variable internal signal (generally low T2 and high b-values, high ADC signal and early contrast enhancement). Sessile lesions have no stalk and a large contact surface with the bladder wall (Fig. 3). If there is chronic inflammation of the lamina propria, a thickening of the superficial layer below the lesion (called the inner layer in the literature) may appear, which may slightly raise a flat or sessile lesion (giving a false image of a pedicle) and may be more extensive than the base of the lesion (Fig. 2). The surface of bladder neoplasms may have papillae (a cystoscopic and histological finding), regardless of whether they

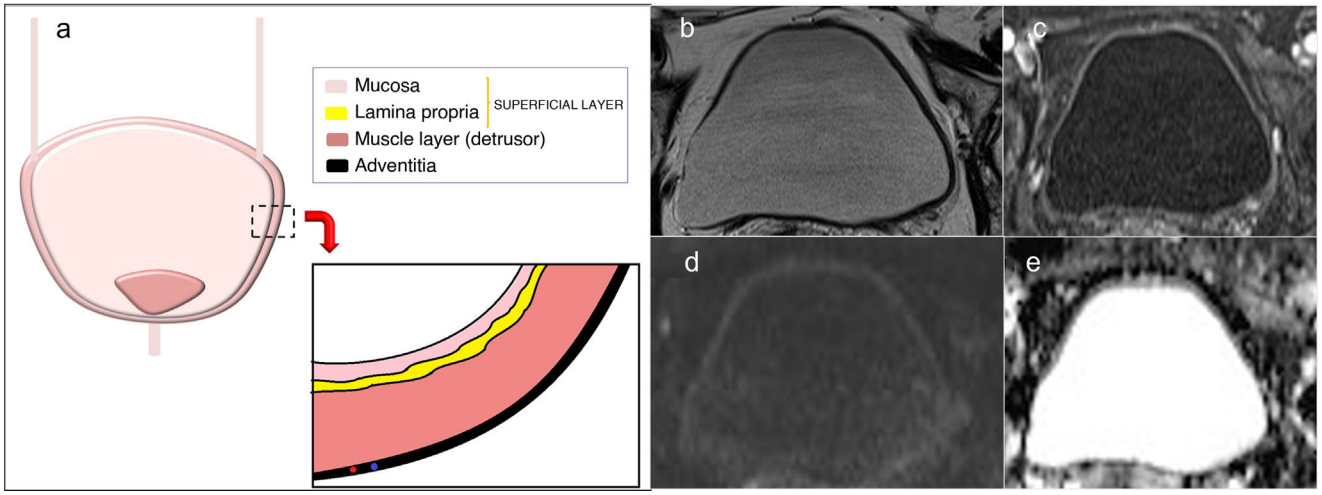

Figure 1 a) Normal anatomical diagram showing the different layers of the bladder. b-e) Normal anatomy of the bladder in MRI. b) Axial T2. c) Dynamic study with early phase contrast. d) Diffusion (b1000). e) ADC. Note the homogeneous and unilamellar appearance of the bladder wall in all sequences.

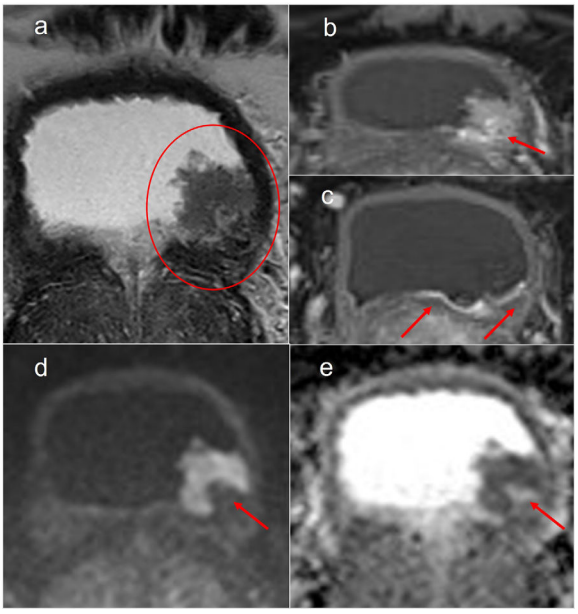

Figure 2 a) Axial T2 showing an exophytic polypoid lesion located on the left posterolateral aspect of the bladder (segments 7-5) (red circle). The lesion presents a hyperintense stalk in T2. b and c) Dynamic study with early-phase contrast showing a maintained linear submucosal enhancement that exceeds the base of the lesion (inner layer) (red arrows). d) Diffusion (b1000). e) ADC. Restriction of the superficial component of the tumour and a lesion stalk without signs of tumour infiltration (red arrows) can be seen. VIRADS® 2 lesion with an outcome of pTa after TUR.

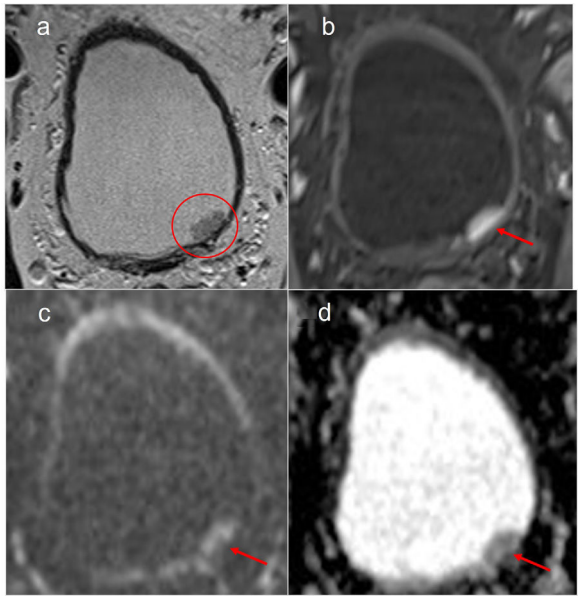

Figure 3 a) Axial T2 showing an exophytic sessile lesion located on the left posterolateral aspect of the bladder (segments 7-5) (red circle). The lesion presents a wide implantation base without signal alteration in the muscular layer. b) Dynamic study with early phase contrast showing a linear submucosal enhancement maintained in the lesion's implantation base (inner layer) (red arrow). c) Diffusion (b1000). d) ADC. Slight restriction is seen in the superficial component of the tumour without signal alteration in the muscle layer (red arrows). VIRADS® 2 lesion with an outcome of pTa after TUR.

are sessile or pedunculated lesions, which can sometimes be observed by different imaging tests.[13]

Differences in the morphology of bladder neoplasms are relevant, as they are related to the likelihood of the lesion invading the muscle layer. Recent studies have analysed the importance of the morphology of the lesion and the extent of contact with the wall in relation to the possibility of invasion of the muscle layer.[12,14,15] Sessile exophytic, endophytic and flat lesions have greater contact with the bladder wall than pedunculated lesions and are more likely to invade the muscle layer[12] (Fig. 4).

Since the superficial layer of the bladder consists of urinary epithelium, the most common malignancy is urothe-

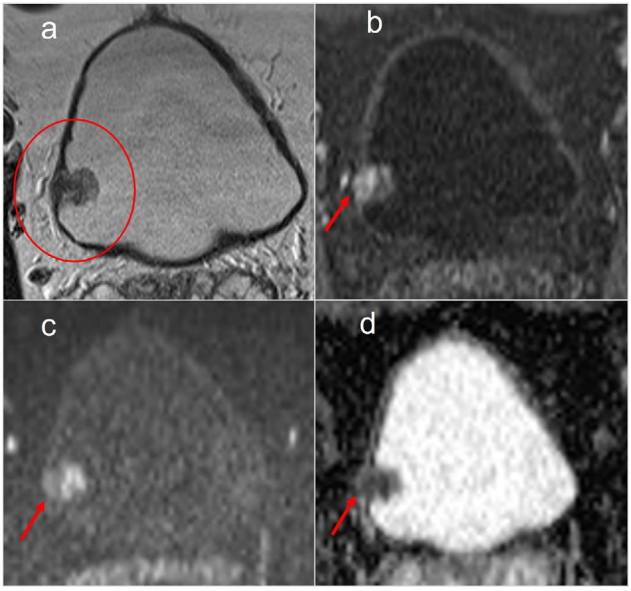

Figure 4 a) Axial T2 showing an exophytic polypoid lesion located on the right lateral aspect of the bladder (segment 6) (red circle). The lesion presents a hypointense pedicle in T2 and associated alteration of the signal intensity in the muscle layer. b) Dynamic study with early phase contrast showing early enhancement in the stalk extending to the muscle layer at the base of the lesion (red arrow). c) Diffusion (b1000). d) ADC. Severe restriction is observed in the superficial component, in the stalk and in the muscle layer at the lesion's implantation base (red arrow). VIRADS® 4 lesion with an outcome of pT2 after TUR.

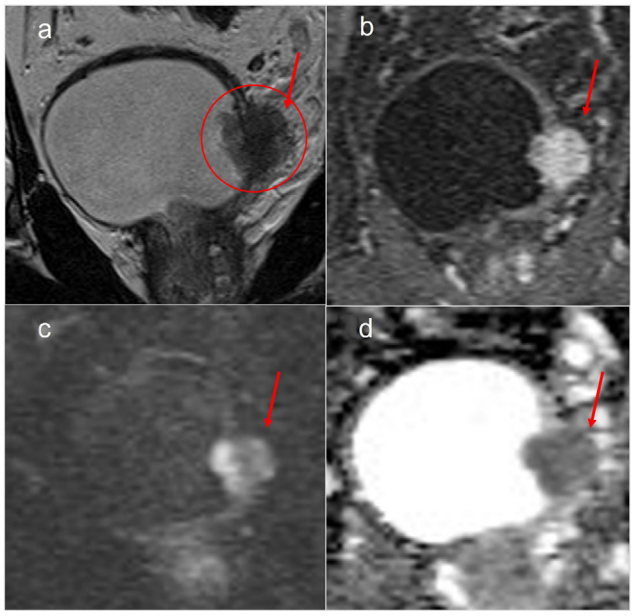

Figure 5 a) Coronal T2 showing an exophytic sessile lesion located on the left lateral wall of the bladder (segment 7) (red circle). The lesion presents a wide implantation base with a marked signal alteration in the muscular layer extending to the perivesical fat (red arrow). b) Dynamic study with early phase contrast showing an early and intense enhancement of the entire lesion encompassing the muscle layer at the implantation base and the tumour component located in the perivesical fat (red arrow). c) Diffusion (b1000). d) ADC. Severe restriction is evident throughout the lesion and in the extravesical spread component (red arrows). VIRADS® 5 lesion with an outcome of pT2 after TUR and pT3 after cystectomy.

lial carcinoma (75–90%). This is most common in men over 60 years of age, smokers and in chronic inflammatory processes in the bladder. In second place is squamous cell carcinoma of the bladder (2–5%). This subtype usually occurs in people with indwelling bladder catheters or chronic parasitosis (mainly schistosomiasis). Adenocarcinoma of the bladder is a rare neoplasm classically associated with patients with urachal abnormalities. Other less frequent histologies are neuroendocrine carcinoma or melanoma.[16,17]

Bladder neoplasm: current management

The usual clinical management of a suspected urothelial tumour includes cystoscopy. If a suspicious lesion is detected, TUR is performed to obtain a histological specimen and remove most of the lesion.[18,19] However, TUR is an invasive technique that carries risks such as bladder perforation and haematuria, and in some cases may promote seeding through bladder perforation or venous embolisms generated by the high pressure at which it is performed (Fig. 5).

TUR may understage the lesion due to various factors such as the sample obtained and the experience of the urologist.[18] Therefore, the European Association of Urology recommends a second TUR (reTUR) within approximately 2–6 weeks in specific situations, such as incomplete resections, when no muscle layer is obtained in the initial specimen (with the exception of TaG1 tumours and primary carcinomas in situ), or in T1 and high-grade tumours.[8,20] This can lead to delays in staging and increased costs and resources. In response to this, the development of non-invasive diagnostic protocols using imaging techniques is being pursued.

In NMIBT, TUR can be diagnostic and therapeutic if the lesion is completely removed and histological findings are favourable. If not, adjuvant treatment is usually required, usually with BCG or intravesical chemotherapy.[21] In MIBT, the standard treatment is radical cystectomy, but 5-year disease-free survival is around 50%.[22–25] To improve the prognosis in cN0M0 MIBT, neoadjuvant treatment with cisplatin is recommended in patients without contraindications.[8] This allows assessment of tumour chemosensitivity, better tolerance to chemotherapy and the possibility of a favourable pathological response with free surgical margins. In responders, overall survival may increase by 5–8% at 5 years,[26,27] while in non-responders the prognosis may be impacted by the delayed cystectomy and side effects of chemotherapy.[28,29] Post-neoadjuvant TUR is not an accurate method of assessing treatment efficacy, as up to 32% of cases may show false negatives compared to histological results obtained after cystectomy.[30]

MRI of the bladder and VIRADS® classification

Basic concepts

The most commonly used imaging techniques for the detection of bladder neoplasms are abdominal ultrasound and intravenous contrast-enhanced computed tomography. Both techniques are useful for identifying lesions suspected of malignancy in the bladder and are highly accurate in distinguishing bladder neoplasms from other intravesical entities such as clots or lithiases.[31] However, their usefulness in local staging is limited.[32] Although computed tomography can identify cases where there is a significant extravesical tumour component (T3b-T4 tumours),[33] these techniques cannot overcome the problems of diagnostic TUR.

In recent years, many studies have been published on the usefulness of MRI in the local staging of urothelial carcinoma of the bladder[34–37] by combining the findings present in different sequences (T2, diffusion and DCE, mainly).[38,39] These studies have shown that the technique has a high diagnostic accuracy in differentiating NMIBT from MIBT, and these results were confirmed in the meta-analysis published by Huang et al.,[34] where sensitivity values of 90% and specificity values of 88% were found in the differentiation of the two groups.

However, although it is an accurate imaging technique, the implementation of MRI in the local staging of bladder tumours has not been without difficulties. One of the most relevant problems is the heterogeneity of existing protocols, as well as the varied language used in the assessment of muscle layer infiltration, which has limited its dissemination.

For this reason, in 2018 the group led by Panebianco et al.[6] published the VIRADS® classification in an attempt to standardise protocols and create a common language for local staging of urothelial bladder neoplasms by MRI. Unlike other radiological classifications, the aim of this classification is not to assess the probability of malignancy of lesions, as it should only be used for malignant lesions. The main purpose is to assess the likelihood of tumour invasion of the muscle layer in urothelial neoplasms (NMIBT vs. MIBT).

Bladder MRI protocol (VIRADS®)

Prior to bladder MRI, adequate bladder repletion is necessary to assess the morphology of the lesions and the behaviour of the bladder layers. In the work of Panebianco et al.[6] it is proposed that patients urinate 1−2 h before the study and drink about 500−1000 ml of water 30 min before the test. The results obtained using the same protocol may vary, as bladder capacity and tolerance to bladder distension differ from patient to patient. The bladder should also not be overdistended, as this promotes motion artefacts and makes assessment of the bladder wall difficult. If this occurs, the patient may urinate and partially empty the bladder. It is advisable to check that the degree of bladder distension is adequate by ultrasound or rapid acquisition sequences (T2 HASTE) before performing the MRI.

Administration of antispasmodic drugs (buscapine) intramuscularly prior to the test helps to decrease intestinal motility.[6] In addition, placement of saturation bands on the anterior abdominal wall reduces artefacts associated with breathing.

Studies should be performed on 1.5 T or 3 T equipment, using a multi-channel surface coil to achieve adequate spatial resolution and good a signal-to-noise ratio.

The VIRADS® protocol consists of three main sequences: one anatomical (T2) and two functional (diffusion-ADC and DCE). The minimum technical characteristics of each sequence are defined in the work published by Panebianco et al.[6] It is advisable to first acquire at least two different T2 planes and then, depending on the location of the lesions, choose in which plane to perform the diffusion and DCE sequences. When necessary, a second diffusion sequence can be performed in another plane, assuming an increase in the duration of the study.

VIRADS® classification. Clinical applications

VIRADS® classification

To evaluate a study using the VIRADS® classification, a category from one to five must be assigned in each sequence to each lesion based on the radiological findings present. Category one indicates a size smaller than 10 mm and a very low probability of muscle invasion, while category five indicates a very high probability of muscle invasion and a component of extravesical spread (Table 1). Finally, the findings from each sequence are combined to give a final VIRADS® value indicating the likelihood of invasion of the muscle layer. It is recommended to assign a VIRADS® value to each lesion in the study and to use the scheme proposed in the work of Panebianco et al.[6] to localise them, which is very useful for planning diagnostic TUR.

Usually, the VIRADS® criteria across the three sequences are congruent and there is no doubt about the final value. However, in some cases we will find discrepancies between sequences. The strict application of the VIRADS® criteria allows for virtually no variation in the final category when findings are discordant, something that is likely to change in future updates of the classification.[40] When in doubt, the sequence with the highest weight in the final VIRADS® category is diffusion, followed by DCE. The T2 sequence frequently gives misleading information about the precise location of the deep margin of the lesion (compared to the other sequences), and may overestimate the existence of tumour invasion of the muscle layer. When assessing each lesion, the main objective is to analyse two specific radiological findings, the lesional stalk or base of the lesion and the thickening of the submucosal layer under the tumour or inner layer. In cases where both of these findings are preserved and show no signs of tumour invasion, NMIBT should be suspected (VIRADS® 2) (Fig. 6).

The main purpose of VIRADS® is differentiation between NMIBT and MIBT. The diagnostic accuracy of the classification has been extensively tested in several studies.[41–43] In the meta-analysis published by Woo et al.,[41] they demonstrated a sensitivity of 83% and a specificity of 90% in differentiating NMIBT from MIBT, with excellent inter-observer agreement. This classification can also provide additional information relevant to local staging, such as the presence of an extravesical tumour component (differentiating T2 tumours from T3 or higher). In contrast to studies categorised as VIRADS® 4

Table 1 VIRADS® categories.

VIRADS®	T2	DWI	DCE
1	Pedunculated lesion < 10 mm without invasion of the muscle layer	Diffusion restriction limited to the lesion, no involvement of the muscle layer	Early enhancement of the lesion, no early enhancement of the muscle layer
2	Pedunculated lesion > 10 mm without invasion of the muscle layer	Diffusion restriction limited to the lesion, no involvement of the muscle layer	Early enhancement of the lesion, no early enhancement of the muscle layer
	Flat lesion of any size with thickening of the submucosal layer (inner layer)	Diffusion restriction limited to the lesion, without involvement of the muscle layer. ADC hypersignal in the inner layer	Early enhancement of the lesion, without early enhancement of the muscle layer. Early enhancement of the inner layer
3	Pedunculated lesion without stalk, no apparent separation of the muscle layer	Restricted diffusion in the lesion, without clear involvement of the muscle layer, although this cannot be ruled out. Restricted diffusion in the stalk (for pedunculated lesions)	Early enhancement of the lesion, without clear invasion of the muscle layer, although this cannot be ruled out. Enhancement of similar intensity and timing to the tumour in the stem (for pedunculated lesions)
	Flat lesion with no thickening of the inner layer, no apparent separation of the muscle layer		
4	Flat or pedunculated lesion with clear involvement of the muscle layer	Diffusion restriction extending to the line of the muscle layer	Early enhancement of the lesion extending to the line of the muscle layer
5	Flat or pedunculated lesion with involvement of the extravesical fat and/or neighbouring organs	Diffusion restriction extending beyond the bladder wall, with involvement of the extravesical fat and/or neighbouring organs	Early enhancement extending beyond the bladder wall, with involvement of the extravesical fat and/or neighbouring organs

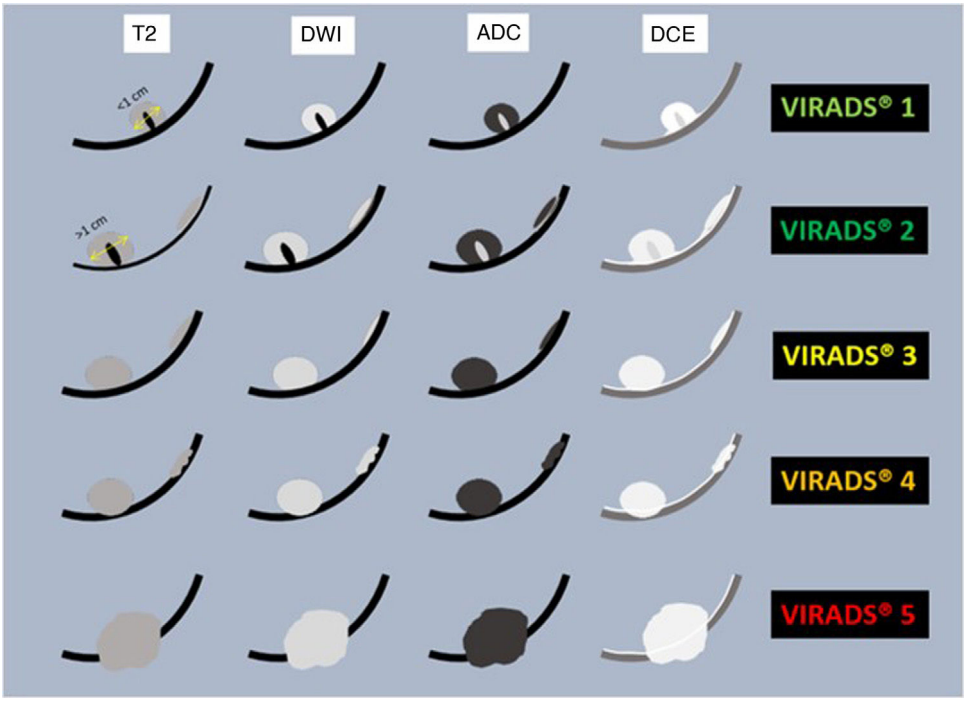

Figure 6 Schematic diagram of bladder lesions and their equivalent on the VIRADS® scale.

that show the tumour stage to be T2, VIRADS® 5 studies indicate T3 or higher with a positive predictive value of about 95%.[44] This is very relevant, as differentiation between T2 and T3 or higher tumours cannot be done preoperatively by TUR.

Clinical applications in local staging

The incorporation of MRI in the local staging of bladder neoplasms can have a great impact on patient management, both improving the accuracy of diagnostic TUR and minimising the morbidity and economic and human resources associated with these neoplasms.[45–48]

Among the clinical applications of MRI performed prior to diagnostic TUR, it should be noted that the findings of this test can support the histological results obtained, achieving a reduction in the percentage of reTUR by combining the two techniques. Lesions categorised as VIRADS® $\leq$ 2 have been shown to have a high negative predictive value of around 90–95%,[41,43] which can help to exclude the possibility of MIBT.[48,49] This combined protocol proposes that once the diagnostic TUR has been performed, if the results indicate the need for reTUR, this can be omitted in VIRADS® $\leq$ 2 lesions. This approach has multiple advantages, such as reducing invasive procedures (reTUR), shortening the total time to diagnosis (reducing the opportunity cost) and reducing the cost of care in terms of economic and human resources. There is currently an ongoing clinical trial evaluating the impact of bladder MRI on these aspects. Although its design is controversial, early results seem to show a favourable outcome in terms of financial resources and total time to diagnosis.[50]

Another potential advantage of using pre-TUR MRI is to minimise the morbidity of diagnostic TUR in cases where there is a high suspicion of muscle invasion on MRI (VIRADS® 5), avoiding deep biopsies that can generate morbidity, preventing local complications and with less lengthy admissions after the procedures. Several studies[43,44] have confirmed the concordance (greater than 95%) of studies categorised as VIRADS® 5 with the presence of MIBT. In these cases, superficial and less aggressive TUR may be considered to confirm the diagnosis of malignancy and to obtain tissue and molecular information, without the need to obtain a sample of the muscle layer to confirm MIBT.

Finally, the clinical impact and management of lesions categorised as VIRADS® 3 and VIRADS® 4 is a controversial issue. Most studies show excellent diagnostic accuracy when both VIRADS® 3 and VIRADS® 4 are used as cut-off points for suspected MIBT, with the sensitivity being higher when VIRADS® 3 is chosen (sensitivity of 96% and specificity of 84%), and the specificity with VIRADS® 4 (sensitivity of 72% and specificity of 92%).[41] Taking into account the relevance of identifying patients with MIBT, it may be preferable to have a higher sensitivity and negative predictive value at the cost of having lower specificity, with the most appropriate cut-off point for considering MIBT being VIRADS® 3. In cases where studies are categorised as VIRADS® 3 or VIRADS® 4 and the result of the first TUR was NMIBT, this result may be taken into account as an indication for reTUR, although this should be assessed in future studies.[45]

Table 2 Main findings observed in post-TUR MRI studies.

1. Morphological alteration of the wall at the TUR site
2. Thickening and increased T2 signal of the underlying muscle layer
3. Inflammatory changes in the perivesical fat around the TUR site
4. Mild diffusion restriction in the muscle layer at the TUR site
5. Enhancement in the muscle layer underlying the TUR changes (may be early and intense enhancement)

As bladder MRI and the application of the VIRADS® criteria are novel concepts, a learning curve is required to reach the sensitivity and specificity figures reported in the literature.[51] Therefore, the most experienced working groups describe the need for training with 100–150 cases in order to bring the degree of accuracy and safety of inexperienced radiologists in line with that of experienced radiologists.[51]

Post-TUR VIRADS® classification

Although the study published by Panebianco et al.[6] describes the possibility of performing MRI before or after diagnostic TUR, it should be noted that this procedure alters both the morphology and the signal of the bladder wall, which should be taken into account when applying the VIRADS® classification (Fig. 7). It is recommended to wait six to eight weeks after TUR to try to minimise changes associated with the procedure. Although this is advisable, it should be borne in mind that the longer the time between the two procedures, the more likely it is that a delay in the final diagnosis may occur.

The recent work by Chai et al.[52] evaluated the role of the VIRADS® scale in patients after TUR, finding worse results than those described in the literature when MRI is performed prior to TUR. This difference is attributed to the inflammatory changes and fibrosis associated with TUR, which can lead to confusion in the assessment of the muscle layer, decreasing the specificity of the scale (Fig. 8). Enhancement can be observed after administration of paramagnetic contrast in the muscle layer weeks after TUR without there being any tumour invasion, and the existence of clear diffusion restriction in this location is the finding most suspected of being MIBT. In the evaluation of these studies, it is essential to know the procedures performed on the patient, the existence of macroscopic tumour remains and the results of the TUR, in order to avoid false positives as far as possible. Imaging findings frequently associated with TUR are summarised in Table 2.

The developers of the VIRADS® scale are aware of the added difficulty in assessing these studies and are trying to overcome this problem.[40]

Assessment of response to neoadjuvant treatments (NAC-VIRADS®)

In patients with MIBT, standard treatment consists of NT followed by cystectomy where patients are candidates.[53,54]

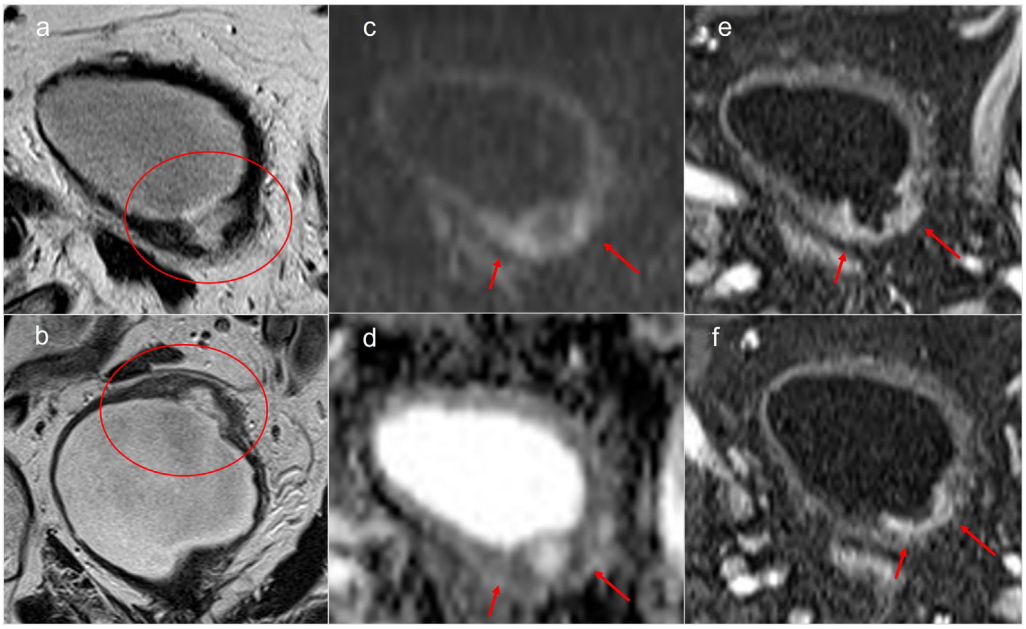

Figure 7 Patient with a history of TUR 4 weeks earlier with an outcome of pT1 in the bladder dome (segment 8). T2 axial (a) and coronal (b) showing the parietal defect, thickening and signal enhancement of the muscular wall of the bladder (red circle). c) Diffusion (b1000). d) ADC showing faint diffusion restriction extending into the muscle layer (red arrows). e and f) Dynamic early phase contrast study showing early enhancement in the muscle layer at the site of the prior TUR (red arrows).

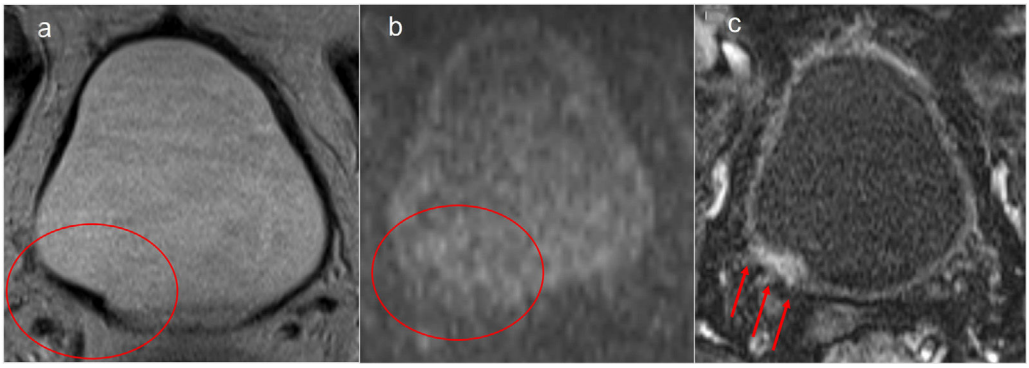

Figure 8 Patient with a history of TUR performed 40 weeks earlier with an outcome of pT1 with suspected local recurrence on control cystoscopy in the posterior wall (segment 5). a) Axial T2. b) Diffusion (b1000). Hypointense thickening in T2 of the posterior wall of the bladder (red circle) with no diffusion restriction in the bladder wall and no suspicious lesion on the T2-weighted sequence. c) Dynamic early phase contrast-enhanced study. Significant contrast enhancement at the site of the prior TUR extending into the muscle layer (red arrows). A subsequent TUR revealed fibrosis and chronic inflammatory changes, with no signs of tumour recurrence.

This combined protocol has led to an increase in survival that is most significant when a complete pathological response is achieved in the surgical specimen (ypT0N0).[26]

However, neither NT administration nor cystectomy is free of complications. The most commonly used neoadjuvant regimens can have severe adverse effects, such as nephrotoxicity or myelosuppression.[54] This is why efforts are being made to develop new, more effective and less toxic regimens, as well as to discover markers that can identify early those patients who will respond to NTs. In addition, cystectomy is associated with a significant risk of perioperative complications and high morbidity due to the need for urinary diversion, which has a major impact on patients' quality of life.[26] In recent years, bladder preservation protocols combining maximal resection of the lesion by TUR and neoadjuvant chemoradiotherapy are being developed. In most multimodal treatment protocols, for a patient to be a candidate for bladder preservation, a complete clinical response is required after completion of treatments.[26,55] For this reason, strategies are being developed to identify patients with a complete pathological response to NTs prior to surgery, in order to try to select the most appropriate treatment for each patient and to avoid cystectomies where possible.[56,57]

In this respect, MRI has proven to be a very useful technique in the assessment of tumour remnants after NT.[58]

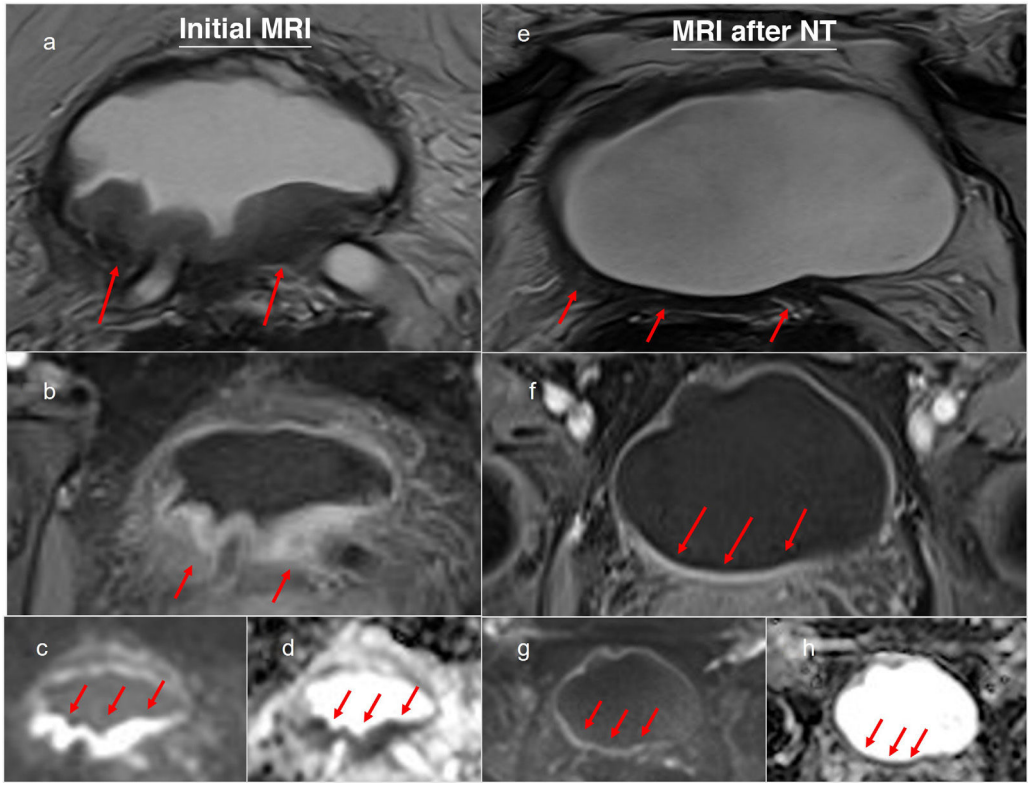

Figure 9 Patient with MIBT who is a candidate for neoadjuvant treatment. Initial pre-TUR MRI 9 (a-d). a) Axial T2. b) Dynamic contrast-enhanced (DCE) study. c) Diffusion (b1000). d) ADC. A sessile parietal thickening involving the posterior aspect, the bladder trigone and both ureters (segments 5, 1, 10, 11) is observed, which appears to replace and infiltrate the muscle wall with retrograde dilatation of both ureters (red arrows). The lesion was categorised as VIRADS® 4. TUR was performed with an anatomopathological outcome of T2. MRI performed after completion of neoadjuvant treatment (e-h). e) Axial T2. f) DCE. g) Diffusion (b1000). h) ADC. There is resolution of the trigonal parietal thickening with diffuse hypointensity of the muscle layer on T2, without diffusion restriction or early enhancement showing tumour remnants (red arrows). It was labelled as NAC-VIRADS® 1. Cystectomy was performed with an anatomopathological outcome of ypT0N0. (Images courtesy of Aránzazu Urresola. Hospital de Cruces, Barakaldo, Bizkaia.).

In the study published by Bandini et al.,[59] MRI was found to have a high diagnostic accuracy in identifying patients with ypT0N0M0, with an area under the curve of 0.74%, which increased to 0.87% on increasing the cut-off point in NMIBT (T1-is-aN0M0). In order to standardise the nomenclature and to be able to carry out studies certifying the usefulness of MRI in the assessment of NT response in MIBT, a variant of the VIRADS® classification (NAC-VIRADS®)[7] has recently been developed. With this classification, by combining the findings present in the pre-TUR MRI and in another MRI performed after completion of neoadjuvant chemotherapy treatment, it is possible to differentiate patients who have responded to the treatments. This classification and the changes in the VIRADS® scale have recently been used in the work published by Necchi et al.,[60] which aimed to evaluate the predictive ability of MRI before and after pembrolizumab to identify responders (ypT0N0 or ypT $\leq$ 1N0) in those with MIBT in the PURE-01 trial, with excellent results (Fig. 9). In this work, the changes in the VIRADS® classification after NT have not only proven to be useful in identifying patients with a complete pathological response, it has also been found that they may be a prognostic factor in disease-free survival and overall survival of patients with MIBT.[60]

Although more studies are needed, current evidence suggests that MRI may be useful in selecting patients who are candidates for bladder preservation after multimodal treatment.[55]

Conclusion

MRI of the bladder together with the VIRADS® classification and its variants represent a dramatic change in the management of patients with bladder neoplasms. Their potential to accurately stage urothelial bladder tumours and to assess the existence of tumour remnants after NT may help multidisciplinary committees select the most appropriate treatment with the least morbidity in each case, while trying to optimise the resources used in this disease.

CRediT authorship contribution statement

1 Responsible for the integrity of the study: JE, ALM.
2 Study concept: JE, ALM.
3 Study design: JE, ALM.
4 Data collection: JE, ALM.
5 Data analysis and interpretation: JE, ALM.

6 Statistical processing: JE, ALM.
7 Literature search: JE, ALM.
8 Drafting of the article: JE, ALM.
9 Critical review of the manuscript with intellectually relevant contributions: JE, ALM.
10 Approval of the final version: JE, ALM.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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