

The accuracy of magnetic resonance imaging (MRI) in predicting the invasion of the tunica albuginea and the urethra during the primary staging of penile cancer

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Objectives

To assess the accuracy of magnetic resonance imaging (MRI) in predicting invasion of the tunica albuginea (TA) and the urethra during the primary staging of penile cancer.

Patients and Methods

In all, 104 consecutive patients with clinical T1–T3 penile cancer had a penile MRI as a part of local staging protocol. An artificial erection was induced before MRI by injecting alprostadil (prostaglandin E₁). Four men with poor quality MRI images were excluded from the study. The preoperative MRI was compared with final histology to assess its accuracy in predicting the invasion of the TA and urethra.

Results

Data of 100 patients who underwent penile MRI before definitive surgery for invasive penile carcinoma were available

for analysis. The mean age was 65 years and number of patients with pathological stage T1, T2 and T3 was 32, 52, and 16, respectively. The sensitivity and specificity of MRI in predicting the invasion of TA and urethra was 82.1% and 73.6%, and 62.5% and 82.1%, respectively. There were no MRI-related complications.

Conclusions

This study shows that penile MRI is an accurate method for assessing TA invasion but is less sensitive in assessing urethral invasion. These results support the use of MRI in the local staging of penile cancer.

Keywords

penile cancer, MRI, primary staging, urethral invasion, tunica albuginea, invasion

Introduction

Primary malignant epithelial tumours of the penis are rare, with the commonest age of presentation being 50–70 years. There is wide variation in the prevalence of penile cancer, ranging from 4 per 100 000 in Africa, Asia and South America to 0.3–1 per 100 000 in North America [1]. In >80% of cases, penile squamous cell carcinoma involves the glans, coronal sulcus or prepuce and is amenable to conservative surgery [2]. Patients with tunica albuginea (TA) or cavernosal invasion are at increased risk of local recurrence (35% vs 17%) and 5-year mortality (30% vs 21%) compared with patients with only glans penis invasion [3]. Furthermore, invasive lesions require more extensive and potentially mutilating surgery.

Over the last decade penile-preserving surgery, with surgical margins of <10 mm compared with the traditional 20-mm margin has become more common. Penile-preserving surgery is reported to firstly achieve excellent oncological control and secondly to improve functional outcomes, although the data for this are limited [4]. Invasion of the TA and the urethra are crucial factors in determining the stage of penile cancer and the feasibility of penile-preserving surgery.

An assessment of the depth of invasion of penile cancer on clinical examination alone may be challenging and is often inaccurate. In such situations, preoperative imaging potentially could be a useful tool in determining invasion of the TA and/or urethra. The intrinsic limitations of high-resolution ultrasound (such as operator dependency and

practical difficulty in assessing ulcerative lesions) led to the proposal of MRI as a tool for the local staging of the penile cancer [5]. Since that original report, there have been limited reports of its utility and the purpose of the present study was to assess the role of penile MRI in assessing both TA and urethral involvement in apparently localised cases of penile cancer.

Patients and Methods

In all, 104 consecutive patients with biopsy confirmed, clinically localised cases of penile cancer (T1–T3) at a tertiary referral centre were assessed. Initial assessment of these patients included a full history and physical examination. All patients underwent a penile MRI as per local hospital protocol (Table 1). An artificial erection was induced before the MRI by intracavernosal injection of 10–20 µg alprostadil (prostaglandin E₁, Caverject®). Patients with severe ischaemic heart disease and presenting with large painful penile tumour were excluded from the Caverject injection. Thus, in all, 56 patients were given alprostadil and 44 patients did not receive alprostadil before penile MRI. Subanalysis of the two groups that did and did not receive artificial erection was performed.

For clinical purposes, a preoperative MRI report was used to guide surgical treatment. For the purposes of the study, each penile MRI was reported prospectively prior to penile surgery by one of two consultant radiologists with at least 10 years specialist uro-radiology experience. The pathology was reported by one of three tertiary centre specialist pathologists with over 10 years training and experience. The pathologist determined pathological T-staging and was blind to the preoperative MRI staging. MRI cases that were reported equivocally were reviewed by both uro-radiologists to obtain a consensus MRI stage.

Based on the clinical examination and preoperative MRI findings various surgical techniques, such as circumcision,

Table 1 Penile MRI protocol for staging of penile cancer.

The penis was maintained in the anatomical or neutral more flaccid state (resting on the anterior abdominal wall)
Artificial erection was induced using injection of 10–20 µg of alprostadil (unless contraindicated)
The primary protocol for penile staging was a high-resolution, thin-slice (1.5 mm), T2-weighted spin-echo sequence in three orthogonal planes
Overview for lymph node staging: Axial T2 turbo spin echo sequence of the pelvis (7 mm slice thickness) and coronal T1 spin echo sequence of the abdomen and pelvis (3–4 mm slice thickness)
Dynamic contrast-enhanced sequences, with 1.5-mm slice thickness and a small field of view, usually in the coronal plane to define the corporal enhancement. Further sequences were added as required
Penile cancer shows low signal on the T2, making it possible to distinguish from the relative hypersignal of the corpora cavernosa. Furthermore, contrast enhancement with i.v. gadolinium on the T1 sequence allows tumour differentiation from normal adjacent tissues

wide local excision and primary closure or split-skin graft glansctomy with split-skin graft, partial penectomy, or total penectomy, were used to treat the primary tumour. The final histological grade and stage of penile cancer were reported by experienced uro-pathologists who were ‘blinded’ to the MRI results. The regional lymph node basin was treated at a later date according to the Yorkshire Cancer penile cancer guidelines.

Demographic data, MRI stage, operative procedure and final histopathological findings were recorded on a database, and the data were analysed to evaluate the accuracy of preoperative MRI in predicting the invasion of the TA and the urethra. Statistical software (statDirect) was used to assess the correlation (κ values) between radiological and pathological diagnosis.

Results

In all, 104 patients with a clinical diagnosis of penile cancer had MRI for local staging. After exclusion of four patients with poor-quality MRI, 100 consecutive patients were included for the final analysis. Patients were treated with the clinically appropriate type of surgery, with most undergoing penile-preserving surgery.

Patient demographics are shown in Table 2. The median (range) age was 65 (39–88) years. Invasion of the TA or the urethra on MRI was present in 38 and 21 patients, respectively. In all, 28 patients were found to have pathological invasion of the TA (Fig. 1; Fig. 2) and invasion of urethra (Fig. 3) was identified in 16 patients. On postoperative tumour staging 32 patients were staged as pT1, 52 as pT2 (T2a-24; T2b-28) and 16 as pT3 penile cancer.

Table 2 Patient demographics.

Variable	Value
Median (range) age, years	66 (39–88)
N	
Preop. MRI findings	
Invasion of TA	42
Invasion of Urethra	25
Surgery	
Circumcision	3
Partial glansctomy	3
Glansctomy	44
Partial penectomy	39
Total penectomy	11
Grade	
G1	13
G2	29
G3	58
pT Stage	
T1	32
T2a	24
T2b	28
T3	16

Fig. 1 T2-weighted thin slice coronal MRI showing a mass within the left glans abutting and deforming the TA consistent with T2a disease. This was confirmed at surgery. Small left glans wart noted.



Fig. 2 T2-weighted thin slice coronal MRI showing a large glans tumour. The TA was seen to be intact (arrow). Radiologically this was reported as T2a but pathologically there was microscopic lymphovascular spread through the TA into the distal corpora bilaterally consistent with microscopic T2b disease.

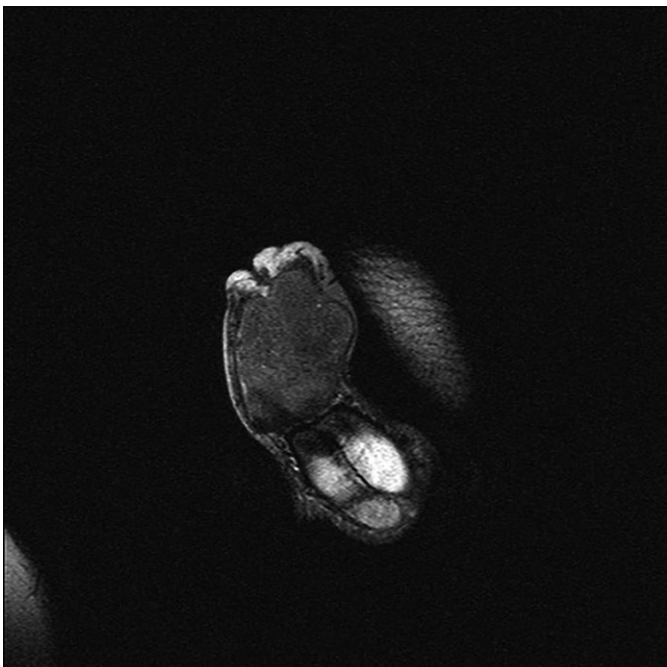
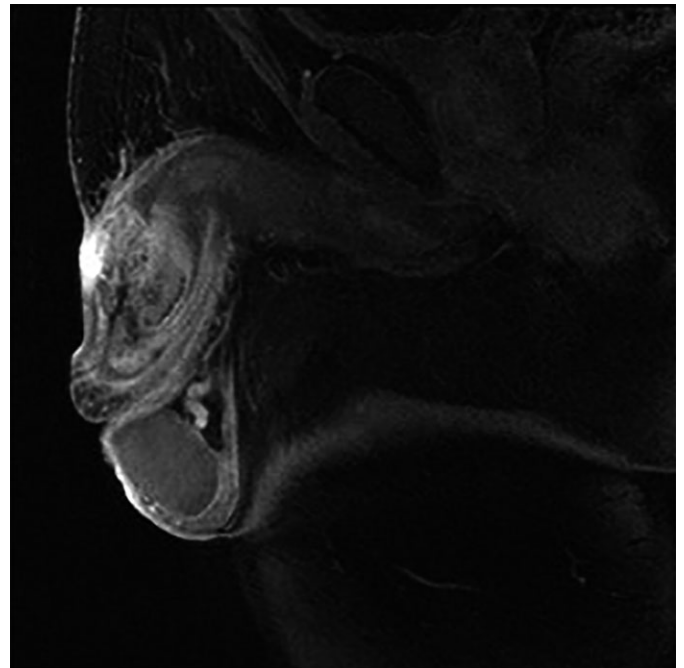


Fig. 3 Post-contrast T1 sagittal MRI showing tumour involving the glans and distal corpora. Tumour abuts the urethra and radiological concern for early T3 disease was reported. Surgery confirmed T2b disease with no urethral infiltration.



The under- and over-staging of the TA invasion on penile MRI was five (8.6%) and 19 (45.2%) respectively. With similar figures for the under- and over-staging of urethra invasion of six (8%) and 15 (60%), respectively (Table 3). The sensitivity, specificity, positive predictive value (PPV) and negative PV (NPV) of penile MRI are shown in Table 4. The sensitivity and specificity of MRI in predicting the invasion of TA and urethra were 82.1% and 79.1%, and 62.5% and 86.9%, respectively. Subanalysis of the two groups that did and did not have an artificial erection showed improved sensitivity and specificity in those patients who received Caverject before MRI (Table 5). Statistically, there was a moderate correlation between radiological and pathological evaluations, with κ values (Table 6) of 0.54 and 0.43 for TA and urethral invasion, respectively. The accuracy of MRI in staging penile cancer is increased by Alprostadil intra-cavernosal injections and should be used routinely unless contraindicated.

There were no complications from the use of intracavernosal alprostadil during the MRI scan.

Discussion

Surgical resection is often curative for men with penile cancer. However, penile amputation carries a significant psychosexual morbidity. Several studies have shown that

Table 3 Comparison of MRI and histology results for 100 cases.

	Histology		Total, <i>n</i>
	TA yes, <i>n</i> (%)	TA no, <i>n</i> (%)	
MRI			
TA yes, <i>n</i> (%)	23 (54.8)	19 (45.2)	42
TA no, <i>n</i> (%)	5 (8.6)	53 (91.4)	58
Total, <i>n</i>	28	72	100
	Urethra yes, <i>n</i> (%)	Urethra no, <i>n</i> (%)	Total, <i>n</i>
MRI			
Urethra yes, <i>n</i> (%)	10 (40)	15 (60)	25
Urethra no, <i>n</i> (%)	6 (8)	69 (92)	75
Total, <i>n</i>	16	84	100

Table 4 Sensitivity, specificity, PPV and NPV of penile MRI in assessing the invasion of the TA and the urethra.

	Sensitivity, %	Specificity, %	PPV, %	NPV, %	κ Value
TA	82.14	79.17	60.53	91.94	0.54
Urethra	62.50	86.90	47.62	86.90	0.43

penile-conserving surgical techniques are feasible in selected patients and allow maximum preservation of functional status without compromising oncological outcome [6,7].

Contemporary series have reported favourable data on the safety of penile-preserving techniques in the medium term [2,8], whilst data on the long-term results have been provided by Philippou et al. [4], who reported a 5-year local recurrence-free rate of 86%.

An accurate preoperative staging is essential before recommending penile-conserving surgery to a patient. The recent European Association of Urology guidelines [9] recommend physical examination of the primary penile lesion with particular attention to morphological and physical characteristics. Interestingly, ultrasound has been shown to have limited value in assessing the invasion of the TA. The TA cannot be easily distinguished from the subepithelial connective tissue, thus creating difficulty in differentiating between T1 and T2 lesions. Indeed, it has been reported that physical examination is more reliable than high-resolution penile ultrasound for the assessment of infiltration of the corpora cavernosa [10]. Similarly, CT does not allow for visualisation of penile tissue planes and therefore is not recommended for local staging, but can be a useful tool for nodal staging and distant metastases. Fütterer [11] evaluated the role of MRI in local staging of prostate cancer, and concluded that the accuracy of detecting T3 disease to be 50–90%. Our present study shows, penile cancer T-staging accuracy using MRI to be similar to MRI T-staging for prostate cancer.

Table 5 Subanalysis of patient's that did and did not receive artificial erection before MRI.

	Artificial erection using Caverject before MRI	
	Yes	No
TA		
Sensitivity, %	93	69
Specificity, %	76	72
Urethra		
Sensitivity, %	86	44
Specificity, %	81	83

Table 6 Significance of κ values (agreement between the MRI and histology).

κ Value	Agreement
<0	No
0–0.2	Slight
0.21–0.4	Fair
0.41–0.6	Moderate
0.61–0.8	Substantial
0.81–1	Perfect

There have been small series evaluating the accuracy of MRI for staging penile cancer [5,12,13] that have mainly investigated the distinction between the T1, T2 and T3 lesions. To date, there have been no studies assessing the accuracy of MRI in TA and urethral invasion. Our present data shows acceptable sensitivity and specificity for penile MRI in predicting invasion of the TA with slightly less good results for predicting urethral invasion.

In conclusion, these data support the use of preoperative MRI in the local staging of men with penile cancer. It is useful in predicting those men who may be suitable for penile-preserving surgery, although the accuracy of identifying urethral involvement is slightly less good than of identifying TA involvement.

Conflicts of Interest

None disclosed.

References

- Barnholtz-Sloan JS, Maldonado JL, Pow-sang J, Giuliano AR. Incidence trends in primary malignant penile cancer. *Urol Oncol* 2007; 25: 361–7
- Minhas S, Kayes O, Hegarty P, Kumar P, Freeman A, Ralph D. What surgical resection margins are required to achieve oncological control in men with primary penile cancer? *BJU Int* 2005; 96: 1040–3
- Rees R, Freeman A, Borley N, Ralf D, Minhas S. PT2 penile squamous cell carcinomas: cavernosus vs. spongiosus invasion. *Eur Urol Suppl* 2008; 7: 111
- Philippou P, Shabbir M, Malone P et al. Conservative surgery for squamous cell carcinoma of the penis: resection margins and long-term oncological control. *J Urol* 2012; 188: 803–8

- 5 Kayes O, Minhas S, Allen C, Hare C, Freeman A, Ralph D. The role of magnetic resonance imaging in the local staging of penile cancer. *Eur Urol* 2007; 51: 1313–9
- 6 Bissada NK, Yakout HH, Fahmy WE et al. Multi-institutional long-term experience with conservative surgery for invasive penile carcinoma. *J Urol* 2003; 169: 500–2
- 7 Feldman AS, McDougal WS. Long-term outcome of excisional organ sparing surgery for carcinoma of the penis. *J Urol* 2011; 186: 1303–7
- 8 Smith Y, Hadway P, Biedrzycki O, Perry MJ, Corbishley C, Watkin NA. Reconstructive surgery for invasive squamous carcinoma of the glans penis. *Eur Urol* 2007; 52: 1179–85
- 9 Pizzocaro G, Algaba F, Solsona E et al. Guidelines on Penile Cancer European Association of Urology 2012. Available at: http://uroweb.org/wp-content/uploads/11_Penile_Cancer_LR-II.pdf. Accessed October 2013
- 10 Horenblas S, Newling DW. Local recurrent tumour after penis-conserving therapy. A plea for long-term follow-up. *Br J Urol* 1993; 72: 976
- 11 Fütterer JJ. MR imaging in local staging of prostate cancer. *Eur J Radiol* 2007; 63: 328–34
- 12 de Kervile E, Ollier P, Desgrandchamps F et al. Magnetic resonance imaging in patients with penile carcinoma. *Br J Radiol* 1995; 68: 704–11
- 13 Scardino E, Villa G, Bonomo G et al. Magnetic resonance imaging combined with artificial erection for local staging of penile cancer. *Urology* 2004; 63: 1158–62

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Abbreviations: (N)(P)PV, (negative) (positive) predictive value; TA, tunica albuginea.