

CONTINUING EDUCATION PROGRAM: FOCUS...

Imaging techniques for local recurrence of prostate cancer: For whom, why and how?

O. Rouvière^{a,*,b}

^a *Department of Urinary and Vascular Imaging, hospices civils de Lyon, hôpital Édouard-Herriot, 5, place d'Arsonval, 69437 Lyon, France*

^b *Faculté de médecine Lyon-Est, université de Lyon, université Lyon 1, 69003 Lyon, France*

KEYWORDS

Male genital system;
Prostate;
Cancer;
MRI;
Ultrasonography

Abstract Since there are salvage solutions, it is important to detect local recurrence of prostate cancer as early as possible. The first sign is “biochemical failure” in that the prostate specific antigen (PSA) concentration rises again. The definition of biochemical failure varies depending on the initial treatment: PSA greater than 0.2 ng/mL after prostatectomy, nadir + 2 ng/mL after radiotherapy. There is no standardised definition of biochemical failure after cryotherapy, focused ultrasound, or brachytherapy. Magnetic resonance imaging (MRI) (particularly dynamic MRI) can detect local recurrence with good sensitivity. The role of spectroscopy is still under discussion. For the moment, ultrasound techniques are less effective than MRI.

© 2012 Éditions françaises de radiologie. Published by Elsevier Masson SAS. All rights reserved.

Over the past 20 years, the therapeutic arsenal against localised prostate cancer has grown considerably. Brachytherapy [1], cryotherapy [2], focused ultrasound ablation [2,3] and photodynamic therapy [4] have been added to the classic treatment methods of prostatectomy and radiotherapy. These therapies are not only new weapons in the initial management of prostate cancer, but also in salvage treatment in cases of local recurrence.

Now, regardless of the initial treatment, there are several salvage solutions if there is a local setback [5].

It is therefore essential to detect local recurrence and locate it precisely so that salvage treatment may be undertaken under the best possible conditions. Imaging local recurrence is currently a growing field, not only because of the clinical need for it, but also because initial assessments have indicated that detection and localisation of tumour foci are paradoxically easier and more precise for local recurrence than for untreated cancer.

* Corresponding author.

E-mail address: olivier.rouviere@netcourrier.com

The purpose of this paper is to review the indications for imaging, the techniques to be used and the possible results for patients with suspected local recurrence after initial treatment of their prostate cancer.

Where it all (re)starts: biochemical failure

Imaging is not indicated for monitoring treated patients. The first warning sign is an increase again in PSA concentration above a given threshold. Precise definition of this biochemical failure depends on the initial treatment (Table 1).

After radical prostatectomy

PSA should theoretically be undetectable. Officially, a patient will be having a biochemical failure when the PSA concentration exceeds 0.2 ng/mL [6].

After radiotherapy

Here, on the contrary, the PSA concentration falls very slowly with a low point (nadir) reached after 2 to 4 years. For a long time, biochemical failure was defined according to the ASTRO guidelines (three successive rises after the nadir, the date of recurrence being backdated as the point halfway between the first and second rise). This criterion correlated poorly with survival and was replaced in 2005 by the Phoenix criterion (a rise in PSA concentration of 2 ng/mL above the nadir) [7].

After focused ultrasound ablation

There is no official definition of recurrence in this case. A strip of anterior prostate tissue is often left and the post-treatment PSA concentration may not be zero, even if a nadir greater than 0.2 ng/mL represents a poor prognosis [8]. Some teams use the Phoenix criteria [3,9]. Recently, the Stuttgart criteria defined recurrence after focused ultrasound as a rise in PSA concentration of 1.2 ng/mL above the nadir [10]. However, the methodology used to arrive at this definition is debatable.

After cryotherapy

Again, there is no definition of biochemical failure after this type of treatment. Many teams use the ASTRO guidelines or a PSA threshold of 0.5 ng/mL, but without any real scientific justification [5]. As cryotherapy produces the same histological lesion as focused ultrasound, it would be logical for the definition of biochemical failure to be the same for both techniques.

After brachytherapy

Changes in the PSA level in this case are complex. It decreases slowly with a nadir reached after 2 to 4 years. Temporary rebound in PSA concentration may occur 12 to 24 months after implantation in 30 to 60% of patients. It rarely exceeds 2 ng/mL and lasts, on average, for 1 year before the PSA concentration falls again. The cause of this rebound is still under discussion, but it does not seem to have prognostic value [11]. The ASTRO guidelines have been abandoned and replaced by the Phoenix criteria, as long as allowances are made for post-therapeutic rebound [12].

A prerequisite: detection of micrometastases

A patient with biochemical failure may have local or metastatic recurrence, or both. Reasonably eliminating metastases is therefore essential before submitting the patient to local salvage treatment, because morbidity due to these treatments is significant.

Current evaluation of the risk of micrometastases

It must indeed be remembered that biochemical failure is a very early indicator that precedes the appearance of clinical metastasis by several years (on average, by 8 years after prostatectomy and 7 years after radiotherapy) [13,14]. If metastases do exist when biochemical failure is found, they are generally microscopic and are highly likely to be missed by the usual imaging techniques (bone scan, abdominopelvic CT).

Table 1 Definition of biochemical failure after prostate cancer treatment.

Treatment	Consensus definition	Definitions proposed but not consensual
Radical prostatectomy	PSA > 0.2 ng/mL	
External beam radiotherapy	PSA > nadir + 2 ng/mL (Phoenix criteria)	
Focused ultrasound		PSA > nadir + 2 ng/mL (Phoenix criteria) PSA > nadir + 1.2 ng/mL (Stuttgart criteria)
Cryotherapy		Three consecutive PSA increases (ASTRO guidelines) PSA > 0.5 ng/mL
Brachytherapy		PSA > nadir + 2 ng/mL (Phoenix criteria)

Table 2 Factors pointing towards metastatic development in the event of biochemical failure.

	Factors favouring metastatic development
Factors related to the initial tumour (before first treatment)	Gleason score ≥ 8 T3-T4 stage PSA ≥ 20 ng/mL
Time interval between initial treatment and biochemical failure	Free interval between treatment and biochemical failure less than 2 to 3 years
Factors related to the PSA concentration at the time of biochemical failure	Concentration ≥ 10 ng/mL Velocity ≥ 2 ng/mL per year Doubling time less than 8 to 12 months

We therefore make do at the present time with probabilistic reasoning founded on clinical/laboratory and histopathological criteria based on the characteristics of the initial tumour and on the PSA kinetics at the time of the biochemical failure (Table 2). The more metastatic risk factors a patient accumulates, the less relevant it becomes to offer him local salvage treatment (and therefore to look for local recurrence using imaging) [5].

New imaging techniques

Many imaging techniques are currently being used to try to move forward from this probabilistic reasoning and detect metastases earlier: NaF scintigraphy, PET-scans with choline or acetate, whole-body diffusion magnetic resonance imaging (MRI), spinal MRI, lymph node MRI with iron oxide particles etc. It is not our intention to study them in detail in this article. While they all offer the prospect of selecting candidates for local salvage treatment better, there is no official recommendation at the present time concerning their use.

In our experience, while MRI of the whole spine and pelvis in conventional sequences (T1, T2, T1 with gadolinium injection) ignores costal metastases, (rare) long bone metastases and lymph node metastases, it does have the advantages of being feasible within a reasonable time, of being more sensitive than scintigraphy and of allowing abnormalities detected to be characterised. We use it more and more in patients with biochemical failure who are considered at risk on the grounds of classic clinical/laboratory and histopathological criteria.

To sum up, because of its potential morbidity, salvage treatment of a local recurrence should only be offered to a patient with little risk of already having micrometastases. Patients considered to be at risk might benefit from new imaging techniques which seek to detect metastases as early as possible, even though there is currently no recommendation on the subject.

Imaging recurrence after radical prostatectomy

The classic scheme

The only treatment currently approved for local recurrence after prostatectomy is radiotherapy, which typically delivers 66 Gy to the prostatic bed. To be effective, radiotherapy must be performed early, if possible while the PSA concentration is less than 1 ng/mL [5,15].

The usefulness of histological evidence of local recurrence is still being debated. Many teams do not take bed biopsies, arguing that a positive biopsy does not rule out the presence of metastases and a negative biopsy does not rule out local recurrence. The classic attitude is therefore to eliminate those patients with biochemical failure with a high risk of metastases and to treat the rest with radiotherapy, with no histological evidence, if possible before the PSA concentration exceeds 1 ng/mL [15].

In this classic scheme of things, there is no place for imaging.

The advantages of imaging

If an imaging method were available which was sensitive enough to detect local recurrence when the PSA concentration is less than 1 ng/mL, and reliable enough to accurately locate the recurrence, then it would be possible to apply a stereotactic boost to the recurrence, focally increasing the dose above 66 Gy.

Transrectal ultrasound

This technique can occasionally show local recurrence as nodular deformation of the tissue coating the urethra, which should normally be regular. It can also show remains of the seminal vesicles (SVs) left in place. They appear either as normal vesicles, with a liquid content and a typical areolar structure, or as less evocative, oblong, hypoechoic nodules in the site formerly occupied by the SVs [16,17]. Unfortunately, ultrasound is not very sensitive. This results in low sensitivity for ultrasound-guided biopsies: 40 to 71% when the PSA concentration is greater than 1 ng/mL and only 14 to 45% when it is below this threshold [18,19].

Magnetic resonance imaging (MRI)

MRI, on the other hand, has recently given excellent results (Figs. 1–3). In T2, peri-urethral fibrosis appears as a coating giving a homogeneous hyposignal. The remains of the SVs may either appear liquid giving a typical hypersignal or fibrous giving a hyposignal. However, it is dynamic MRI that differentiates well between local recurrences (which are enhanced early and intensely) and postoperative fibrosis (which is not or very little enhanced). Two studies involving 51 and 72 patients with a mean PSA of 1.9 and 1.23 ng/mL respectively, reported sensitivity and specificity of 48 to 61.4% and 52 to 82.1% for T2 imaging and 84.1 to 88% and 89.3 to 100% for T2 combined with dynamic imaging [20,21]. Looking for high choline peaks using spectroscopy (there is no longer any citrate as, in theory, no healthy prostate tissue remains) can also be useful. In a study on

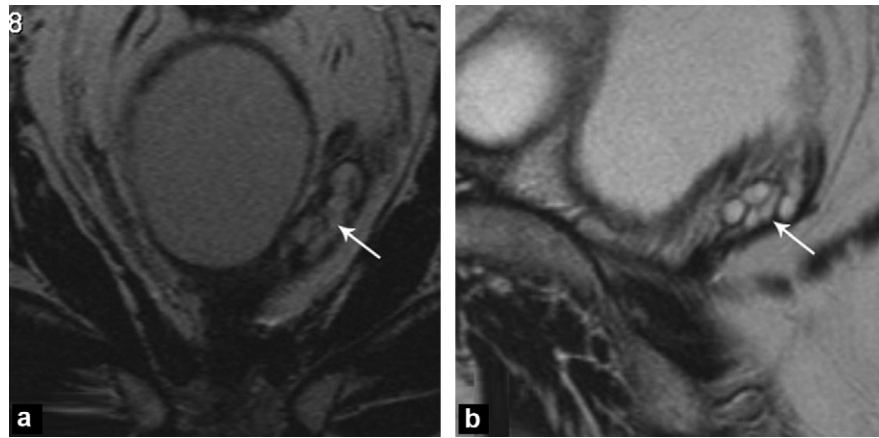


Figure 1. A 70-year-old patient who had had a radical prostatectomy 3 years previously for a Gleason 8 prostatic adenocarcinoma. After surgery, the PSA nadir was 0.09 ng/mL. Gradual increase again to 0.2 ng/mL: a: T2-weighted coronal slice; b: T2-weighted sagittal slice. The magnetic resonance imaging (MRI) shows an almost intact seminal vesicle (SV) on the left. It has a normal T2 fluid signal (white arrow). Dynamic MRI (not shown) did not show any suspect enhancement of this seminal vesicle.

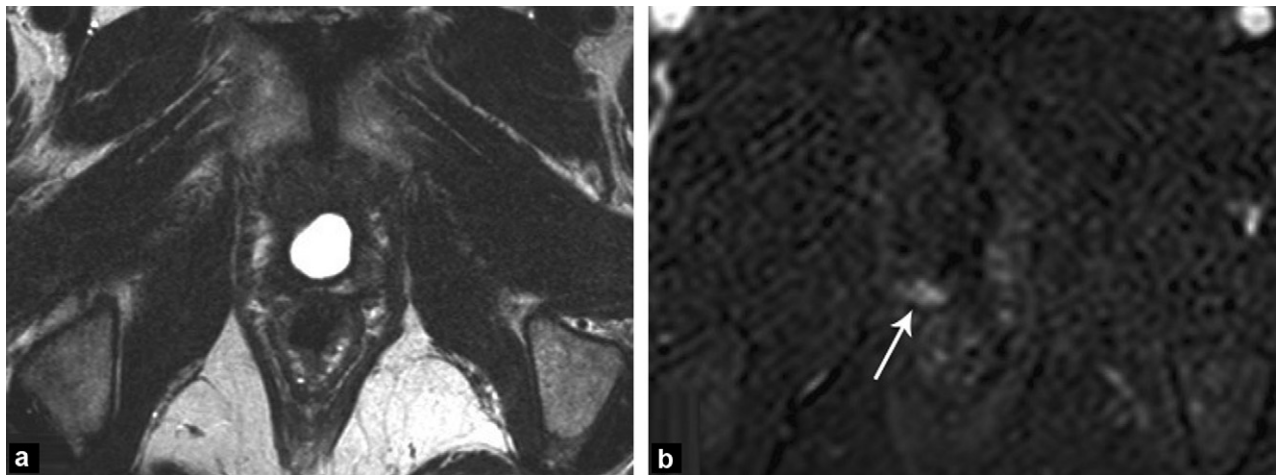


Figure 2. A 57-year-old patient who had had a prostatectomy 3 years previously for a Gleason 7 prostatic adenocarcinoma. After surgery, the PSA nadir was 0 ng/mL. Gradual increase again to 0.32 ng/mL: a: T2-weighted axial magnetic resonance imaging (MRI) shows no abnormality; b: the dynamic axial slice subtracted after injection of contrast agent detected early enhancement of the right side of the neck of the bladder (arrow); targeted biopsies showed a Gleason 7 adenocarcinoma.

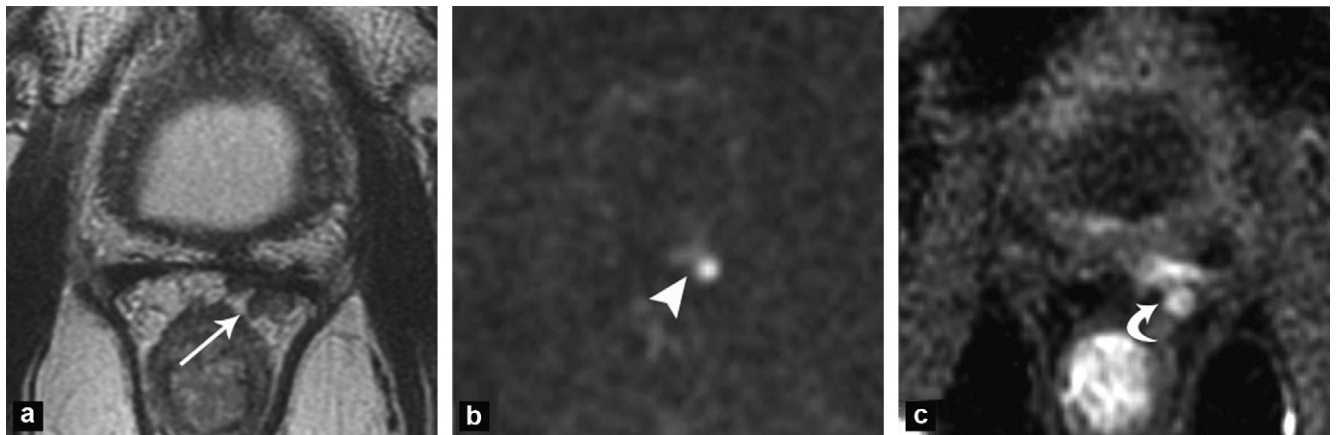


Figure 3. A 70-year-old patient who had had a radical prostatectomy and radiotherapy 3 years previously for a Gleason 7 pT3a prostatic adenocarcinoma. The PSA nadir was 0 ng/mL. Gradual increase to 1.48 ng/mL, with the appearance of a left nodule on DRE: a: T2-weighted axial magnetic resonance imaging (MRI) showing a nodule with an intermediate signal in the left vesicorectal angle (arrow); b: diffusion-weighted axial slice ($b = 2000\text{s/mm}^2$): the nodule exhibits clear diffusion restriction (arrowhead); c: dynamic axial slice after contrast agent injection: enhancement is early and intense (curved arrow). Biopsy of the nodule showed a Gleason 8 adenocarcinoma.

70 patients, the sensitivity and specificity of dynamic MRI combined with spectroscopy was 87% and 94% respectively (as against 71% and 94% for dynamic imaging only) [22].

In theory, PET-CT using choline or acetate could also detect local recurrence [23,24] but the problem is its low spatial resolution which does not provide precise localisation. Moreover, it seems less sensitive than MRI when the PSA concentration is below 1 ng/mL [25].

MRI-guided stereotactic radiotherapy protocols should emerge in the coming years. They could significantly improve radiotherapy results by delivering high doses to the tumour while minimising side effects [26].

Imaging recurrence after radiotherapy

The different salvage treatments

Treatment of local recurrence after radiotherapy is difficult. Salvage prostatectomy is possible but is associated with considerable morbidity and in practice only a few teams in the world practice it [27,28]. Cryotherapy, focused ultrasound and even brachytherapy have been used. These treatments are still associated with a much higher rate of morbidity when used in irradiated patients than when used as first-line treatment [5]. However, it should be noted that for focused ultrasound, it has been possible to define parameters for specific shots in irradiated patients, which has substantially reduced morbidity. The rate of grade 3 urinary incontinence decreased from 11% to 9%, the need to fit an artificial sphincter from 20% to 6% and the rate of urethrorectal fistula from 9% to 0% [29].

Nevertheless, there remains a risk with salvage treatment after radiotherapy, and in the first place, patients with a low risk of metastasis should be selected and secondly, the recurrence should be located as early and as precisely as possible. Because of the morbidity of salvage therapy, it is also important to treat only patients for whom there is biopsy evidence of recurrence, since it is now clear that a biopsy after radiotherapy can be interpreted as long as this is done at least 18 months after the radiation treatment.

The advantages of imaging

If an imaging technique can detect local recurrence early with accurate localisation, it will play an essential role in managing these patients, confirming the recurrence and guiding biopsies and possible salvage treatment.

Ultrasonography

Unfortunately, ultrasonography is not reliable enough to hope to play this role.

Magnetic resonance imaging (MRI)

A T2-weighted MRI shows a prostate as a diffuse hyposignal, with loss of the differentiation between the peripheral and transition zones, and detection of recurrences (which also appear as a hyposignal) remains difficult. On the other hand, dynamic MRI, in which there is excellent contrast

between the recurrence (which is often hypervascular) and post-radiation fibrosis (hypovascular) has given very promising results (Figs. 4–6) [30,31]. Indeed, it correlates well with biopsy results and has good inter-reader agreement [30].

Here again, spectroscopy could be of assistance. After effective radiotherapy, there is metabolic atrophy with disappearance of the choline, creatine, citrate and polyamine peaks. The reappearance of a choline peak appears to be a good sign of recurrence [32]. However, for reasons that are still unknown, it seems that some irradiated benign glands can retain high levels of choline. The specificity of spectroscopy may not therefore be perfect. In a short series of nine patients who underwent salvage prostatectomy, the sensitivity and specificity of T2 MRI was 68% and 96% respectively, compared with 77% and 78% for spectroscopy [33].

Diffusion imaging also appears to show recurrence. Its association with T2 MRI increases the detection sensitivity from 25% to 62% and specificity from 92% to 97% [34].

Gradually, therefore, it is becoming possible to offer multiparametric MRI combining T2, dynamic and diffusion imaging. By combining these three sequences, Arumainayagam et al. obtained excellent correlation with saturation biopsies in 13 patients. The area under the ROC curve was 0.77 to 0.89 depending on the readers for all cancers and 0.86 to 0.93 for recurrences associated with biopsies invaded over more than 3 mm [35].

These good results should make multiparametric MRI an essential examination in all patients with suspected recurrence after radiotherapy.

Imaging recurrence after focused ultrasound treatment

The different salvage treatments

One of the advantages of focused ultrasound treatment is that it can be repeated. It only delivers heat; there is no cumulative dose problem as with radiotherapy so that repeating treatment as often as necessary can be envisaged. In practice, morbidity increases with the number of treatments [36] so that two treatment sessions are the limit. Another alternative in the event of local recurrence after focused ultrasound is to use radiotherapy, which gives good results with acceptable morbidity [37].

One of the limitations of focused ultrasound treatment is that with current equipment, we cannot destroy tissue beyond the fixed focal point. As the transducer is intra-rectal, anterior tumours may be poorly destroyed. It is therefore important to accurately locate the recurrence, particularly whether it is anterior, to decide between retreatment with focused ultrasound, or radiotherapy.

The advantages of imaging

An imaging technique detecting and locating recurrences is thus essential.

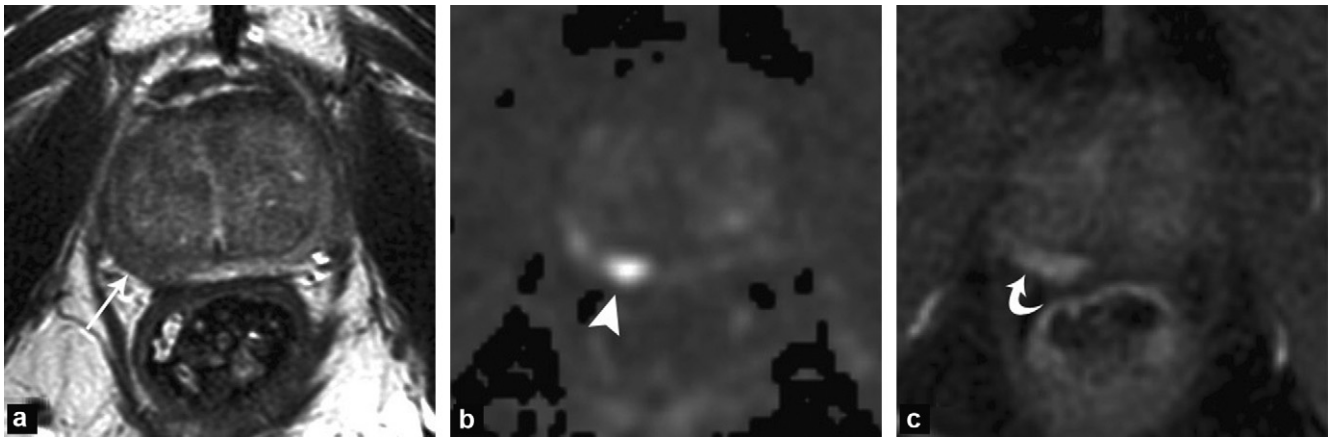


Figure 4. A 79-year-old patient who had had external beam radiotherapy (76 Gy) and hormone treatment 6 years previously for a Gleason 7 prostate adenocarcinoma. The PSA nadir was 0.6 ng/mL, then the level gradually climbed again to 2.7 ng/mL: a: T2-weighted axial magnetic resonance imaging (MRI) shows a suspect hypointense area in the right mid part of the peripheral zone (arrow); b: diffusion-weighted axial slice ($b = 2000 \text{ s/mm}^2$); this area exhibits clear diffusion restriction (arrowhead); c: the dynamic axial slice after contrast agent injection shows early enhancement (curved arrow). Targeted biopsies showed a right mid Gleason 7 adenocarcinoma.

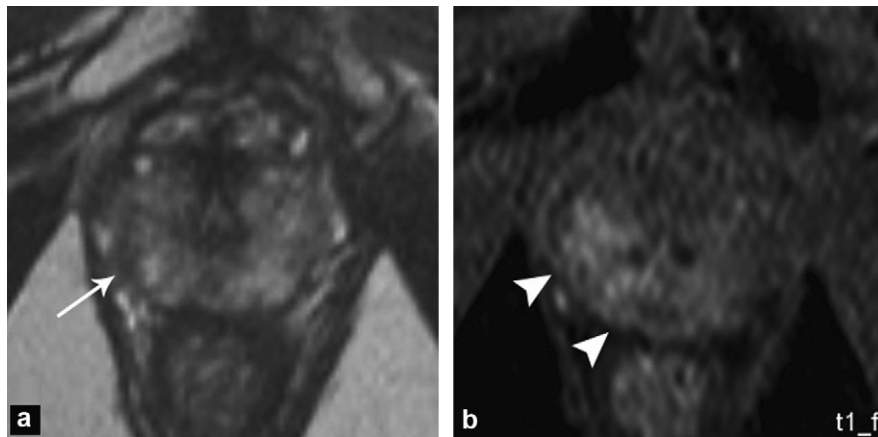


Figure 5. A 73-year-old patient treated with external beam radiotherapy for prostate adenocarcinoma 8 years previously. The nadir PSA was 0.85 ng/mL 2 years after radiotherapy, then the level gradually climbed again to 1.67 ng/mL. Biopsies of the prostate showed a Gleason 6 adenocarcinoma in the right apex, right and left mid parts of the prostate: a: T2-weighted axial magnetic resonance imaging (MRI) shows a suspect hypointense area in the right mid part of the peripheral zone (arrow); b: dynamic axial slice after contrast agent injection shows early enhancement of the apex and the right mid part crossing the midline towards the left (arrowheads).

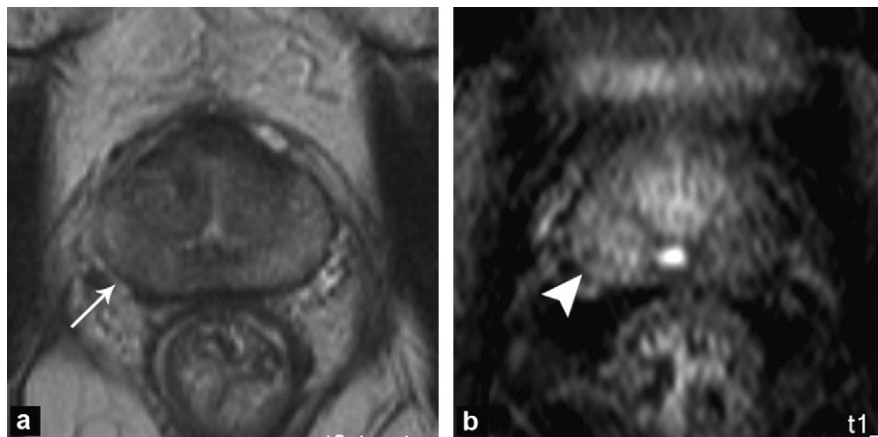


Figure 6. A 65-year-old patient treated with radio-hormonal therapy 4 years previously for a Gleason 6 prostatic adenocarcinoma with a PSA of 20 ng/mL. The PSA nadir was 0.1 ng/mL and the level gradually climbed again to 3.5 ng/mL: a: T2-weighted axial magnetic resonance imaging (MRI) shows a discrete hypointense area in the right mid part of the peripheral zone (arrow); b: the dynamic axial slice after contrast agent injection shows early enhancement of the entire right mid part (arrowhead). Biopsies showed a Gleason 7 prostatic adenocarcinoma of the right mid part.

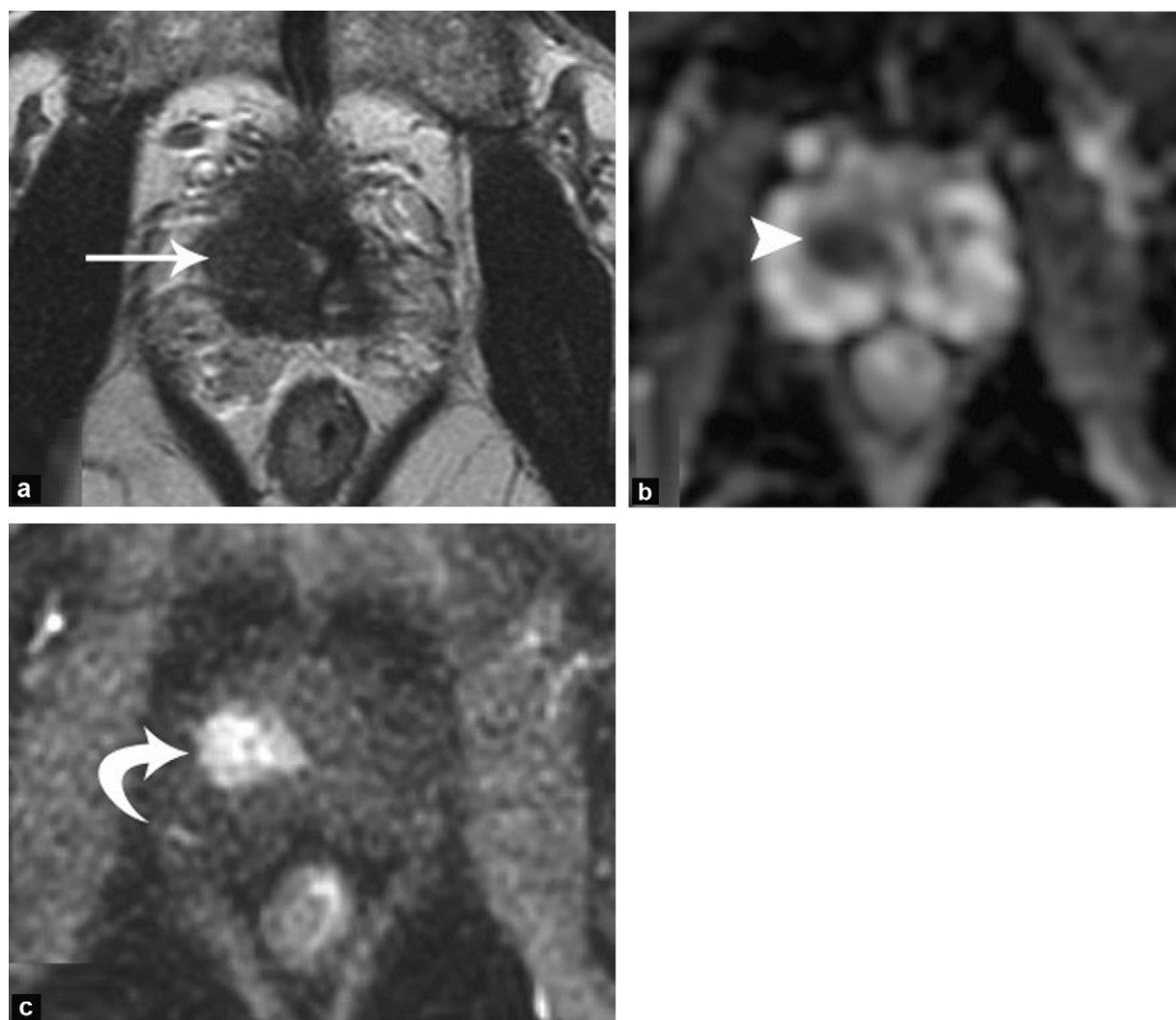


Figure 7. A 78-year-old patient treated with focused ultrasound 6 years previously for a Gleason 7 prostatic adenocarcinoma with a PSA of 20 ng/mL. After a PSA nadir at 0 ng/mL, the level rose again progressively to 3 ng/mL: a: T2-weighted axial slice showing a right basal nodule as a discrete hypointense (arrow); b: axial section, ADC map: the nodule is much more visible (arrowhead); c: the dynamic axial slice after contrast agent injection also shows this nodule better (curved arrow). Targeted biopsies showed a Gleason 7 adenocarcinoma of the mid part and the right base.

Ultrasonography

This technique is not reliable, but Doppler colour makes detection of recurrent cancers a little more sensitive, although the sensitivity of the ultrasound/Doppler combination is still low (around 30%) [38].

Magnetic resonance imaging (MRI)

T2-weighted MRI is not very reliable. Dynamic MRI greatly increases detection sensitivity by showing foci of recurrence as nodules with early enhancement (Figs. 7 and 8) [39]. T2-weighted dynamic MRI is thus significantly more sensitive than the ultrasound/Doppler combination [40]. However, dynamic MRI is a little lacking in specificity. It is difficult to categorically decide between a recurrent cancer and any poorly destroyed anterior adenomatous tissue. Diffusion imaging appears to be more specific than dynamic imaging, but it is decidedly less sensitive [41]. Spectroscopy does not

seem to be useful, but there are only few data on the subject [42].

In practice, dynamic MRI still appears to be the most useful for detecting suspect foci. Given its lack of specificity, guided biopsies should always be used to confirm a recurrent cancer before deciding on salvage treatment.

Imaging recurrence after cryotherapy

There are very few data on the imaging of recurrence after cryotherapy. Ultrasound and T2-weighted MRI are not very reliable [43,44]. As the histological lesions induced by focused ultrasound and cryotherapy are the same, it is likely that dynamic MRI would also be reliable for detecting recurrence after cryotherapy.

Spectroscopy might be useful [43], but that remains to be confirmed.

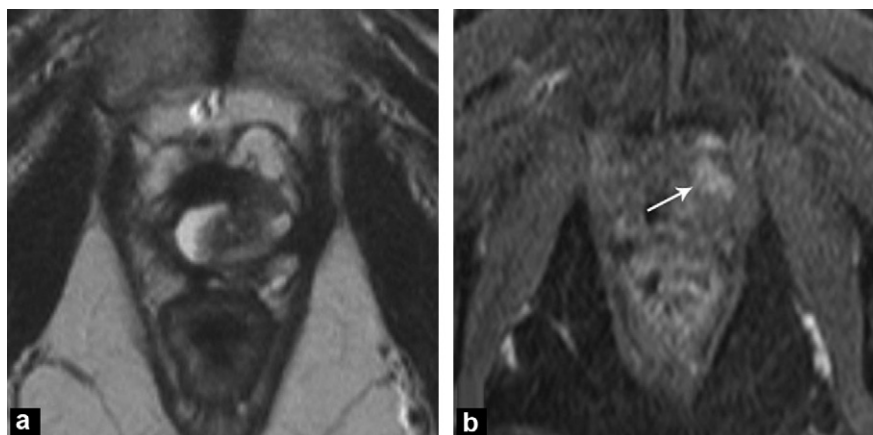


Figure 8. A 75-year-old patient treated with focused ultrasound 2 years previously for a Gleason 6 prostate adenocarcinoma with a PSA of 8.3 ng/mL. The persistence of high PSA concentrations (5 ng/mL) led to discovery in the biopsy of residual cancer of the right mid part treated by a second course of focused ultrasound. Despite this second treatment, the PSA concentration remained at 5 ng/mL: a: T2-weighted axial slice showing no clear anomaly; b: the dynamic axial slice after contrast agent injection shows a left anterior-basal nodule with early enhancement (arrow). Targeted biopsies of the nodule showed a Gleason 6 prostatic adenocarcinoma.

Imaging recurrence after brachytherapy

The different salvage treatments

Once again, the literature contains very few data on the subject of post-brachytherapy local recurrence because, for a long time, there was no treatment for it and hence, no interest in its early detection.

Things change, and brachytherapy failures are no longer therapeutic dead ends. Prostatectomy is possible but difficult. A few trials of high dose rate brachytherapy salvage treatment have been reported [45]. Focused ultrasound can also be used, with very good results, according to our experience.

Because there are beginning to be salvage solutions, early detection of local recurrence is becoming important. Uncertainty about the best criterion of biochemical failure, the problem of PSA rebound between 12 and 24 months, means that it is wise to obtain biopsies before speaking of recurrence. In addition, when the PSA level remains high or rises more than 30 months after treatment, biopsies should be performed to search for recurrence [46,47].

Advantages of magnetic resonance imaging (MRI)

In a T2-weighted MRI, the prostate is dedifferentiated with a diffuse hyposignal [48]. This sequence is thus of little use.

Spectroscopy can show metabolic atrophy, as after radiotherapy. The persistence of metabolic activity beyond 2 years points to recurrence, especially if it is focused [47,49].

Dynamic MRI can also show that cancers have disappeared after treatment and detect recurrence as persistent areas of early enhancement or areas reappearing at a distance from the implantation [5]. In our experience, this is a simple and sensitive method for detecting recurrence (Fig. 9).

Focal treatments: the radiologist in the front line?

Dynamic magnetic resonance imaging (MRI): the most reliable sequence

In short, dynamic MRI seems currently to be the most useful technique for detecting local recurrence of prostate cancer early, regardless of the initial treatment. Diffusion MRI and spectroscopy may be able to improve the diagnosis, but that remains to be confirmed. In general, it appears that detecting local recurrence by imaging is easier, paradoxically, than initial detection of a cancer. This is above all due to the very different enhancement patterns of recurrent cancer and fibrosis (post-surgical, post-radiation or post-coagulation necrosis). The indications for imaging after treatment could therefore have to change rapidly.

Indications for imaging in the future

A new development may in fact somewhat complicate the situation. It is becoming clear that a number of patients with limited prostate cancer could be offered focal treatment in which only the focus of the tumour is targeted [50]: between the two extremes of active surveillance and radical treatment, there must be a middle way.

However, if, instead of removing or destroying the entire gland, only a sector containing the tumour is destroyed (e.g. using focused ultrasound or brachytherapy), it is probable that the PSA concentration will vary little after treatment. The very notion of biochemical failure could henceforth lose its meaning and imaging will find itself in the front line for monitoring changes in the area treated, verifying destruction of the tumour and ensuring there are no recurrences.

What will be the best imaging techniques for this follow-up? How often should we monitor patients? It is

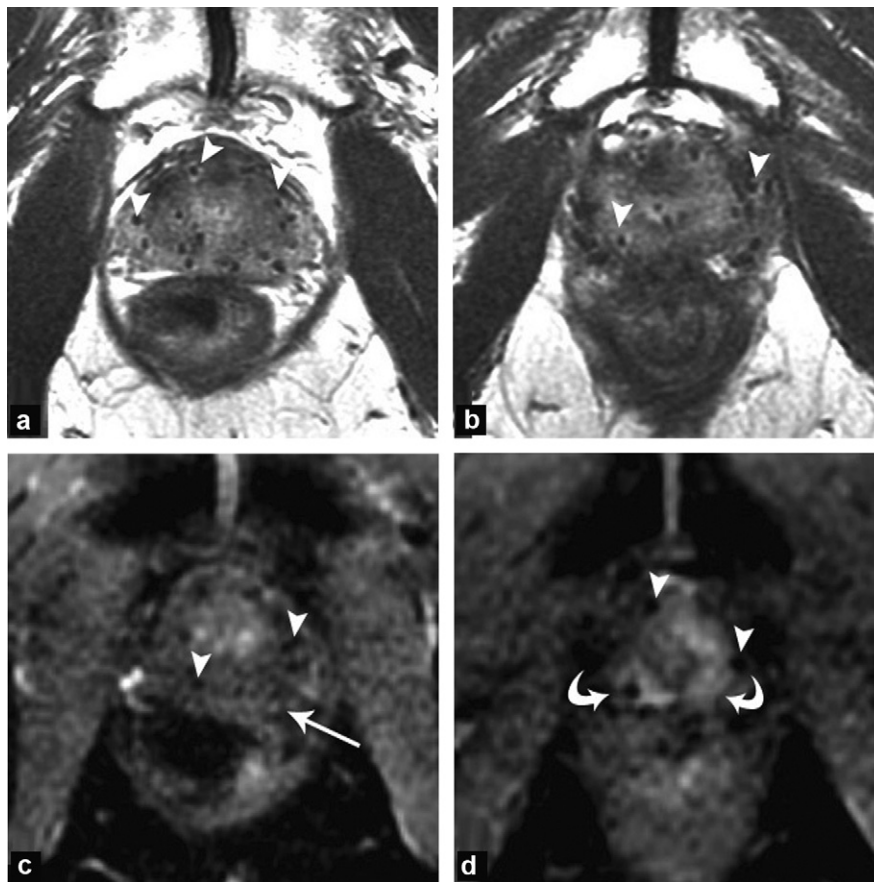


Figure 9. A 71-year-old patient treated with brachytherapy 8 years previously for a Gleason 6 prostatic adenocarcinoma with a PSA concentration of 8 ng/mL. Slow increase again in PSA to 5 ng/mL; a and b: T2-weighted axial magnetic resonance imaging (MRI) revealing a dedifferentiated prostate with no suspect area; c and d: dynamic axial slices after injection of contrast agent showing a peripheral area which is not enhanced (Fig. 9c, arrow), except at the apex where there is bilateral early enhancement (Fig. 9d, curved arrows). Note that the brachytherapy grains appear as small signal voids (Fig. 9a–d, arrowheads).

too early to answer these questions, but the issue of evaluation of focal treatment of prostate cancer is certain to be one of the burning questions of the next few years.

TAKE-HOME MESSAGES

General concepts

- Whatever the initial treatment, there are now salvage solutions for cases of local recurrence of prostate cancer.
- The definition of biochemical failure after radical prostatectomy is: PSA greater than 0.2 ng/mL.
- The definition of biochemical failure after radiotherapy is: PSA greater than nadir + 2 ng/mL.
- There is no consensus definition of biochemical failure after treatment with focused ultrasound, cryotherapy or brachytherapy.

Detection of local recurrence by imaging

- Ultrasound and techniques derived from it are not at present reliable.

- T2-weighted MRI is generally not very accurate.
- Dynamic MRI has shown very promising results after prostatectomy, after radiotherapy and after focused ultrasound, given the good contrast between the hypervascular recurrent cancer and typically hypovascular post-treatment fibrosis.
- The role of diffusion MRI and spectroscopy remains to be defined.

Clinical case

This 63-year-old patient was treated 11 years previously for a Gleason 6 T3N0M0 prostatic adenocarcinoma by radiotherapy (65 Gy). The PSA concentration before treatment was 23.5 ng/mL. The PSA nadir (1.81 ng/mL) was obtained after 3 years. PSA concentration is currently 3.91 ng/mL.

Questions

1. Does the patient categorically have a biochemical failure?
2. A multiparametric MRI was performed (Fig. 10). How do you interpret it?

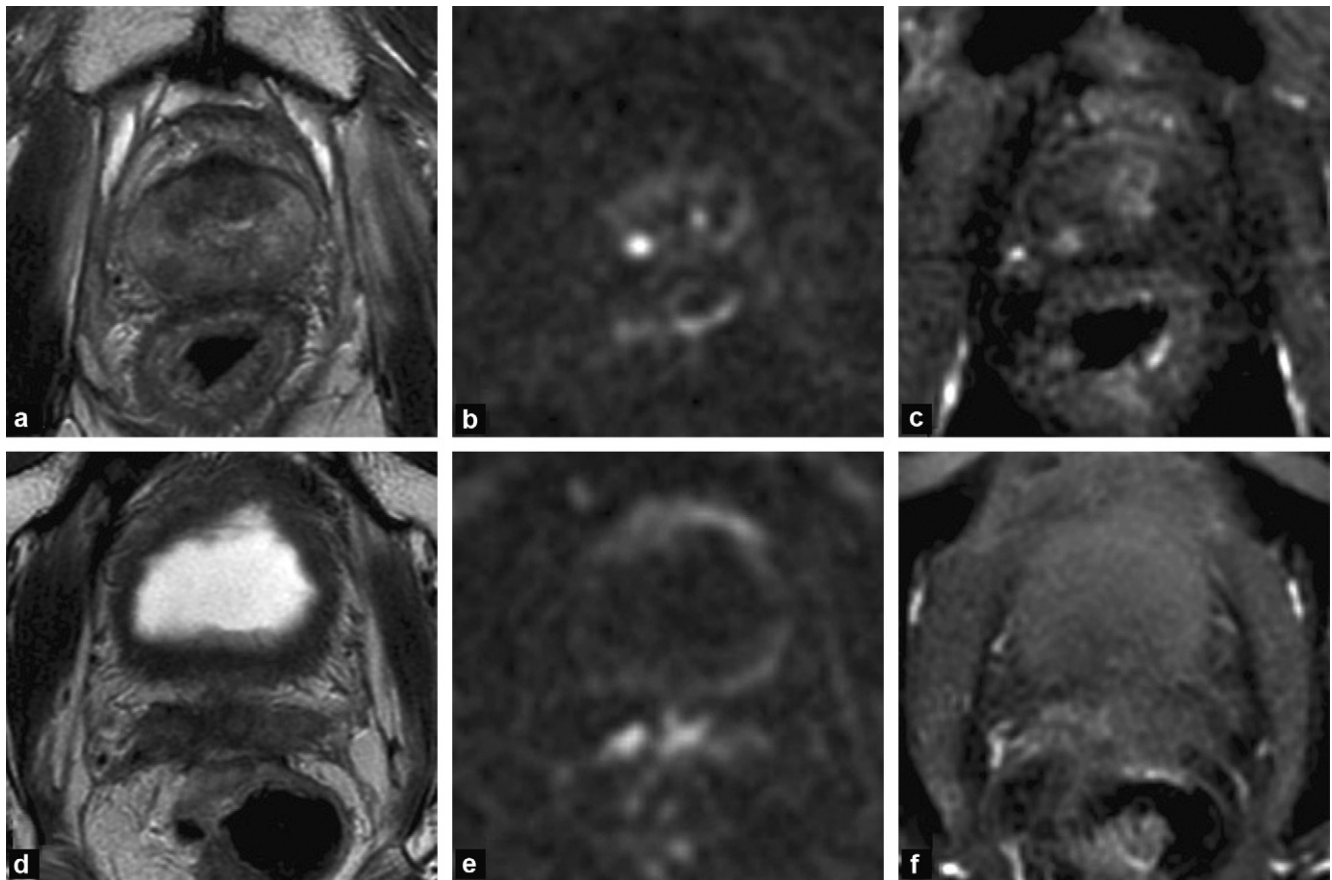


Figure 10. Axial multiparametric magnetic resonance imaging (MRI) of the prostate passing through the middle part the gland (a–c) and through the root of the seminal vesicles (SV) (d–f), T2-weighted (a and d), in diffusion (b = 2000s/mm², b and e) and in T1 after contrast agent injection (dynamic imaging, c and f).

3. What do you recommend before being able to decide on the best management?

Answers

1. After radiotherapy, the current definition of biochemical failure is nadir + 2 ng/mL (Phoenix criteria). The patient therefore has a biochemical failure;
2. Two abnormalities can be seen:
 - a nodule in the right mid part of the peripheral area with all the characteristics of a tumour lesion: T2 hyposignal (Fig. 10a), diffusion restriction (Fig. 10b) and early contrast uptake (Fig. 10c),
 - the appearance of the right SV is suspect: it likewise has the features of a tumour lesion in the three sequences (Fig. 10d–f);
3. Prostate biopsies are needed for evidence of the local recurrence. They will be randomised samples scattered over the prostate and biopsies guided by the MRI data (mid right part and right SV).

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

- [1] Peiffert D. Brachytherapy for localised prostate cancer. *Cancer Radiother* 2007;11:373–8.
- [2] Aus G. Current status of HIFU and cryotherapy in prostate cancer – a review. *Eur Urol* 2006;50:927–34.
- [3] Crouzet S, Rebillard X, Chevallier D, Rischmann P, Pasticier G, Garcia G, et al. Multicentric oncologic outcomes of high-intensity focused ultrasound for localized prostate cancer in 803 patients. *Eur Urol* 2010;58:559–66.
- [4] Arumainayagam N, Moore CM, Ahmed HU, Emberton M. Photodynamic therapy for focal ablation of the prostate. *World J Urol* 2010;28:571–6.
- [5] Rouviere O, Vitry T, Lyonnet D. Imaging of prostate cancer local recurrences: why and how? *Eur Radiol* 2010;20:1254–66.
- [6] Heidenreich A, Aus G, Bolla M, Joniau S, Matveev VB, Schmid HP, et al. EAU guidelines on prostate cancer. *Eur Urol* 2008;53:68–80.
- [7] Roach 3rd M, Hanks G, Thames Jr H, Schellhammer P, Shipley WU, Sokol GH, et al. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix consensus conference. *Int J Radiat Oncol Biol Phys* 2006;65:965–74.
- [8] Rouviere O, Souchon R, Salomir R, Gelet A, Chapelon JY, Lyonnet D. Transrectal high-intensity focused ultrasound ablation of prostate cancer: effective treatment requiring accurate imaging. *Eur J Radiol* 2007;63:317–27.

- [9] Blana A, Murat FJ, Walter B, Thuroff S, Wieland WF, Chaussy C, et al. First analysis of the long-term results with transrectal HIFU in patients with localised prostate cancer. *Eur Urol* 2008;53:1194–201.
- [10] Blana A, Brown SC, Chaussy C, Conti GN, Eastham JA, Ganzer R, et al. High-intensity focused ultrasound for prostate cancer: comparative definitions of biochemical failure. *BJU Int* 2009;104:1058–62.
- [11] Carey B, Swift S. The current role of imaging for prostate brachytherapy. *Cancer Imaging* 2007;7:27–33.
- [12] Kuban KDA, Levy LB, Potters L, Beyer DC, Blasko JC, Moran BJ, et al. Comparison of biochemical failure definitions for permanent prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2006;65:1487–93.
- [13] Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. *JAMA* 1999;281:1591–7.
- [14] Zagars GK, Pollack A. Kinetics of serum prostate-specific antigen after external beam radiation for clinically localized prostate cancer. *Radiother Oncol* 1997;44:213–21.
- [15] Naito S. Evaluation and management of prostate-specific antigen recurrence after radical prostatectomy for localized prostate cancer. *Jpn J Clin Oncol* 2005;35:365–74.
- [16] Wasserman NF, Kapoor DA, Hildebrandt WC, Zhang G, Born KM, Eppel SM, et al. Transrectal US in evaluation of patients after radical prostatectomy. Part I. Normal postoperative anatomy. *Radiology* 1992;185:361–6.
- [17] Wasserman NF, Kapoor DA, Hildebrandt WC, Zhang G, Born KM, Eppel SM, et al. Transrectal US in evaluation of patients after radical prostatectomy. Part II. Transrectal US and biopsy findings in the presence of residual and early recurrent prostatic cancer. *Radiology* 1992;185:367–72.
- [18] Leventis AK, Shariat SF, Kattan MW, Butler EB, Wheeler TM, Slawin KM. Prediction of response to salvage radiation therapy in patients with prostate cancer recurrence after radical prostatectomy. *J Clin Oncol* 2001;19:1030–9.
- [19] Deliveliotis C, Manousakas T, Chrisofos M, Skolarikos A, Delis A, Dimopoulos C. Diagnostic efficacy of transrectal ultrasound-guided biopsy of the prostatic fossa in patients with rising PSA following radical prostatectomy. *World J Urol* 2007;25:309–13.
- [20] Casciani E, Poletini E, Carmenini E, Floriani I, Masselli G, Bertini L, et al. Endorectal and dynamic contrast-enhanced MRI for detection of local recurrence after radical prostatectomy. *AJR Am J Roentgenol* 2008;190:1187–92.
- [21] Cirillo S, Petracchini M, Scotti L, Gallo T, Macera A, Bona MC, et al. Endorectal magnetic resonance imaging at 1.5 Tesla to assess local recurrence following radical prostatectomy using T2-weighted and contrast-enhanced imaging. *Eur Radiol* 2009;19:761–9.
- [22] Sciarra A, Panebianco V, Salciccia S, Osmani M, Lisi D, Ciccariello M, et al. Role of dynamic contrast-enhanced magnetic resonance (MR) imaging and proton MR spectroscopic imaging in the detection of local recurrence after radical prostatectomy for prostate cancer. *Eur Urol* 2008;54:589–600.
- [23] Reske SN, Blumstein NM, Glatting G. [(11)C]choline PET/CT imaging in occult local relapse of prostate cancer after radical prostatectomy. *Eur J Nucl Med Mol Imaging* 2008;35:9–17.
- [24] Cimitan M, Bortolus R, Morassut S, Canzonieri V, Garbeglio A, Baresic T, et al. [18F]fluorocholine PET/CT imaging for the detection of recurrent prostate cancer at PSA relapse: experience in 100 consecutive patients. *Eur J Nucl Med Mol Imaging* 2006;33:1387–98.
- [25] Veas H, Buchegger F, Albrecht S, Khan H, Husarik D, Zaidi H, et al. 18F-choline and/or 11C-acetate positron emission tomography: detection of residual or progressive subclinical disease at very low prostate-specific antigen values (<1 ng/mL) after radical prostatectomy. *BJU Int* 2007;99:1415–20.
- [26] Miralbell R, Veas H, Lozano J, Khan H, Mollà M, Hidalgo A, et al. Endorectal MRI assessment of local relapse after surgery for prostate cancer: A model to define treatment field guidelines for adjuvant radiotherapy in patients at high risk for local failure. *Int J Radiat Oncol Biol Phys* 2007;67:356–61.
- [27] Touma NJ, Izawa JI, Chin JL. Current status of local salvage therapies following radiation failure for prostate cancer. *J Urol* 2005;173:373–9.
- [28] Heidenreich A, Richter S, Thuer D, Pfister D. Prognostic parameters, complications, and oncologic and functional outcome of salvage radical prostatectomy for locally recurrent prostate cancer after 21st-century radiotherapy. *Eur Urol* 2010;57:437–43.
- [29] Murat FJ, Poissonnier L, Rabilloud M, Belot A, Bouvier R, Rouviere O, et al. Mid-term results demonstrate salvage high-intensity focused ultrasound (HIFU) as an effective and acceptably morbid salvage treatment option for locally radiorecurrent prostate cancer. *Eur Urol* 2009;55:640–7.
- [30] Rouvière O, Valette O, Grivolat S, Colin-Pangaud C, Bouvier R, Chapelon JY, et al. Recurrent prostate cancer after external beam radiotherapy: value of contrast-enhanced dynamic MRI in localizing intraprostatic tumor – correlation with biopsy findings. *Urology* 2004;63:922–7.
- [31] Haider MA, Chung P, Sweet J, Toi A, Jhaveri K, Ménard C, et al. Dynamic contrast-enhanced magnetic resonance imaging for localization of recurrent prostate cancer after external beam radiotherapy. *Int J Radiat Oncol Biol Phys* 2008;70:425–30.
- [32] Coakley FV, Teh HS, Qayyum A, Swanson MG, Lu Y, Roach 3rd M, et al. Endorectal MR imaging and MR spectroscopic imaging for locally recurrent prostate cancer after external beam radiation therapy: preliminary experience. *Radiology* 2004;233:441–8.
- [33] Pucar D, Shukla-Dave A, Hricak H, Moskowitz CS, Kuroiwa K, Olgac S, et al. Prostate cancer: correlation of MR imaging and MR spectroscopy with pathologic findings after radiation therapy-initial experience. *Radiology* 2005;236:545–53.
- [34] Kim CK, Park BK, Lee HM. Prediction of locally recurrent prostate cancer after radiation therapy: incremental value of 3T diffusion-weighted MRI. *J Magn Reson Imaging* 2009;29:391–7.
- [35] Arumainayagam N, Kumaar S, Ahmed HU, Moore C, Payne H, Freeman A, et al. Accuracy of multiparametric magnetic resonance imaging in detecting recurrent prostate cancer after radiotherapy. *BJU Int* 2010;106:991–7.
- [36] Blana A, Rogenhofer S, Ganzer R, Wild PJ, Wieland WF, Walter B. Morbidity associated with repeated transrectal high-intensity focused ultrasound treatment of localized prostate cancer. *World J Urol* 2006;24:585–90.
- [37] Pasticier G, Chapet O, Badet L, Ardiet JM, Poissonnier L, Murat FJ, et al. Salvage radiotherapy after high-intensity focused ultrasound for localized prostate cancer: early clinical results. *Urology* 2008;72:1305–9.
- [38] Rouvière O, Mège-Lechevallier F, Chapelon JY, Gelet A, Bouvier R, Boutitie F, et al. Evaluation of color doppler in guiding prostate biopsy after HIFU ablation. *Eur Urol* 2006;50:490–7.
- [39] Ben Cheikh A, Girouin N, Ryon-Taponnier P, Mège-Lechevallier F, Gelet A, Chapelon JY, et al. Détection par IRM des récidives locales du cancer de prostate après traitement par ultrasons focalisés de haute intensité (HIFU) transrectaux: étude préliminaire. *J Radiol* 2008;89:571–7.
- [40] Rouvière O, Girouin N, Glas L, Ben Cheikh A, Gelet A, Mège-Lechevallier F, et al. Prostate cancer transrectal HIFU ablation: detection of local recurrences using T2-weighted and dynamic contrast-enhanced MRI. *Eur Radiol* 2010;20:48–55.
- [41] Kim CK, Park BK, Lee HM, Kim SS, Kim E. MRI techniques for prediction of local tumor progression after high-intensity focused ultrasonic ablation of prostate cancer. *AJR Am J Roentgenol* 2008;190:1180–6.

- [42] Cirillo S, Petracchini M, D'Urso L, Dellamonica P, Illing R, Regge D, et al. Endorectal magnetic resonance imaging and magnetic resonance spectroscopy to monitor the prostate for residual disease or local cancer recurrence after transrectal high-intensity focused ultrasound. *BJU Int* 2008;102:452–8.
- [43] Parivar F, Hricak H, Shinohara K, Kurhanewicz J, Vigneron DB, Nelson SJ, et al. Detection of locally recurrent prostate cancer after cryosurgery: evaluation by transrectal ultrasound, magnetic resonance imaging, and three-dimensional proton magnetic resonance spectroscopy. *Urology* 1996;48:594–9.
- [44] Kalbhen CL, Hricak H, Shinohara K, Chen M, Parivar F, Kurhanewicz J, et al. Prostate carcinoma: MR imaging findings after cryosurgery. *Radiology* 1996;198:807–11.
- [45] Tharp M, Hardacre M, Bennett R, Jones WT, Stuhldreher D, Vaught J. Prostate high-dose-rate brachytherapy as salvage treatment of local failure after previous external or permanent seed irradiation for prostate cancer. *Brachytherapy* 2008;7:231–6.
- [46] Toledano A, Chauveinc L, Flam T, Thiounn N, Solignac S, Timbert M, et al. PSA bounce after permanent implant prostate brachytherapy may mimic a biochemical failure: a study of 295 patients with a minimum 3-year follow-up. *Cancer Radiother* 2007;11:105–10.
- [47] Kirilova A, Damyanovich A, Crook J, Jezioranski J, Wallace K, Pintilie M. 3D MR spectroscopic imaging assessment of metabolic activity in the prostate during the PSA “bounce” following 125iodine brachytherapy. *Int J Radiat Oncol Biol Phys* 2011;79:371–8.
- [48] Coakley FV, Hricak H, Wefer AE, Speight JL, Kurhanewicz J, Roach M. Brachytherapy for prostate cancer: endorectal MR imaging of local treatment-related changes. *Radiology* 2001;219:817–21.
- [49] Pickett B, Ten Haken RK, Kurhanewicz J, Qayyum A, Shinohara K, Fein B, et al. Time to metabolic atrophy after permanent prostate seed implantation based on magnetic resonance spectroscopic imaging. *Int J Radiat Oncol Biol Phys* 2004;59:665–73.
- [50] Lecornet E, Ahmed HU, Moore CM, Emberton M. Conceptual basis for focal therapy in prostate cancer. *J Endourol* 2010;24:811–8.