ACTA ONCOLOGICA, 2017
VOL. 56, NO. 1, 27–32
http://dx.doi.org/10.1080/0284186X.2016.1223342

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ORIGINAL ARTICLE

# Proposal for magnetic resonance imaging-guided salvage radiotherapy for prostate cancer*

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**ABSTRACT**

**Background:** A subset of patients experience a biochemical recurrence following radical prostatectomy. Radiotherapy can salvage those patients, provided that all disease is encompassed within the target volume. We hypothesized that this can be achieved more adequately with magnetic resonance imaging (MRI)-guided treatment planning.

**Material and methods:** From January 2009 to April 2014, 183 patients were referred to our department for salvage radiotherapy (SRT). According to protocol, patients received a planning computed tomography (CT) as well as an MRI in treatment position. All MRI scans were retrospectively reviewed by an experienced uro-radiologist.

**Results:** Median prostate-specific antigen (PSA) value at time of referral was 0.3 ng/ml (range 0.02–4.7 ng/ml). MRI did not show any suspected macroscopic disease in 137 patients (75%). In 46 (25%) patients, MRI did indicate a pelvic recurrence. The mean PSA level was significantly higher in patients with a suspected recurrence on MRI (0.4 vs. 1.4 ng/ml, $p < .001$) on a Student's t-test. The mean follow-up was 33 months (range 5–69 months). Biochemical disease-free survival (bDFS) was significantly worse in patients with suspected disease on MRI [hazard ratio (HR) 2.9, $p < .0001$]. bDFS was significantly worse in the subgroup where the macroscopic recurrences on MRI received a lower radiation dose (HR 3.4, $p = .01$).

**Conclusion:** MRI detects loco-regional disease in a substantial subset of patients with a biochemical recurrence after prostatectomy, especially in a PSA above 0.5 μg/l. Lack of MRI-based dose escalation on these macroscopic recurrences could explain some of the biochemical progression observed after SRT.

**ARTICLE HISTORY**
Received 9 December 2015
Revised 15 July 2016
Accepted 29 July 2016
Published online 1 September 2016

The predominant treatment failure site after radical prostatectomy is local [1]. Therefore, salvage radiotherapy (SRT) is a potentially curative option in patients with a biochemical recurrence after prostatectomy, especially when patients are referred early and when sufficiently high radiation doses are delivered [2,3]. Obviously, definition of the appropriate target volume is equally important, and there is concern that geographical miss could cause inadequate local control, resulting in further biochemical progression after SRT.

At least four working group guidelines for the delineation of the post-prostatectomy clinical target volume (CTV) on the planning computed tomography (CT) scan exist [4–7]. There are considerable discrepancies between those guidelines [8]. Moreover, all of the current guidelines sometimes inadequately cover the prostate bed and/or the pre-operative gross tumor volume [9]. Furthermore, even when the guidelines are followed closely, considerable inter-observer variability can be observed [10].

During the last decade, magnetic resonance imaging (MRI) has become commonly used in the planning of prostate radiotherapy, and compared with planning CT provides improved soft tissue resolution, allowing more consistent delineation of the prostate apex, anterior rectal wall, and penile bulb. These last two structures are also important when outlining the prostate bed. Additionally, identification of the vesico-urethral anastomosis is better on T2-weighted MRI sagittal slices. Comparable to what is observed with prostate CTV delineation, Sefrova and colleagues demonstrated a significant reduction of the overall post-prostatectomy CTV on planning MRI compared with CT [11].

Multi-parametric MRI, especially with diffusion-weighted (DW) and/or dynamic contrast-enhanced (DCE) sequences, is a powerful tool for detection of local recurrences after radical prostatectomy, even at low prostate-specific antigen (PSA) values [12,13]. Generally, DCE-MRI is considered the most reliable technique in detecting local prostate cancer

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*Presented as an oral presentation OC-0592 at the 3rd ESTRO forum 2015 in Barcelona.

Supplementary data for this article can be accessed here.

recurrence after radical prostatectomy, although DW-MRI can be proposed as a reliable alternative [13]. Recently, both showed sensitivity and specificity >90% for local recurrence detection in 126 surgically treated patients with a PSA <1.7 ng/ml [13]. A recent comparison between $^{11}$C-Choline positron emission tomography (PET)-CT and multi-parametric MRI for detection of recurrent prostate cancer after radical prostatectomy, albeit at relatively high PSA levels (mean PSA of 2.5 ng/ml at time of imaging), suggested that: 1) MRI is superior to PET-CT for detection of a local recurrence in the prostate bed; 2) MRI is less adequate for diagnosis of lymph node metastases and probably inferior to PET-CT in that regard; and 3) both are excellent for the diagnosis of pelvic bone metastases [14].

Since 2009, patients referred for SRT routinely received a planning MRI (with T1-, T2- and DW sequences) in treatment position in our institution. We hypothesized that in some patients, a local and/or regional recurrence could have been detected on those images, which were in fact solely used for CTV delineation.

## Material and methods

### Study population

From January 2009 to April 2014, 238 patients with a biochemical recurrence after radical prostatectomy were referred to our department for SRT. None of the patients had a suspected local recurrence on digital rectal examination (DRE) or trans-rectal ultrasound (TRUS). Patients were generally not re-staged with bone scintigraphy or CT of the pelvis, therefore patients with a PSA level >5.0 ng/ml (n = 16) were excluded from the analysis. Time (and PSA level) of referral depended solely on the referring urologist.

Medical history and physical examination (including DRE) were obtained by the treating radiation oncologist from each patient at the start of the treatment. According to our protocol, patients received a planning CT without intravenous (IV) contrast as well as a planning MRI in treatment position, with consistent bladder and rectal filling. A very strict bladder and rectal filling procedure was followed in all patients. Patients were advised to place a Microlax® Fleet enema before leaving home. At the same time, they were asked to empty their bladder and then drink 400 cm$^3$ of water. Bladder voidance should thereafter be avoided. For both CT and MRI patients were positioned on a flat table top with knee and feet support to limit rotations. Registration, delineation and planning were performed on the Eclipse® (version 11) treatment planning system from Varian Inc. (Palo Alto, CA). For various reasons, e.g. claustrophobia, pacemaker, incompatible prosthesis, etc., 39 patients only received a planning CT, and were therefore also excluded from this analysis.

The study protocol was approved by the local ethics committee.

### Patient and disease characteristics

Of the final study population of 183 patients with a PSA value ≤5.0 ng/ml and both planning CT as well as MRI images, 113 patients had pathological T2-classification (16 pT2a-b vs. 97 pT2c), 48 had pT3a disease, 21 had pT3b disease, and one patient had pT4 disease, respectively (Table 1). In 112 (61%) patients, no pelvic lymph nodes were removed during surgery. In 71 (39%) patients, some lymph node sampling was performed. Ultimately, 11 patients had pN1 disease. Median time between surgery and referral was 33 months (range 6–161 months). Median PSA at time of referral was 0.3 ng/ml (range 0.02–4.7 ng/ml).

### Radiation technique

The post-prostatectomy CTV was delineated on MRI according to the European Organization for Research and Treatment of Cancer (EORTC) guidelines [4]. No elective lymph nodes were irradiated in 132 (72%) patients. In 51 (28%) patients, some elective nodal irradiation (ENI) was performed, generally only covering a limited field (mini-pelvis) including the bilateral obturator, internal and external iliac nodes up to the lower border of the sacro-iliacal joint. Isotropic planning target volume (PTV) margins of 1 cm were used for both prostate bed and nodal CTV. Dose to the prostate bed was 66.0 Gy in 33 daily fractions of 2.0 Gy for all patients, delivered through intensity-modulated radiotherapy (IMRT). If elective nodal radiotherapy was performed, dose to the nodal regions was 52.8 Gy in 33 fractions of 1.6 Gy through a simultaneous integrated boost approach.

**Table 1.** Patient and disease characteristics (n = 183).

| | All (n = 183) | | MRI negative (n = 137) | | MRI positive (n = 46) | | |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | p-Value ($\chi^2$-test) |
| LND | | | | | | | .27 |
| Yes | 71 | 39 | 50 | 36 | 21 | 46 | |
| No | 112 | 61 | 87 | 64 | 25 | 54 | |
| Pathological Gleason score | | | | | | | .03 |
| 6 | 47 | 26 | 37 | 27 | 10 | 22 | |
| 7 | 102 | 56 | 80 | 58 | 22 | 48 | |
| 8 | 22 | 12 | 15 | 11 | 7 | 15 | |
| 9 | 12 | 7 | 5 | 4 | 7 | 15 | |
| Pathological T-stage | | | | | | | .02 |
| pT2 | 113 | 62 | 87 | 64 | 26 | 57 | |
| pT2a | 6 | 3 | 6 | 4 | 0 | 0 | |
| pT2b | 10 | 5 | 9 | 7 | 1 | 2 | |
| pT2c | 97 | 53 | 72 | 53 | 25 | 54 | |
| pT3 | 69 | 38 | 49 | 36 | 20 | 44 | |
| pT3a | 48 | 26 | 39 | 29 | 9 | 20 | |
| pT3b | 21 | 12 | 10 | 7 | 11 | 24 | |
| pT4 | 1 | 1 | 1 | 1 | 0 | 0 | |
| Pathological N-stage | | | | | | | .01 |
| pN0 | 60 | 33 | 46 | 34 | 14 | 30 | |
| pN1 | 11 | 6 | 4 | 3 | 7 | 15 | |
| pNx | 112 | 61 | 87 | 64 | 25 | 54 | |
| PSA (ng/ml) at RT | | | | | | | <.00001 |
| <0.2 | 55 | 30 | 53 | 39 | 2 | 4 | |
| [0.2–0.5] | 61 | 33 | 50 | 37 | 11 | 24 | |
| [0.5–1.0] | 34 | 19 | 16 | 12 | 18 | 39 | |
| >1.0 | 33 | 18, | 18 | 13 | 15 | 33 | |
| Mean time (months) after surgery | 33 months (range 6–161) | | 32 months (range 6–161) | | 34 months (range 10–138) | | |

LND: lymph node dissection; MRI: magnetic resonance imaging; SRT: salvage radiotherapy.

**Table 2.** Univariate and multivariate analysis.

| | | Biochemical disease-free survival | | |
|---|---|---|---|---|
| | | HR | 95% CI | p-Value |
| All patients (n = 183): | | | | |
| Univariate | MRI (suspect vs. not) | 2.9 | 2.3–3.4 | <.0001 |
| | pT-stage (pT3-4 vs. pT2) | 1.7 | 1.0–3.0 | .06 |
| | Pre-radiotherapy PSA (>0.5 vs. ≤0.5 ng/ml) | 1.5 | 0.9–2.6 | .15 |
| | Gleason (8–9 vs. 6–7) | 3.8 | 1.5–10.0 | .004 |
| | LND (yes vs. no) | 0.7 | 0.4–1.2 | .19 |
| | ENI (yes vs. no) | 2.5 | 1.2–5.0 | .01 |
| Multivariate | MRI (suspect vs. not) | 2.8 | 1.0–4.0 | .04 |
| | Gleason (8–9 vs. 6–7) | 2.0 | 1.6–5.0 | .03 |
| Subgroup of patients with a suspected recurrence on MRI (n = 46): | | | | |
| Univariate | ID vs. HD | 1.1 | 0.4–3.2 | .86 |
| | LD vs. HD | 3.4 | 1.4–8.4 | .01 |

CI: confidence interval; ENI: elective nodal irradiation; HD: high (mean dose above 60 Gy) dose to the suspected recurrence on MRI; HR: hazard ratio; ID: intermediate (mean dose between 50 and 60 Gy) to the suspected recurrence on MRI, LD: low (mean dose <50 Gy) to the suspected recurrence on MRI; LND: lymph node dissection; MRI: magnetic resonance imaging; PSA: prostate specific-antigen.

### *Imaging protocol*

MRI consisted of T1-, T2-, and DW [with an apparent diffusion coefficient (ADC) map] sequences. MRI was performed on a 3T scanner (Magnetom Verio, Siemens AG, Erlangen, Germany). The MRI protocol consisted of axial DW images using b-values of 0 and 1000 s/mm$^2$ [repetition time (TR)/ echo time (TE) 4500 ms/63 ms, 5-mm slice thickness], axial and coronal turbo spin-echo (TSE) T2-weighted images (TR/ TE 3000 ms/149 ms, 5-mm slice thickness) and axial three-dimensional (3D) gradient echo T1-weighted images (TR/TE 6.52 ms/2.86 ms, 2.5-mm slice thickness). All MRI scans were sent to the radiotherapy planning system and used for CTV delineation. They were retrospectively reviewed for the presence of a local and/or regional recurrence by an experienced uro-radiologist (FD or FVM) for the purpose of this investigation. The recurrence was delineated retrospectively on the MRI and its dose and relation to the delineated CTV was calculated.

### *Statistical analysis*

Patient and tumor characteristics as well as PSA values were recorded at start of treatment. After radiotherapy, patients were again followed by their referring urologist. Disease control data were retrospectively collected: information was sought on subsequent PSA evolution. A biochemical relapse after SRT was defined as a PSA level that had increased to ≥0.2 ng/ml from the post-SRT nadir confirmed by one more consecutive result at least two weeks later [15]. The time to biochemical relapse after SRT was defined as the period from the end of SRT to the confirmatory PSA measurement. The close-out date for survival analysis was October 2014. Mean follow-up was 33 months (range 5–69 months).

The data were analyzed using R (version 3.2.1). Cumulative survival and disease control rates were calculated using the Kaplan-Meier product-limited (actuarial) method. Biochemical relapse was compared regarding MRI findings, pre-radiotherapy PSA (PSA ≤0.5 vs. >0.5 ng/ml), pathological Gleason score (6–7 vs. 8–9), pathological T-stage (pT2 vs. pT3-4), nodal dissection (yes vs. no), and ENI (yes vs. no) using univariate Cox regression analysis. Significant results (p-value <.05) were compared in multivariate Cox regression analysis. For the subset of patients with a local recurrence on MRI, biochemical relapse was compared regarding mean dose to the recurrence: low dose (mean dose <50.0 Gy) versus intermediate dose (mean dose 50.0–60.0 Gy) versus high dose (mean dose >60.0 Gy).

## Results

The MRI was negative in 137 (75%) patients. In 46 patients (25%), the planning MRI did indicate a suspected macroscopic recurrence. This recurrence consisted of local disease in 22 (49%) patients, lymph node metastases in 23 (50%) patients, and pelvic bone metastases in two (4%) patients. One patient had a combined local and nodal relapse (Supplementary Figure S1, available online at http://www.informahealthcare.com). The mean PSA was significantly higher in patients with a suspected recurrence on MRI than in patients with a negative planning MRI (1.4 vs. 0.4 ng/ml, p < .001) on a Student's t-test.

Of the 22 patients with suspected local disease, in 11 patients (50%) the recurrence was found in the peri-anastomotic region, in two patients (9%) in the retrovesical space, and in nine patients (41%) in the seminal vesicle bed. Looking at the definitive pathology of the nine patients with a suspected recurrence in the seminal vesicle bed, only three of those had seminal vesicle invasion (SVI) on the surgical pathology specimen.

Of the 23 patients with suspected pelvic lymph nodes, the involved nodal region was obturator in seven patients (30%), internal iliac in seven patients (30%), external iliac in nine patients (39%), presacral in two patients (9%), and common iliac in two patients (9%). Looking at the definitive pathology of the 23 patients with a nodal recurrence, it is striking that eight had SVI on the surgical pathology specimen. Also, five patients were pN1, eight were pN0 (albeit often with a limited dissection), and 10 were pNx.

For the patients with a local recurrence (n = 22), the macroscopic lesion was included in the high-dose (i.e. prostate bed) CTV in 17 (77%) patients, whereas in all patients it was included in the high-dose PTV. In all five

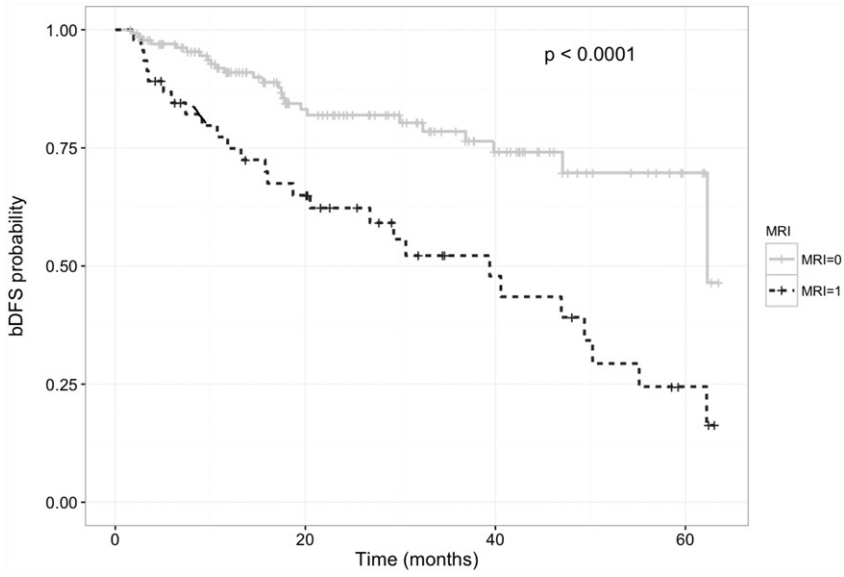


**Figure 1.** Kaplan-Meier estimates of biochemical disease-free survival (bDFS) in patients with a suspected recurrence on MRI (n = 46) versus a negative MRI (n = 137). bDFS: biochemical disease-free survival; MRI: magnetic resonance imaging; MRI = 0: no suspected recurrence on MRI; MRI =1: suspected recurrence on MRI.

patients with a recurrence outside the high-dose CTV, the local relapse was located in the seminal vesicle bed.

Of the 23 patients with a regional (i.e. pelvic) recurrence, nine patients received ENI. The recurrence was included in the high-dose PTV in 10 (43%) patients, in two (9%) and five (22%) patients it was covered by the intermediate-dose (elective) CTV and PTV respectively, the remaining six (26%) cases where located outside the PTV.

Obviously, both bone metastases were outside the PTV. Ultimately, the calculated mean dose delivered to the macroscopic disease was 55 Gy (range 1–68 Gy).

At two-years follow-up, biochemical disease-free survival (bDFS) was 81.3% for patients without a recurrence on MRI and 62.5% for patients with a recurrence on MRI (Figure 1). In univariate analysis, bDFS was significantly worse in patients with suspected macroscopic disease on MRI [hazard ratio (HR) 2.9, 95% confidence interval (CI) 2.3–3.4, $p < .0001$,], in patients who received ENI (HR 2.5, 95% CI 1.2–5.0, $p = .01$), and in patients with higher Gleason score (HR 3.8, 95% CI 1.5–10.0, $p = .004$). There was a trend towards worse bDFS for patients with more advanced pathological T-classification (HR 1.7, 95% CI 1.0–3.0, $p = .06$). In multivariate analysis, both MRI findings (HR 2.8, 95% CI 1.0–4.0, $p = .04$) as well as Gleason score (HR 2.0, 95% CI 1.6–5.0, $p = .03$) remained independently significant (Table 2).

In the subset of patients with a recurrence on MRI, bDFS was significantly worse if the macroscopic recurrences received a low (<50.0 Gy) mean radiation dose (HR 3.4, 95% CI 1.4–8.4, $p = .01$, Figure 2). However, there was no significant difference between an intermediate (50.0–60.0 Gy) versus high mean radiation dose (HR 1.1, 95% CI 0.4–3.2, $p = .86$).

## Discussion

A biochemical recurrence after radical prostatectomy represents a very difficult dilemma to the threating physician. If the disease recurrence is suspected to be local and/or regional, SRT is best initiated as early as possible. Cutoff PSA values for referral of 0.1–0.5 ng/ml at the very latest are usually suggested [16]. With those PSA values, the chances of finding the exact location of the relapse on imaging are slim. However, if the recurrence is in fact distant, the patient is unnecessarily exposed to the toxicity of radiotherapy. Local failure is generally considered to be more probable if the PSA increase occurs more than three years after surgery, if the PSA doubling time is more than 11 months, if the pathological Gleason score was below 8, and if there was extra-capsular extension or a positive surgical margin. Systemic failure is to be expected if the biochemical relapse occurs within a year after surgery, if the PSA doubling time is less than six months, if the pathological Gleason score was 8 or more, and if there was SVI or involved lymph nodes [16]. Of course, these are just very broad suggestions and do not really allow for individualized decision making. What is really needed is reliable imaging that shows the location of the disease at very low PSA values.

Regrettably, choline PET-CT is not very useful for PSA values below 1.0 or even 1.5 ng/ml [16,17]. Encouragingly, prostate-specific membrane antigen (PSMA) PET-CT seems to show substantially higher detection rates than reported for the other PET tracers. Most importantly, it reveals a high number of positive findings in the clinically important range of low PSA values (<0.5 ng/ml). For instance, in a retrospective analysis of 248 patients with a median PSA level of 2.0 ng/ml (range 0.2–59.4 ng/ml) after radical prostatectomy, 222 (90%) patients showed pathologic findings on $^{68}$Ga-PSMA PET-CT. The detection rate was still 58% for PSA levels of between 0.2 and 0.5 ng/ml [18]. Obviously, these promising findings still need to be confirmed by other groups and prospectively validated.

Compared to choline PET-CT at least, multi-parametric MRI is clearly superior for the detection of local recurrences, and currently remains the standard for local restaging [12–14]. Retrospectively, 25% of patients referred for SRT did indeed harbor a suspected recurrence on MRI. This is consistent with

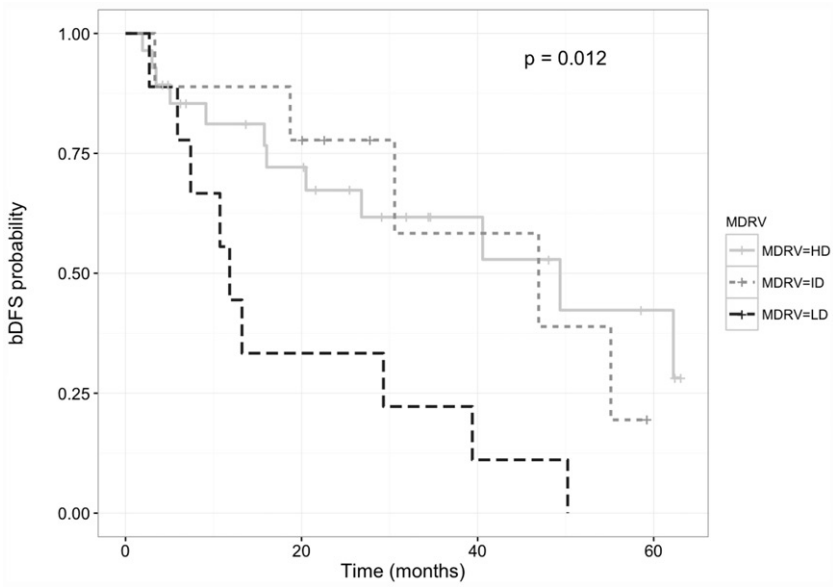


**Figure 2.** Kaplan-Meier estimates of biochemical disease-free survival (bDFS) for a high (>60.0 Gy), intermediate (50.0–60.0 Gy), and low (<50.0 Gy) mean dose to the suspected recurrence on MRI. bDFS: biochemical disease-free survival; HD: high dose; ID: intermediate dose; LD: low dose; MDRV: mean dose to the recurrence volume.

the study by Liauw et al., who observed a local recurrence on MRI in 24% of 88 patients referred for SRT after radical prostatectomy [19]. Median PSA level in that analysis was 0.3 ng/ml (interquartile range 0.2–0.7 ng/ml), almost exactly the same as in our group (median PSA level 0.3 ng/ml). This suggests that in about one in four patients referred for SRT in a routine clinical setting, a macroscopic recurrence could potentially be detected on MRI.

Worryingly, in 5 of 22 patients with a local recurrence on MRI, the macroscopic tumor was located outside the post-operative CTV as based on the EORTC guidelines. This confirms the inadequacies of the current delineation guidelines [4–10]. The definition of new consensus guidelines, based on the previous efforts by the four working groups but also taking results from modern surgical series (since the pelvic anatomy after robotic-assisted radical prostatectomy is considerably different from that after open prostatectomy) as well as from MRI planning into account, seems appropriate. Recently, Park et al. suggested an 'optimal' post-prostatectomy target volume based on 118 suspect tumor recurrences on MRI [20].

An interesting observation from our study is that nine of 22 local recurrences occurred at the level of the seminal vesicles, although only three of those nine patients had SVI. This has important repercussions on the superior border of the CTV, which is markedly different in the consensus guidelines papers. The superior boundary of the CTV is defined as follows: by the bladder neck in the EORTC guideline (although in patients with seminal vesicle involvement, the original position and/or remnants of the seminal vesicles should be included in the CTV); as encompassing the entire seminal vesicle bed and distal portion of the vas deferens in the Faculty of Radiation Oncology Genito-Urinary Group (FROGG) guideline; as the level of the cut end of vas deferens or 3–4 cm above the top of the symphysis in the Radiation Therapy Oncology Group (RTOG) guideline; and as the superior surgical clips or 5 mm above the vas deferens in the Princess Margaret Hospital (PMH) guideline [4–7]. Our data suggest that it might be opportune to include the seminal vesicle bed in all patients.

Clearly, there is potential to individualize SRT planning on the basis of MRI. It is to be expected that a dose of 66.0 Gy is insufficient for eradicating macroscopic prostate cancer, as was demonstrated by the significantly worse bDFS in patients with a suspected recurrence. Several authors have advocated for dose escalation in the post-operative setting. Their arguments were also confirmed by our study, where bDFS was clearly correlated to the dose delivered to the suspected recurrence. We currently deliver a dose of 70.0 Gy (35 fractions of 2.0 Gy) to the post-operative CTV, with escalated doses of 77.0 Gy through an integrated boost (2.2 fractions) on any macroscopic recurrence. Such a dose-adapted, MRI-based approach was already prospectively evaluated by Zilli and colleagues, with very encouraging results [21].

Although the indication for pelvic radiotherapy in pN1 patients is becoming well established, it is still unclear whether the pelvic lymph nodes need to be electively irradiated in patients who have had no or inadequate lymph node sampling. Retrospective results suggest it might improve bDFS, especially in patients with a higher PSA [22,23]. Ten of 23 regional recurrences were 'accidentally' included in the high-dose PTV due to the relatively large PTV margin (1 cm). Still, our data suggest that a least 13% of our patients would have benefitted from pelvic radiotherapy. Also, our results confirm the importance of the presacral lymph nodes in the treatment of prostate cancer [24]. However, it should be noted that MRI, even with DW sequences, has low sensitivity (albeit very high specificity) for lymph nodes metastases [24]. Consequently, this percentage could be an underestimation. Although it is probably prudent to await results from RTOG 05-34, pelvic radiotherapy with integrated boost to the prostate bed can be considered in selected patients with high-risk features [25].

There are several limitations to this study. First of all, all the important caveats with a retrospective analysis apply.

There are some important data missing such as the PSA doubling time and the surgical margins due to the retrospective nature of this study. Also, there is an important imbalance between patients with and without a potential recurrence on MRI regarding. Patients with a suspected recurrence had a higher proportion Gleason 9 score (15% vs. 4%), pT3b stage (24% vs. 7%), pathological N1-stage (15% vs. 3%), and pre-SRT PSA >1.0 ng/ml (33% vs. 13%), as can be observed in Table 1. Obviously, these differences confirm the high-risk nature of the disease in those patients and could explain the worse bDFS. Second, there was no pathological confirmation of any of the recurrences. However, MRI has very high specificity for pelvic recurrences (whether local, nodal or in bone), with only a very limited number of false positive results [12–14]. Third, no systemic staging was performed to rule out metastatic disease. Still, bDFS was around 70% at five years after SRT for patients with a negative MRI, suggesting that the indications for SRT were mostly correct. It is to be expected that combined PET/MRI imaging, preferably with $^{68}$Ga-PSMA as the PET tracer and DCE as well as DW-MRI sequences, will allow true individualization of salvage treatment. Prospective studies evaluating this possibility are urgently warranted.

MRI detects loco-regional disease in a substantial subset of patients with a biochemical recurrence after prostatectomy, especially in a PSA above 0.5 μg/L. Of the local recurrences, around 25% were located outside the post-operative CTV. This suggests that the current delineation guidelines need to be reconsidered and should incorporate MRI data. Lack of MRI-based dose escalation on these macroscopic recurrences could explain some of the biochemical progression observed after SRT.

## Disclosure statement

We have no conflict of interest to declare.

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