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Shrinkage of the non-malignant prostate gland volume after receiving incidental radiotherapy for rectal cancer

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Abstract

Background: The purpose of this study was to assess the impact of coincidental radiotherapy on the volume of the non-malignant prostate gland in rectal cancer patients treated with neo-adjuvant radiotherapy.

Materials and methods: In this retrospective analysis, thirty male patients with rectal cancer who had neoadjuvant radiotherapy met the inclusion criteria. These patients had pre-treatment magnetic resonance imaging (MRI) and at least one post-treatment MRI of the pelvis and the whole of their prostate volume received the full prescribed radiotherapy dose; 45 Gy in 25 fractions (n = 22), 45 Gy in 20 fractions (n = 4) and 25 Gy in 5 fractions (n = 4).

Results: The median age of this patient cohort was 66 years (range: 30–87). With a median interval between pre-treatment MRI and first MRI post-treatment of 2 months (range: 1–11), the mean prostate volume reduced from 36.1 cm^3 [standard deviation (SD) 14.2] pre-radiotherapy to 31.3 cm^3 (SD 13.0) post radiotherapy and this difference was significant ($p = 0.0004$).

Conclusion: Radiotherapy may cause shrinkage in volume of normal (non-malignant) prostate. Further research is required in this field, since these results may be of some comfort to men contemplating the consequences of radiotherapy on their quality of life. The authors suggest recording flow-rate and international prostate symptom score (IPSS) during rectal radiotherapy as a next step.

Key words: prostate hyperplasia; radiotherapy; benign disease

Introduction

Neo-adjuvant (chemo)radiotherapy is recommended for locally advanced rectal cancer [1, 2]. In male patients with rectal cancer, the prostate gland often receives an incidental radiation dose, due to its proximity to the target volume. It appears possible that this will affect the prostate gland physically or structurally, which may lead to physiological side-effects for patients being treated.

In this study, we wished to assess the physical effects of incidental radiotherapy on the prostate; if such effects exist, this would motivate a future investigation of physiological consequences. We hypothesized that there would be a difference in the prostate volume before and after receiving radiotherapy for rectal cancer.

Materials and methods

Inclusion criteria

On review of the records of all 215 male patients treated with neo-adjuvant radiotherapy for rectal carcinoma in our centre between 01/01/2010 and 31/12/2019, we included patients who had:

- a pre-treatment magnetic resonance image (MRI) of the pelvis; and
- at least one post-treatment MRI of the pelvis.

Exclusion criteria

We excluded patients where:

- the MRI quality did not allow precise identification of prostate anatomy;
- the radiotherapy dose was not delivered to the entire prostate;
- rectal cancer infiltrated the urinary tract;
- there was any urological condition that impacted the prostate.

Radiotherapy treatment

In our centre, neo-adjuvant radiotherapy comprises either a short course of 25 Gy in 5 daily fractions, or a long course of 45 Gy in 20–25 daily fractions over 4–5 weeks.

Prostate contouring

Each prostate volume was contoured on the pre-treatment and post-treatment MRIs by an experienced consultant in radiation oncology. The volumes were independently peer-reviewed by a second consultant.

Statistical analysis

We used Student's paired t-test to assess the change in prostate volume from pre- to post-radiotherapy. We used Student's unpaired t-test to assess whether the change in prostate volume was related to radiotherapy regime (short- *vs.* long-course). We used Pearson's correlation coefficient to assess whether the change in prostate volume was related to the patient's age. For all tests, statistical significance was assumed at $p < 0.05$.

Ethical approval

As per institutional policy, this project was registered and approved by our institutional clinical governance body. Project number was 10159.

Results

In 40 of 215 patients, a pre-treatment MRI and at least one post-treatment MRI of the pelvis were available. Subsequently, 10 of these patients were excluded as per Figure 1.

Therefore, we report on thirty men with histologically proven rectal carcinoma. They had a median age of 66 years (range: 30–87), and all had World health Organization (WHO) performance status 0 to 2. The ages and pre-treatment prostate volumes are shown in Figure 2.

Radiotherapy treatment

All patients were treated with radical intent with neo-adjuvant (chemo)radiotherapy followed by radical surgery. Six patients were treated with 3-dimentional conformal radiotherapy (3D CRT), and 24 patients with intensity modulated radiotherapy (IMRT). Treatment plans with dose distribution were available with exact dose to the prostate gland (Fig. 3). Dose mapping on each case confirmed that the whole prostate was included in the volume treated. Treatments were as follows:

- four patients were treated with 25Gy in 5 daily fractions (short course);
- four patients were treated with 45Gy in 20 daily fractions (long course);
- twenty-two patients were treated with 45Gy in 25 daily fractions (long course);
- these 22 patients received concomitant capecitabine chemotherapy. In one of these 22 patients, chemotherapy was stopped during the last week of treatment due to toxicity (grade III diarrhoea).

Prostate volumes per time point

The prostate volumes at each time point are summarized in Table 1. Changes to prostate volumes between the first two time points are illustrated in Figure 4.

The effect of radiotherapy regimen and age on prostate size

Neither radiotherapy regime ($r = -0.04$; $p = 0.8$) nor the patient's age ($p = 0.9$) had a significant effect on the change in prostate volume.

Discussion

We report statistically significant reductions in prostate volume following radiotherapy; 8 months after treatment we found a mean 17% (6.2 mL) reduction of prostate volume from a mean of 36.1 mL.

With aging, prostate volume increases due to benign prostatic hyperplasia (BPH). Two longitudinal studies report a prostate growth rate of 2.0–2.5% per year in older men [3,4], and this growth is evident in our data (Fig. 2). It is known that radiotherapy can shrink prostate volume, as well as cause prostatic parenchymal change and function. Therefore, referring specifically to our findings on the change in volume, radiotherapy may reverse 6–8 years of prostate volume growth.

In later life the hypertrophied prostate, obstructs the urethra, compromising flow of urine [5]. Urine flow declines by 1–2 mL/second every 5 years, and by the age of 80 a man's maximum flow rate is typically 5.5 mL/second [6]. Through the reduction on prostate volume alone, we would anticipate up to a 2 mL/second improvement in urine flow rate. This change should be detected by pre- and post-treatment uroflowmetry, though likely of no consequence to an asymptomatic man with a normal flow rate.

The prevalence of BPH rises with increasing age, from 50% in the 6th decade of life to 80% in the 9th decade of life [7]. Untreated BPH will eventually manifest as lower urinary tract symptoms (LUTS) of poor stream, hesitancy and urine retention which lead to urinary frequency and urgency. Indeed, 9/30 of this cohort would meet the EAU criteria for surgical treatment (prostate volume > 35 mL) [8]. In these men, an improvement in flow rate of 2 ml/s is comparable with that reported for alpha-blocker treatment. Therefore, we might anticipate some mild benefits for their lower urinary tract symptoms after radiotherapy.

Possible clinical implications

To be clear, we are not advocating radiotherapy as a treatment for bladder outlet obstruction. The relatively mild benefits are likely to be comparable to first-line medical management, but the gold standard surgical treatment of BPH is transurethral resection of the prostate (TURP). In terms of flow rate, the benefit from TURP is typically 5 times that reported here.

Nevertheless, men being counselled for (chemo)radiotherapy for rectal cancer may have concerns about survivorship once the acute treatment phase is complete. Urinary tract function plays an important role in quality of life for older men, and so reassurance about this aspect of their recovery would be of some importance. In our patient group, we speculate that men may have measurable improvement in their lower urinary tract function once the acute effects of radiotherapy have resolved.

In order to assess this effect, we would advocate a simple package of objective and patient-reported measures; for example, uroflowmetry to measure urine flow rate and voided volume, and the International Prostate Symptoms Score (IPSS) questionnaire.

Limitations of the report

In this report we describe an interesting set of observations from 10 years of historic data. The data have not been collected with this report in mind, and aspects such as target volume, organ-at-risk contouring approaches, the type of MRI scanning, and radiotherapy techniques have developed as current knowledge and best practice have changed.

Nevertheless, our data are hard to come by, since we treat only about 20 such men per year; we found no comparable data in the literature. Moreover, despite changes in practice, there has been a consistent effect of radiotherapy on prostate volume. We hope our report will serve to generate further debate and perhaps, be the pilot for better-planned investigations.

Conclusion

An incidental radiotherapy dose to the prostate reduces its volume. We hypothesise that this may result in a mild but measurable improvement in lower urinary tract function and hope to test this hypothesis in the future.

Conflict of interest

None declared.

Funding

None declared.

Data sharing statement

Anonymised data can be made available on individual request.

Disclosures

None.

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Table 1. Prostate volume (**A**) and changes in prostate volume (**B**) for 4 time-points. All 30 patients had at least one post-treatment magnetic resonance imaging (MRI), and some had two or three MRIs

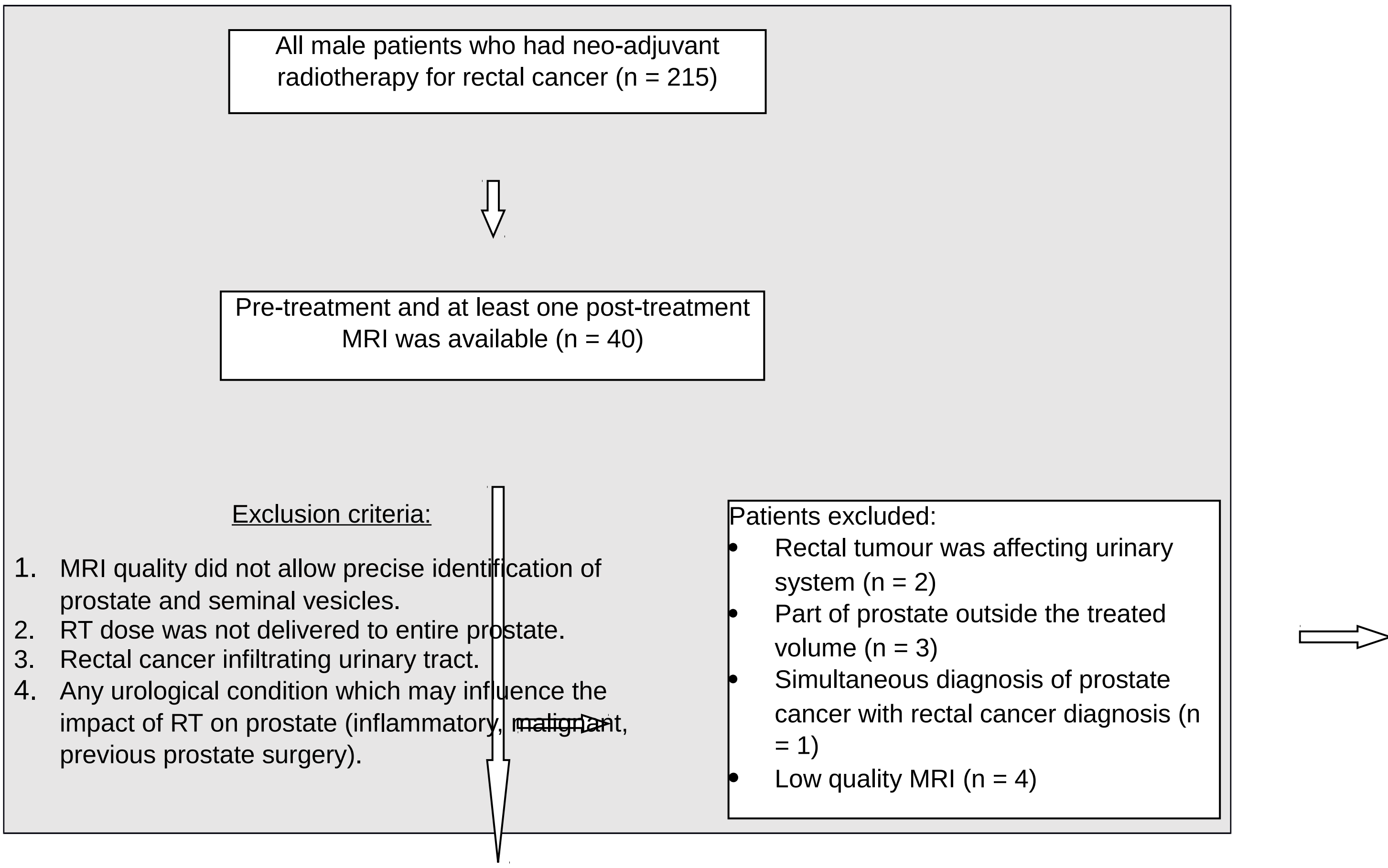
A				
	Pre-RT	**1st post-RT**	**2nd post-RT**	**3rd post-RT**
Number of patients	30	30	7	4
Median (range) time of MRI (months)	0	2 (1 to 11)	8 (3 to 26)	14 (5 to 17)

Mean (SD) prostate volume [mL]	36.1 (14.6)	31.3 (13.3)	29.5 (12.1)	26.3 (1.8)
95% CI [mL]	30.9 to 41.3	26.6 to 36.1	20.5 to 38.5	25.0 to 27.6

B

	Pre- to 1st post	**1st post to 2nd post**	**2nd post to 3rd post**
Number of patients	30	7	4
Median (range) time between MRIs (months)	2 (1 to 11)	4 (2 to 18)	11 (3 to 14)
Mean (SD) change in prostate volume (ml)	–4.8 (4.6)	–1.4 (1.1)	+0.5 (1.8)
95% CI [ml]	–3.1 to –6.5	–0.5 to –2.2	–1.3 to +2.2
p	0.000004	0.02	0.7

SD — standard deviation; CI — confidence interval



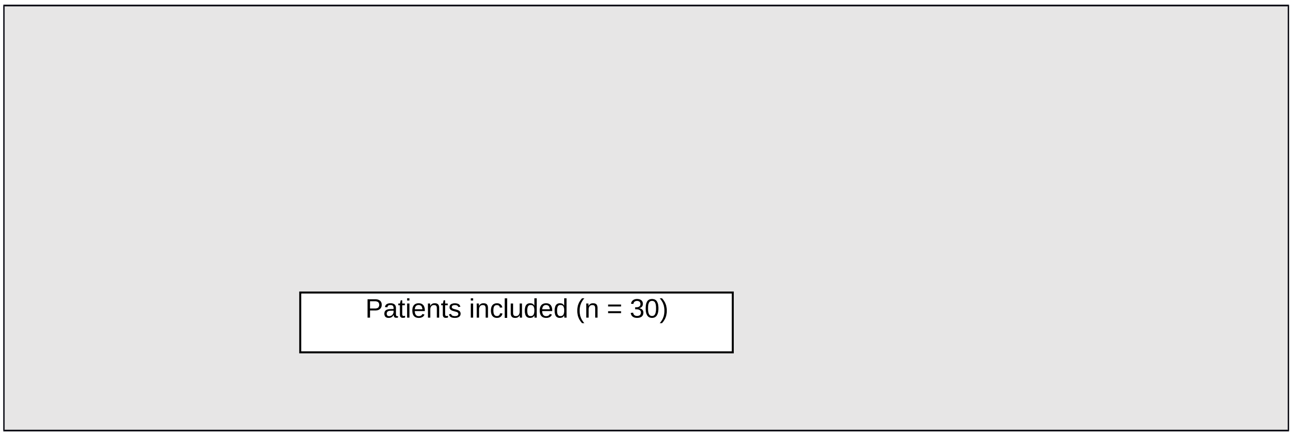


Figure 1. A consort diagram of patient selection

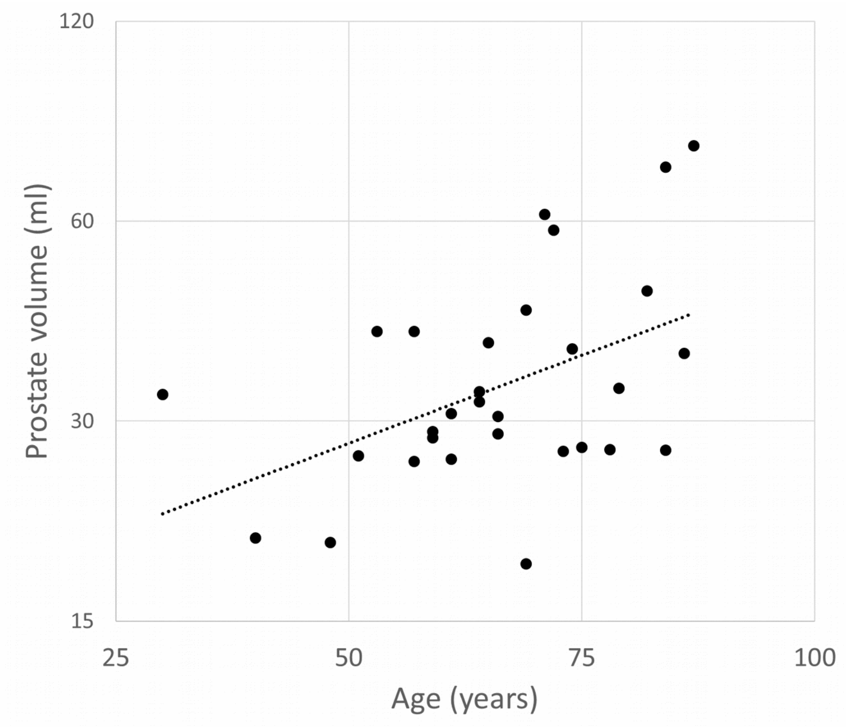


Figure 2. The relation of pre-treatment prostate volume with age. The line of best-fit indicates a volume growth rate of 1.25% per year

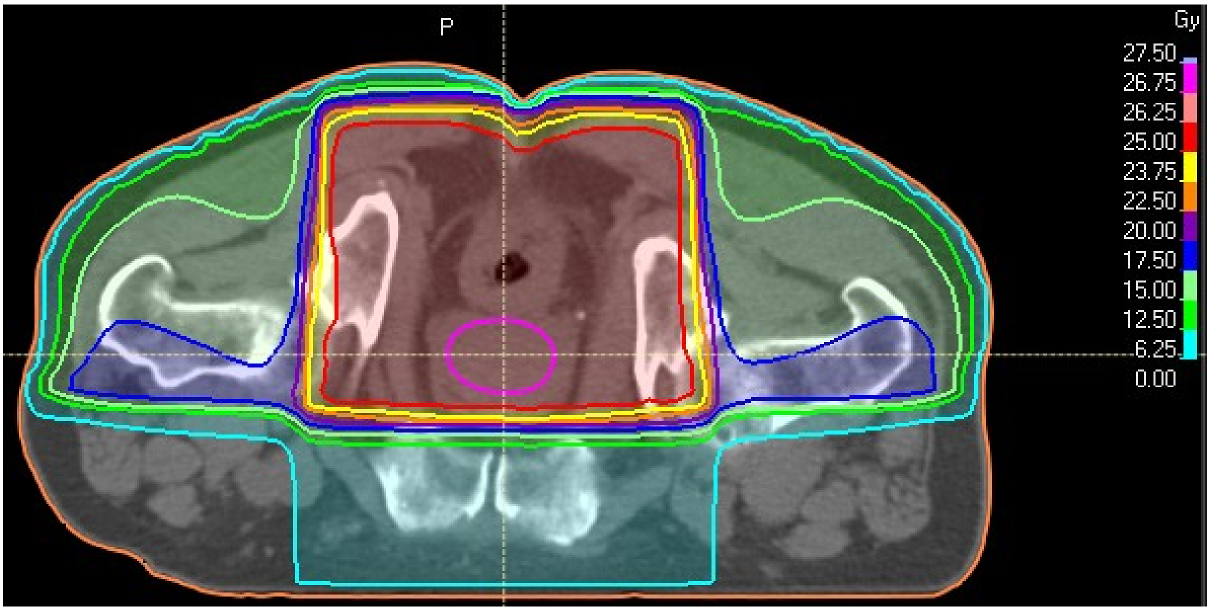


Figure 3. An example of a treatment plan with dose distribution shown and the prostate outlined

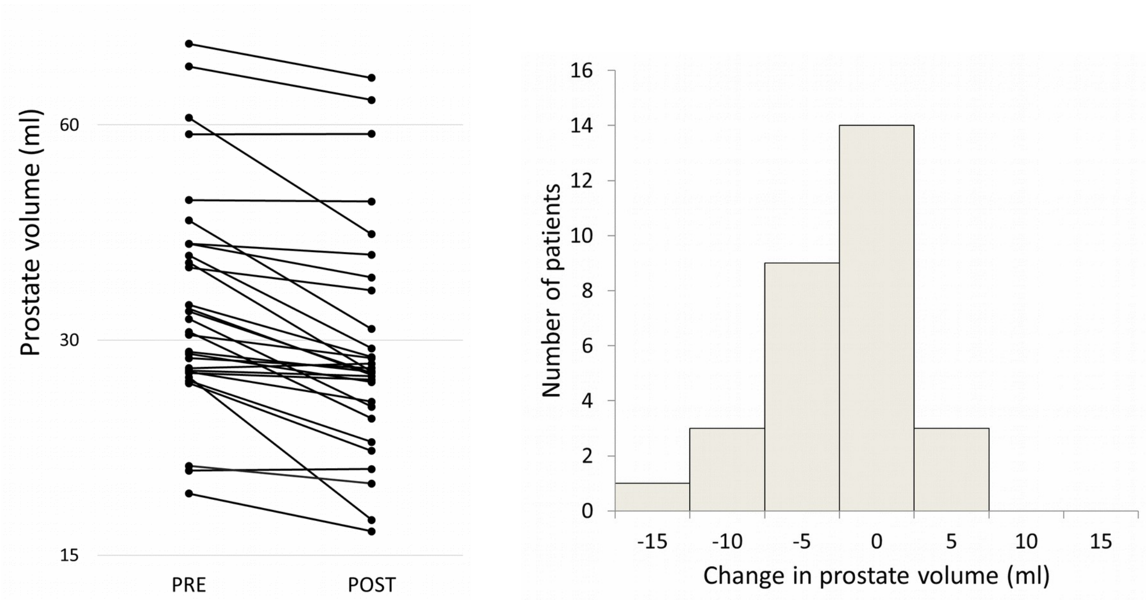


Figure 4. Changes in prostate volume between first and second time-points; **A.** The pre-and-post treatment volumes for each patient; **B.** A histogram of the changes in these patients