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FULL PAPER

PEG spacer gel and adaptive planning vs single plan in external prostate radiotherapy—clinical dosimetry evaluation

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Objective: Spacer gel is used to reduce the rectal dose in prostate radiotherapy. It is injected to increase the distance between the prostate and rectum. During the course of external radiotherapy treatment, physiological changes in rectal volume exist. When using polyethylene glycol material, such as DuraSeal® (Covidien, Mansfield, MA), gel resorption also occurs. Together, these factors alter the original dose plan distribution. **Methods:** External dose planning and calculations were simulated using images acquired from 10 patients who were treated with brachytherapy and gel. The CT series was taken relative to gel injection: pre 1 day, post 1 day, post 1 month and post 2 months. Adaptive planning was compared with a single plan.

Results: Adaptive planning shows better results compared with the single plan used in the total treatment course; however, the effect is minor.

Conclusion: Gel usage is clearly favourable to rectal DVH. Using adaptive planning with gel improves rectal DVH but is not necessary according to this study.

Advances in knowledge: Spacer gel is used in prostate radiotherapy to increase distance between the prostate and the rectum, thus reducing the rectal doses. During the treatment course, gel resorption exists which affects the rectal doses. The usefulness of adaptive planning to compensate this resorption effect has not been studied before.

INTRODUCTION

Prostate cancer is the most common cancer among males in industrialized Western countries, including Finland. In 2009, 4596 new cases were diagnosed, which equates to 31.2% of all cancers in males.¹ In the USA, the corresponding number was estimated to be 217,730 in 2010, which equates to 27.6% of all cancers in males.² The majority of cancer foci (74%) are found in biopsies taken from the peripheral zone,³ which is mainly located beside the rectum. Commonly used treatment options with radical intent are radical prostatectomy and external or internal radiation therapy. Treatment results are approximately the same using surgery or radiotherapy alone when comparing survival rate or side effects.⁴ To achieve the best result in radiotherapy, the prostate needs to have a sufficiently high-absorbed dose. In external radiotherapy and conventional fractionation (1.8–2.0 Gy), the European Association of Urology recommends ≥ 74 Gy⁵ and the National Comprehensive Cancer Network recommends 75.6–79.2 Gy.⁶ Treatment technique is typically intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy using fiducial gold markers or an radiofrequency (rf)-marker, as in Calypso® Extracranial Tracking (Varian® Medical

Systems, Palo Alto, CA). The desired dose to the prostate is mostly limited by rectal and bladder doses. Side effects may emerge even after years.

Dose–volume histograms (DVH) are used to evaluate the dose plan. Different recommended constraint values on DVH exist depending on individual treatment centres and organizations. The Quantec publication on radiation-induced rectal injury provides practical instructions.⁷ Although IMRT techniques have given us tools to increase the highest conceivable dose to the prostate without giving too much of the dose to healthy tissues, the vicinity of the rectum and prostate is still challenging. The anterior rectal wall is at the greatest risk of injury.⁸ Various methods, such as biodegradable spacer balloons,⁹ human collagen¹⁰ and different gels,^{11–13} have been presented to increase the space between the prostate and rectum in order to reduce the rectal dose.

The prostate tends to move, and the shape can vary intra-fractionally and interfractionally, mainly depending on rectal filling and gas. The markers help to target the prostate, but the rectal dose distribution can be very different in comparison

Figure 1. Gel resorption (a) after 1 month and (b) after 2 months.

with the original dose plan. This can be partially compensated for by using adaptive planning and treatment.^{14,15} Endorectal balloon (ERB) is also used to reduce both intrafraction motion of the prostate and rectal doses. The reduction of the posterior and lateral rectal wall dose is obvious because of the increased distance from the high-dose regions.¹⁶ The anterior rectal wall tends to be pressed tightly against prostate, exposing it to higher doses. There is, however, some evidence that the anterior rectal wall dose might be reduced also because of the build-up effect caused by air-filled balloon.¹⁷ Errors in ERB positioning and balloon size can cause prostate deformation and dosimetric changes.¹⁸ Also, the gas and stool in the rectum beside the balloon can cause large random interfraction prostate displacements.¹⁹ Some of the patients find the daily use of ERB uncomfortable although tolerable.²⁰

In conventional fractionation, the treatment course lasts 8–10 weeks from the implantation of markers to the last treatment fraction including waiting times between marker implantation (gel implantation), acquiring planning images, and dose planning and treatment fractions. Polyethylene glycol (PEG) gel, such as DuraSeal® (Covidien, Mansfield, MA), remains intact for 4–8 weeks after application, is degraded by the hydrolysis of ester bonds and is then excreted renally.²¹ According to the literature,^{22,23} the PEG gel clearance time varies from 1 to

6 months. Thus, during the treatment course, some gel resorption occurs. Heikkilä et al²⁴ measured a clearance half-life of 47 days but found prostate–rectum separation half-life as high as 110 days. Other studies also suggest that separation does not change significantly during the treatment course.^{25–27} However, no studies of calculated values on DVH changes in external radiotherapy treatment owing to gel resorption are presented. Hyaluronic acid as a spacer gel is reported to be stable up to 1 year and would, therefore, have no resorption effect on dose distribution during the external radiotherapy course.¹³ However, hyaluronic acid is considered more viscous than PEG, causing possible changes in gel position.¹⁰ The aim of this study was to examine PEG gel: what is the gel resorption effect on rectal DVH, and does the use of the spacer gel reduce or even remove the need for the adaptive planning?

METHODS AND MATERIALS

The study was conducted using simulated dose plans. The image series from 10 patients who received actual low dose rate brachytherapy seed implantation with PEG spacer gel were used.²⁴ The gel resorption effect (Figure 1) on dose plans is, hence, present.

Two different approaches were used: (1) dose optimization and planning using each image series (post-implantation 1 day

Figure 2. Single plan (fusion, Method 2) rectal dose–volume histograms as a function of time: (a) no volume normalization and (b) volume normalization. post1d, post-implantation 1 day; post1mth, post 1 month; post2mth, post 2 months.

Figure 3. Adaptive planning rectal dose-volume histograms as a function of time: (a) no volume normalization and (b) volume normalization. post1d, post-implantation 1 day; post1mth, post 1 month; post2mth, post 2 months.

(post1d), post 1 month (post1mth), post 2 months (post2mth)) separately and (2) dose optimization and planning using the 1 day post image series, which was then fused to other image series. The first method represents adaptive planning. All varying parameters influencing the dose plan are included (e.g. gel volume, rectal filling and bladder filling). The second method represents the situation when a single dose plan is used during the whole treatment course. The gel effect on reducing rectal doses during the whole treatment could be seen by comparing the dose plans made on the image series before (pre1d) and after gel implantation (post1d). The rectal DVH values were also normalized to absolute rectal volumes (post1d) to separate the gel resorption effect. The schedule for image series was determined on the economic and resource basis: before the gel injection and at the beginning, in the middle and at the end of the treatment course.

Dose optimization

IMRT treatment plans with dynamic multileaf collimator leaves were made using dose-planning software Eclipse™ DVO/AAA-algorithms 11.0.31 (Varian Medical Systems). From the images, the prostate was defined as clinical target volume. Planning target volume (PTV) was then created from clinical target volume using a 0.5-cm margin. The spacer gel was not separated from the PTV. The rectum was segmented 1 cm longer from

both ends compared with PTV in the craniocaudal direction and including the rectal content. The anterior rectal wall was defined from the rectum by creating a contour asymmetric inner margin 3 mm in the anteroposterior direction. Thus, the received contour was then subtracted from the original rectum contour, resulting in anterior rectal wall. The prescribed dose was 76 Gy in 38 fractions, primary reference point PTV and no normalization used. The plan template consists of seven fields and gantry angles: 215/268/303/0/62/95/135. The dose constraints to PTV were: upper 0% 77 Gy and lower 100% 76 Gy, both having a weight factor of 80. Rectal upper dose constraints were used according to the Fox Chase Center,²⁸ 5% 75 Gy/15% 70 Gy/25% 65 Gy/35% 60 Gy/45% 50 Gy, each with a weight factor of 50. Bladder upper dose constraints were: 5% 75 Gy/25% 60 Gy/50% 50 Gy. Normal tissue objective was used with a weight factor of 150. Optimization was run until the progression plateau was reached. The same person did all the structure contouring, and all the dose plans were made by one planner.

In Method 1, optimization, dose calculation and structure recontouring were performed to each image series separately.

In Method 2, the plan from the image series was that the 1-day post image was fused to other image series. Image fusion was aligned

Table 1. Unnormalized and normalized rectal dose-volume histogram (DVH) values

Method	Unnormalized rectal DVH					Normalized rectal DVH (ref post1d)				
	75	70	65	60	50	75	70	65	60	50
No gel	3.2 ± 1.8	9.6 ± 2.8	14.4 ± 3.8	18.6 ± 4.8	30.0 ± 8.1	4.0 ± 2.8	11.4 ± 5.5	17.2 ± 8.2	22.0 ± 10.6	35.7 ± 18.2
Post1d	0.6 ± 0.6	2.7 ± 2.0	4.9 ± 2.7	8.4 ± 3.8	21.2 ± 7.8	0.6 ± 0.6	2.7 ± 2.0	4.9 ± 2.7	8.4 ± 3.8	21.2 ± 7.8
Fu1mth	1.1 ± 0.8	4.7 ± 2.9	8.3 ± 3.8	11.9 ± 4.5	24.4 ± 7.9	1.0 ± 1.0	4.4 ± 3.6	9.8 ± 7.2	12.5 ± 7.2	25.5 ± 14.1
Fu2mth	2.0 ± 2.4	5.7 ± 4.5	10.1 ± 5.1	14.2 ± 5.5	28.8 ± 8.1	1.7 ± 1.7	4.9 ± 3.8	8.4 ± 5.0	11.9 ± 5.9	23.9 ± 10.1
Ad1mth	0.4 ± 0.5	2.8 ± 2.1	6.0 ± 3.4	9.4 ± 4.6	20.7 ± 7.8	0.5 ± 0.5	3.0 ± 2.1	6.3 ± 3.5	9.8 ± 4.8	21.7 ± 9.8
Ad2mth	0.7 ± 0.7	4.4 ± 1.7	8.4 ± 2.5	12.3 ± 3.2	25.5 ± 6.6	1.7 ± 0.7	3.9 ± 1.7	7.4 ± 2.8	10.6 ± 4.0	21.8 ± 7.7

Ad1mth, 1-month adaptive plan; Ad2mth, 2-month adaptive plan; Fu1mth, 1-month fusion plan; Fu2mth, 2-month fusion plan; Post1d, post-implantation 1 day.

Figure 4. Adaptive vs single plan (fusion) rectal dose-volume histograms: (a) no volume normalization and (b) volume normalization.

using the prostate posterior edge with the help of brachyseeds. This was chosen in order to reduce the influence of prostate swelling because of brachytherapy seed implantation in the original images. The rigid registration was performed. Leaf motion and monitor units were kept intact, but the final calculation was performed to determine the actual dose distribution. This method represents a situation when a single plan is used for the total treatment course. The variations in the rectum and bladder filling and their effect on DVH can be seen.

The influence of adaptive planning was studied by comparing DVH results from Method 1 and Method 2. The individual patient has the same image and structure volumes in both methods. Changes in DVH are, therefore, due to optimization and should produce better results (lower DVH values to the rectum).

The swelling effect caused by the seed implantation and its impact on dose distribution was studied using regression analysis. The oedema magnitude was compared with rectal DVH values in each case to see whether any correlation existed.

Rectal volumes were studied to estimate their effect on DVH. A volume increase tends to shift the rectal DVH curve to the left (artificial improvement). Rectal DVH values were normalized using post1d rectal volume as a reference value.

Statistics

A Wilcoxon signed-rank test was used to compare fusion and adaptive plan DVH values.

RESULTS

Rectum

Unnormalized and normalized mean rectal DVH values as a function of time and planning method are presented in Figures 2 and 3 and Table 1. The use of gel distinctly reduces the rectal DVH values. The difference is clear during the whole treatment course with both methods (adaptive and single plan), even though it becomes smaller towards the end of the treatment course. Rectal DVH values were normalized against post1d rectal volume to separate the gel resorption effect from the rectal volume change effect. Adaptive planning removes or reduces the gel resorption and the rectal volume change effect as expected, but in Method 2 (single plan), the DVH values are higher as a function of time. The plain gel resorption effect can be seen in Figure 2b.

Adaptive planning allows for some benefits as compared with a single plan used throughout the whole treatment course. The values are significantly different ($p = 0.043$). Figure 4 shows mean rectal DVH, but the differences and significance values remain the same when comparing patients separately. Figure 5 shows 45-Gy isodose lines in sagittal images for post1d plan, post2mth fusion plan and post2mth adaptive plan. The gel resorption can also be seen.

Figure 5. 45-Gy isodose line in (a) original post-implantation 1-day plan, (b) post 2-month fusion plan, (c) post 2-month adaptive plan. Rectum, gel and 45-Gy isodose lines are delineated. Arrows show the regions of interest.

Figure 6. Anterior rectal wall dose-volume histograms with (a) single plan (fusion) and (b) adaptive planning. post1d, post 1 day; post1mth, post 1 month; post2mth, post 2 months.

The swelling effect on doses was studied by regression analysis in each case. No correlation in oedema volume and DVH dose pairs was found ($R = 0.0006-0.07$). Thus, the swelling effect is not significant.

Anterior rectal wall

The use of gel also reduces anterior rectal wall DVH values compared with the plan without gel, and the gel resorption effect on DVH values can be seen (Figure 6). However, adaptive planning does not improve the DVH values, most likely because the anterior rectal wall was not used in optimization constraints.

Rectal volume

Median rectal volume during the treatment course was 45, 48, 48 and 32 cm³ (pre 1 day, post1d, post1mth and post2mth, respectively).

DISCUSSION

Using spacer gel shows clear improvements to rectal and anterior rectal wall DVH as compared with treatment without gel. Although rectal DVH constraints were achieved also without gel, the use of gel gives more margin to dose planning, which is especially tempting when using a hypofractionated treatment. From a treatment planning perspective, using gel could give the opportunity to increase the prostate total dose without exceeding rectum DVH tolerances. This should be evaluated clinically.

Theoretically, the change in rectal volume shifts the DVH to the right when volume decreases and to the left when volume increases. In this study, the rectal volume change effect was minimized using rectal volume (post1d) normalization, leaving the gel resorption effect as a primary factor in rectal DVH changes.

Standard deviation (SD) values in Table 1 are a bit misleading and should not be taken here as error values. This is because in the dose-planning optimization process, only upper constraints are used. The DVH values that are very low and the DVH values that are near the upper constraints are both acceptable but can lead to large SD values. The mean values can be used because the same images are used in both comparable planning methods.

There is some benefit to using gel and adaptive planning on rectal DVH, but not on anterior rectal wall DVH. This is likely because dose-planning optimization was performed using only rectum constraints. Using anterior rectal wall constraints would probably improve DVH.

Adaptive planning requires multiple CT-image series and dose plans and can, thus, be quite laborious. In the treatment process, choosing the appropriate dose plan can be difficult because it requires cone beam CT and preferably one or two explicit measurements in order to use real-time adaptive plans efficiently. Gel resorption happens during the treatment course, and its effect can be seen in DVH. Adaptive planning decreases the gel resorption effect and improves rectal DVH during the treatment course. However, the use of the spacer gel only is sufficient to reach described rectal DVH tolerances with given treatment doses. The benefit of adaptive planning with the spacer gel comes with higher doses.

CONCLUSION

Gel usage is clearly favourable to rectal DVH. Gel resorption occurs during an external treatment course even though it is minor. Using adaptive planning with gel improves rectal DVH but is not necessary according to this study.

REFERENCES

1. Cancer Society of Finland. *Cancer in Finland 2008 and 2009. Publication No. 84*. Helsinki, Finland: 2011.
2. American Cancer Society. *Cancer facts & figures 2010*. Atlanta, GA: 2010.
3. Chen ME, Johnston DA, Tang K, Babaian RJ, Troncoso P. Detailed mapping of prostate carcinoma foci, biopsy strategy implications. *Cancer* 2000; **89**: 1800–9. doi: [10.1002/1097-0142\(20001015\)89:8<1800::AID-CNCR21>3.0.CO;2-D](https://doi.org/10.1002/1097-0142(20001015)89:8<1800::AID-CNCR21>3.0.CO;2-D)
4. Klein E, Ciezki J, Kupelian P, Mahadevan A. Outcomes for intermediate risk prostate cancer: are there advantages for surgery, external radiation, or brachytherapy. *Urol Oncol* 2009; **27**: 67–71. doi: [10.1016/j.urolonc.2008.04.001](https://doi.org/10.1016/j.urolonc.2008.04.001)
5. Mottet N, Bastian PJ, Bellmunt J, van den Bergh RCN, Bolla M, van Casteren N, et al. *Guidelines on prostate cancer*. Arnhem, Netherlands: European Association of Urology; 2014.

6. Mohler JL, Kantoff PW, Armstrong AJ, Bahnson RR, Cohen M, D'Amico AV, et al. *NCCN clinical practice guidelines in oncology (NCCN guideline®) prostate cancer*. Fort William, PA: National Comprehensive Cancer Network, Inc.; 2014.
7. Michalski JM, Gay H, Jackson A, Tucker SL, Dasy JO. Radiation dose-volume effects in radiation-induced rectal injury. *Int J Radiat Oncol Biol Phys* 2010; **76**: S123–9. doi: [10.1016/j.ijrobp.2009.03.078](https://doi.org/10.1016/j.ijrobp.2009.03.078)
8. Peterson J, Buskirk S, Heckman M, Diehl N, Bernard J Jr, Tzou K, et al. Image-guided intensity-modulated radiotherapy for prostate cancer: dose constraints for the anterior rectal wall to minimize rectal toxicity. *Med Dosimetry* 2014; **39**: 12–17. doi: [10.1016/j.meddos.2013.08.007](https://doi.org/10.1016/j.meddos.2013.08.007)
9. Levy Y, Paz A, Yosef R, Corn BW, Vaisman B, Shuhat S, et al. Biodegradable inflatable balloon for reducing radiation adverse effects in prostate cancer. *J Biomed Mater Res B Appl Biomater* 2009; **91B**: 855–67. doi: [10.1002/jbm.b.31467](https://doi.org/10.1002/jbm.b.31467)
10. Noyes W, Hosford C, Schultz S. Human collagen injections to reduce rectal dose during radiotherapy. *Int J Radiat Oncol Biol Phys* 2012; **82**: 1918–22. doi: [10.1016/j.ijrobp.2011.02.034](https://doi.org/10.1016/j.ijrobp.2011.02.034)
11. Weber DC, Zilli T, Vallee JP, Rouzaud M, Miralbell R, Cozzi L. Intensity modulated proton and photon therapy for early prostate cancer with or without transperineal injection of a polyethylen glycol spacer: a treatment planning comparison study. *Int J Radiat Oncol Biol Phys* 2012; **84**: e311–18. doi: [10.1016/j.ijrobp.2012.03.028](https://doi.org/10.1016/j.ijrobp.2012.03.028)
12. Chapet O, Udrescu C, Tanguy R, Ruffion A, Fenoglietto P, Sotton MP, et al. Dosimetric implications of an injection of hyaluronic acid for preserving the rectal wall in prostate stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys* 2014; **88**: 425–32. doi: [10.1016/j.ijrobp.2013.10.039](https://doi.org/10.1016/j.ijrobp.2013.10.039)
13. Prada P, Fernández J, Martínez A, de la Rúa A, Gonzalez JM, Fernandez JM, et al. Transperineal injection of hyaluronic acid in anterior perirectal fat to decrease rectal toxicity from radiation delivered with intensity modulated brachytherapy or EBRT for prostate cancer patients. *Int J Radiat Oncol Biol Phys* 2007; **69**: 95–102. doi: [10.1016/j.ijrobp.2007.02.034](https://doi.org/10.1016/j.ijrobp.2007.02.034)
14. Diding B, Nikoghosyan A, Schulz-Ertner D, Zierhut D, Schlegel W, Wannenmacher M. Benefit of adaptive inverse planning during intensity modulated radiotherapy of prostate cancer—a comparative DVH-analysis. *Int J Radiat Oncol Biol Phys* 2001; **51**: 300. doi: [10.1016/S0360-3016\(01\)02375-6](https://doi.org/10.1016/S0360-3016(01)02375-6)
15. Nuver T, Hoogeman M, Remeijer P, van Herk M, Lebesque J. An adaptive off-line procedure for radiotherapy of prostate cancer. *Int J Radiat Oncol Biol Phys* 2007; **67**: 1559–67. doi: [10.1016/j.ijrobp.2006.12.010](https://doi.org/10.1016/j.ijrobp.2006.12.010)
16. Smeenk R, van Lin E, Kollenburg P, McColl G, Kunze-Busch M, Kaanders J. Endorectal balloon reduces anorectal doses in post-prostatectomy intensity-modulated radiotherapy. *Radiother Oncol* 2011; **101**: 465–70. doi: [10.1016/j.radonc.2011.07.019](https://doi.org/10.1016/j.radonc.2011.07.019)
17. Teh B, McGary J, Dong L, Mai WY, Carpenter S, Lu H. The use of rectal balloon during the delivery of intensity modulated radiotherapy (IMRT) for prostate cancer: more than just a prostate gland immobilization device? *Cancer J* 2002; **8**: 476–83. doi: [10.1097/00130404-200211000-00012](https://doi.org/10.1097/00130404-200211000-00012)
18. Jones B, Gan G, Kavanagh B, Miften M. Effect of endorectal balloon positioning errors on target deformation and dosimetric quality during prostate SBRT. *Phys Med Biol* 2013; **58**: 7995–8006. doi: [10.1088/0031-9155/58/22/7995](https://doi.org/10.1088/0031-9155/58/22/7995)
19. van Lin E, van der Vicht L, Witjes J, Huisman H, Leer J, Visser A. The effect of an endorectal balloon and off-line correction on the interfraction systematic and random prostate position variations: a comparative study. *Int J Radiat Oncol Biol Phys* 2005; **61**: 278–88. doi: [10.1016/j.ijrobp.2004.09.042](https://doi.org/10.1016/j.ijrobp.2004.09.042)
20. McGary J, Teh B, Butler B, Grant W. Prostate immobilization using a rectal balloon. *J Appl Clin Med Phys* 2002; **3**: 6–11. doi: [10.1120/1.1421749](https://doi.org/10.1120/1.1421749)
21. Susil RC, McNutt TR, DeWeese TL, Song D. Effects of prostate-rectum separation on rectal dose from external beam radiotherapy. *Int J Radiat Oncol Biol Phys* 2010; **76**: 1251–8. doi: [10.1016/j.ijrobp.2009.07.1679](https://doi.org/10.1016/j.ijrobp.2009.07.1679)
22. SpaceOAR®. Waltham, MA: Augmenix Inc. [Updated 8 April 2015.] Available from: <http://www.augmenix.com/products/spaceoar/>
23. DuraSeal®, FAQ. Mansfield, MA: Covidien. [Updated 4 January 2015.] Available from: <http://www.durasealinfo.com/durasealcra-nial/pages.aspx?page=WhatIsDuraSealCra-nial/FAQ>
24. Heikkilä V-P, Kärnä A, Vaarala M. DuraSeal as a spacer to reduce rectal doses in low-dose rate brachytherapy for prostate cancer. *Radiother Oncol* 2014; **112**: 233–6. doi: [10.1016/j.radonc.2014.08.012](https://doi.org/10.1016/j.radonc.2014.08.012)
25. Song DY, Herfarth KK, Uhl M, Eble MJ, Pinkawa M, van Triest B, et al. A multi-institutional clinical trial of rectal dose reduction via injected polyethylene-glycol hydrogel during intensity modulated radiation therapy for prostate cancer: analysis of dosimetric outcomes. *Int J Radiat Oncol Biol Phys* 2013; **87**: 81–7. doi: [10.1016/j.ijrobp.2012.12.019](https://doi.org/10.1016/j.ijrobp.2012.12.019)
26. Pinkawa M, Piroth MD, Holy R, Escobar-Corral N, Caffaro M, Djukic V, et al. Spacer stability and prostate position variability during radiotherapy for prostate cancer applying a hydrogel to protect the rectal wall. *Radiother Oncol* 2013; **106**: 220–4. doi: [10.1016/j.radonc.2012.11.010](https://doi.org/10.1016/j.radonc.2012.11.010)
27. Uhl M, van Triest B, Eble M, Weber D, Herfarth K, De Weese T. Low rectal toxicity after dose escalated IMRT treatment of prostate cancer using an absorbable hydrogel for increasing and maintaining space between the rectum and prostate: results of a multi-institutional phase II trial. *Radiother Oncol* 2013; **106**: 215–19. doi: [10.1016/j.radonc.2012.11.009](https://doi.org/10.1016/j.radonc.2012.11.009)
28. Feigenberg SJ, Pollack A, Price RA, McNeeley SW, Horwitz EM. Prostate. In: Chao KSC, Apisarnthanarax S, Ozyigit G, eds. *Practical essentials of intensity modulated radiation therapy*. 3rd edn. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. pp. 308–24.