

Literature Review: Dietary and Pharmaceutical Interventions for Bowel Preparation in Prostate Cancer Irradiation

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1. Introduction

Prostate cancer is the most common form of cancer in Canadian men, with an estimated incidence of 23,300 new cases in 2020 alone ^[1]. With so many prostate cancer patients receiving radiation therapy as a treatment modality, there is a desire to limit the frequency and severity of patient side effects. These adverse reactions include, but are not limited to, proctitis, diarrhea, cystitis, and impotence ^[2]. In order to reduce the severity of these side effects, it is important that patients follow bladder and bowel preparation prior to radiation treatment on a daily basis. Bladder and bowel preparation are essential steps in the treatment of almost all patients receiving radiation to the pelvic region. Changes to these organs can affect anatomical positioning and, thus, accuracy of radiation delivery. It is important to note that anatomical reproducibility and prostate motion are key players in prostate cancer treatment since rectal size may be easily changed by gas or bowel content. In an effort to regulate these factors, a high-fiber or anti-flatulent diet, perhaps in conjunction with other interventions, may be applied to reduce rectal size and, therefore dose to the rectum. Instances of these interventions include, microenema prescriptions, a high fiber or anti-flatulent diet, pharmaceutical interventions and milk of magnesia (MoM) ^[3]. The standard protocol at the Princess Margaret Cancer Center establishes that the bladder should be comfortably full, and the rectum empty so that organs at risk are positioned away from the treatment field ^[2]. In this case, hydration, regular bowel movements and an anti-flatulent diet are recommended ^[2].

Currently, rectal preparation for the purposes of radiation treatment to the prostate is routine for patients, yet there is no standardized protocol delineating a most effective strategy. This research is especially crucial for patients who are unable to have daily bowel movements. The methodologies practiced at each institution vary, but they all aim to increase the accuracy of treatment

delivery and decrease side effects by limiting the area of the rectum receiving radiation. The aim of this literature review is to examine the effectiveness of diet and other forms of interventions to address the issue of extraneous rectal dose during radiation treatment to the prostate.

2. Methodology

For the purpose of this literature search, various databases – including PubMed, Science Direct, EBSCOhost and Google Scholar – were used in combination with predetermined key words. Key words included: “*prostate cancer*”, “*bowel prep*”, “*diet*”, “*nutrition*”, “*image-guided radiation therapy*”, “*prostate motion*”, and “*reproducibility*” in various combinations. The literature selected were limited to English articles published from 2010 to the present year, 2020, to ensure that the information retrieved would be relatively up to date. Article topics were focused on the impact of diet on image-guided prostate cancer treatment and excluded various literature concerning the influence of diet on bowel preparation for other procedures, such as colonoscopies. An initial exploration for literature using key words “prostate cancer” and “diet” yielded a plethora of articles discussing the effects of diet on the risk of prostate cancer development and/or progression. To amend this, “bowel” and “motion” key words were used in conjunction, which generated more definitive search results. A total of 974 journal articles were initially identified from a general search across all four aforementioned databases. From these search results, an additional search with specific key words was performed to narrow down options, resulting in 49 relevant journal articles. At this point, duplicate results were removed, and specific abstract keywords were reviewed again. (Table 1) Literature Search Strategy below outlines the keywords used and the number of search results from each database used. The final articles were chosen based on topic relevance, date of publication and interventions implemented.

Table 1. Literature Search Strategy

Search Database	Key words	Publication Date	Publication Type	Results (1)	Refined Search	Results (2)
PubMed (NCBI)	"Prostate Cancer" AND "Diet" AND "Imaging"	2010 – 2020	Journal Article	41	Journal Review	7
PubMed (NCBI)	"Prostate Cancer" AND "Diet" AND "Motion"	2010 – 2020	Journal Article	5	Keyword in Abstract ("Bowel" or "Rectal")	3
Science Direct	"Prostate Cancer" AND "Diet"	2010 – 2020	Journal Article	898	Key word ("reproducibility")	20
Google Scholar	"Prostate Cancer" AND "Diet" AND "Motion" AND "Bowel Preparation"	2010 – 2020	Journal Article	30	Keyword ("CT")	19

RESULTS

Table 2. Summary of Articles below summarizes the intervention(s) implemented in each study, background and methods, main findings, and the implications on practice.

Table 2. Summary of Articles

Publication (year)	Intervention Implemented in Study	Background and Methods	Main Results or Findings	Implications on Practice
Yahya et al. (2013) ^[8]	<ul style="list-style-type: none"> - No bowel preparation - High-fibre diet information leaflet - Daily micro enema 	<ul style="list-style-type: none"> - 3 cohorts of 10 patients followed various dietary interventions for bowel preparation in prostate cancer patients - Cone beam CTs were used to quantify interfractional changes in rectal distention and prostate shifts 	<ul style="list-style-type: none"> - Patients in the micro enema cohort showed significant reduction in mean prostate shifts and geometric miss of $\geq 5\text{mm}$ 	<ul style="list-style-type: none"> - Use of micro enema is effective in decreasing prostate shift and rectal cross-sectional area - Use of smaller expansion margins could potentially reduce toxicities in normal tissue, it can also increase the risk of geographical miss to the target - A further prospective randomized study was suggested to validate the study results

Oates, et al. (2013) ^[6]

- Low fiber and anti-flatulent diet was implemented
- Patients were recommended to avoid spicy foods and dairy products, and to limit lipid intake as well
- 30 patients were enrolled in this study
- All participants were over the age of 50 and receiving external beam radiotherapy to an intact prostate
- The study found that dietary intervention reduced rectal filling variability, in comparison to standard therapy
- The results supported the use of dietary intervention for bowel prep and provided the basis for a future study with a larger sample size of 100 participants

Hosni, et al. (2017) ^[11]

- Rectal filling was compared for populations on an anti-flatulence diet that did and did not supplement with milk of magnesia
- Two groups of 40 patients were retrospectively identified:
 - The first group followed an anti-flatulence diet with MoM implemented 3 days before CT simulation and continued throughout radiation treatment
 - The second group only followed anti-flatulence diet
- A weekly CBCT was used to evaluate rectum between the upper and lower limits of the CTV
- There were no significant differences in rectal volume, average cross-sectional rectal area, and anterior-posterior diameter of rectum contours, following implementation of MoM
- 60% of patients in the MoM cohort experienced diarrhea, compared to only 22.5% of patients in the non-MoM cohort
- 40% of patients in the MoM discontinued use of MoM
- Use of MoM, in addition to anti-flatulence diet, did not reduce interfractional variation to rectal volume

		<ul style="list-style-type: none"> - Rectal filling in the anterior-posterior direction, rectal volume and average cross-sectional rectal area was also evaluated 	<ul style="list-style-type: none"> by the end of radiation treatment 	
<i>Lips, et al. (2011)</i> ^[10]	<ul style="list-style-type: none"> - Follows the effects of anti-flatulent dietary advice - Dietary guidelines aimed to reduce intestinal gas by limiting certain foods and air swallowing 	<ul style="list-style-type: none"> - Portal images were used to evaluate the effects of anti-flatulent dietary advice on intrafraction prostate movement - Clinically relevant motion was defined as $\geq 50\%$ of the fractions with an intrafraction motion outside a range of 3mm 	<ul style="list-style-type: none"> - 19.1% of patients without dietary changes recorded increased, clinically relevant intrafraction motion 	<ul style="list-style-type: none"> - Anti-flatulent dietary advice is not recommended in clinical practice for the purpose of limiting intrafraction prostate movement
<i>Schaefer, et al (2020)</i> ^[7]	<ul style="list-style-type: none"> - Follows a low FODMAP Diet (LFD) - FODMAP stands for fermentable oligo-, di-, monosaccharides and polyols 	<ul style="list-style-type: none"> - Patients were asked to follow an LFD during radiation treatment, with a retrospective control group who did not receive any dietary advice - Rectal volume was measured in the planning CT simulation scan and all available CT scans - Rectal gas was evaluated using a scale of 1-5 	<ul style="list-style-type: none"> - The prospective intervention group (with LFD) showed lower scores of rectal gas scores and decreased rectal volume than the control group - Mean standard deviation of rectal volume variability was 22cm³ in the intervention group and 23cm³ in the control group 	<ul style="list-style-type: none"> - The use of LFD reduced both rectal gas and rectal volume - Prospective trials with increased number of patients and evaluation of gastrointestinal toxicity and quality of life was suggested

- Patient compliance was also recorded and evaluated via a self-assessment questionnaire

McGuffin, et al (2018)
[12]

- Intervention with anti-flatulent medication

- 78 participants were randomly assigned to either an intervention cohort or a control cohort
- Rectal diameters were measured on CT simulation and treatment CBCT scans
- Acute rectal toxicities were also evaluated

- There was no significant variation in rectal diameter between the two cohorts
- No acute rectal toxicities > Grade 2 were recorded

- There were no clinically significant findings
- The study concluded that the standardized bowel preparation developed was sufficient for reducing rectal size variation

Nichol, et al (2010)
[5]

- Milk of magnesia in conjunction with an anti-flatulent diet

- 42 patients were evaluated with a cinematic MRI without bowel preparation for determine baseline
- Participants were evaluated again before CT planning with an interventional bowel regimen (MR-CT)
- Participants were then randomly assigned a RT fraction (with bowel regimen), and displacement of the posterior midpoint of the prostate was tracked (MR-RT)

- The mean rectal area was 13.5cm at MR-Baseline, 12.7 at MR-CT and 12.3cm at MR-RT

- Milk of magnesia laxative with an anti-flatulent diet did not significantly reduce intrafraction prostate motion or reduce rectal area

McNair, et al. (2011)
[9]

- Individualized fluid and fiber prescription in conjunction with constant treatment
- Fiber, fluid intake and bowel function were evaluated in 22 patients and individualized dietary advice was prescribed
- Patients were to record frequency and type of bowel movements, in addition to daily fiber and fluid intake
- Rectal volume and gas were measured in the planning CT and treatment CT scans
- Two subsequent CT scans were also taken at 7 days (CCT1) and 10 days (CCT2) after the planning scan
- The mean change in volume between the planning scan to CCT1 and CCT1 to CCT2 was 5.68cm^3 and -8.6cm^3 , respectively
- Most patients were able to achieve or exceeded the prescription
- Patients were able to self-report bowel movement and diet intake, but there was no improvement in rectal filling consistency

Perna, et al. (2019) [13]

- Patients were prescribed microenemas or laxatives (Sodium Docusate)
- Retrospective data was collected to oversee the use of micro enemas and/or laxatives for whole pelvis, prostate bed and prostate radiation treatments
- A radiographer-led clinic was established for patients
- Intervention via laxatives reduced patient rescans from 23% to 16.4%
- Prescribed laxatives were tolerated well by patients
- Prescription of laxatives reduced the need for patients to be rescanned, which decreases radiation exposure to patients

to determine if patients
should be prescribed
additional laxatives

3. Discussion

The interventions in the literature chosen for this review included: dietary interventions [6, 7, 9, 10], with or without the use of MoM [5, 11], pharmaceutical intervention [12, 13] and microenemas [8, 13]. The effectiveness of an intervention was evaluated by one or more of the following: treatment and intervention side effects, interfractional anatomical changes, number of rescans and rectal filling consistency. The significance of the literature findings is relevant to patient side effects and radiotherapy treatment efficiency. It also influences the frequency of avoidable CT rescans and the number of potential interruptions during patients' treatments. For example, Princess Margaret Cancer Center patients with inadequate bladder and bowel prep may be scanned up to three times for their initial CT appointment [2], which exposes the patient to unnecessary radiation and increases overall stress. Effective bowel preparation can, thus, help increase efficiency and workflow in radiation therapy departments.

Dietary interventions were either high in fibre (to increase bowel movements) or aimed to reduce the amount of gas by implementing an anti-flatulent diet or low FDP (fermentable oligo-, di-, monosaccharides and polyols) diet. Studies with high fiber dietary interventions showed an improvement in image quality and reduced overall prostate motion variability [6] or had inconclusive rectal filling consistency [9]. Anti-flatulent diets did not show any improvements in reducing prostate motion [11], but a low FODMAP diet showed decreased rectal gas and rectal volume [7]. Two studies examined the effect of anti-flatulence diets in conjunction with a pharmaceutical, MoM. Both findings demonstrated that there was no significant change in rectal volume nor prostate motion following intervention with MoM [5, 11]. Dietary interventions were difficult to quantify as there is no definitive outline of what fulfills the criteria of a particular diet. As a result, many of the recommended diets simply involved promotion of certain foods that were high in fiber via pamphlets [6, 7, 8], or individual consultations [9]. There is also the issue of patient compliance; while some patients were asked to self-record and evaluate via questionnaires [7], other patients were only given diet information leaflets [8]. The compliance of patients to the suggested diets plays an important role in the presented results. Intervention via pharmaceuticals without dietary changes was another division in the included studies. Studies that had intervention with medication alone showed

no clinically significant findings [12] but were able to reduce the number of times patients were sent to be rescanned in CT simulation when combined with microenemas [13]. Laxatives were also documented to be tolerated well by patients [13]. The use of micronemes as an intervention strategy was proved effective in two studies included [8, 13].

Overall, interventional strategies showed promising but mixed results as many of these studies used various methods to measure results. For instance, Perna [13] used number of CT rescans, while McNair [9] and Oates [6] measured rectal filling variability. Patient sample size also varied. The literature findings are also limited by several factors that are unaccounted for: access to pharmaceutical interventions, modified diets and/or patient willingness to adapt to these strategies are only some of the barriers that deter standardization of bowel preparation. The demand for bowel preparation may also be less urgent at various cancer centres if the protocol dictates more lenient tolerances for rectal volume dose during the treatment planning stages.

4. Conclusion

Despite the wide variety of possible techniques, there does not seem to be a single most effective method or consensus among radiation oncologist on how patients should carry out rectal preparation for radiation treatment. An existing literature review published in 2014 on the effect of intervention on rectal emptying preparation for prostate cancer patients is inconclusive as well [3], and none had been published in recent years or focused on combinational (e.g., diet and laxatives) interventions for bowel preparation.

There are challenges associated with each method, and even combinations of techniques do not always produce clinically significant results. Future studies with larger sample sizes and stricter dietary guidelines are needed to produce more accurate results.

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