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The Effect of Contrast Material in Three Dimensional Conformal and Helical Treatment Plans in Rectal Radiotherapy

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Abstract

The aim of this study to investigate the impact of contrast agent used for imaging purposes in the treatment of neoadjuvant rectal cancer patients. In rectal radiotherapy, contrast agent is used during the treatment simulation but the patient treated without contrast. In our study, we will examine whether CTs taken with contrast agent are sufficient for clinical application. A total of eighteen patients who had undergone neoadjuvant treatment with rectal cancer randomly selected. Two different CT scans were performed for each patient. The contours were delineated on a non-contrast CT images with the help of image fusion with contrast CT images. Then, the contours drawn on the non-contrast CT were copied to the contrast-enhanced CT with the help of fusion to be used in contrast CT plans for our retrospective study. Subsequently, all plans were generated in Eclipse TPS and Accuray Precision TPS. Finally the plans with contrast agent and non-constrat agent were compared. 3DCRT plans were compared for contrast and non-contrast images, no significant differences were observed in either the PTV or the maximum and mean values of critical organs. It was observed that the average post-contrast doses increased significantly for small bowel only in helical therapy ($p = 0.019$). As a result, no significant difference was observed in terms of PTV and critical organs in the comparison of 3DCRT plans. In the comparison of helical plans, there was only a significant difference in the bladder. Based on these results, we suggest that planning can be done with a single contrast CT for 3DCRT treatments, both to avoid further discomfort for the patient and to prevent additional tomography doses. On the other hand, for helical therapy, we believe that it can be clinically evaluated whether the treatment will be performed with contrast CT depending on the patient's condition.

Keywords: Contrast, conformal radiotherapy, helical therapy, rectum.

1. Introduction

Rectal cancer is a disease that significantly affects the quality of life. The incidence of rectal cancer in the world in 2020 was 3.8%[1]. The incidence of rectal cancer is affected by factors, including heredity, obesity, dietary habits, smoking and other factors. The illness is becoming more common, with a rise in both the number of cases and deaths each year[2]. With advances in medical technology and development of new treatment techniques, the combination of neoadjuvant therapy and surgery has become widely used for the treatment of the rectum cancer[3, 4].

Recent studies have shown that patients with locally advanced rectal cancer who received radiotherapy and chemotherapy before total mesorectal excision (TME) exhibited improved outcomes in terms of tumour response and survival[5, 6]. Initially postoperative or preoperative radiotherapy (RT) studies and recent studies of combinations of concurrent chemotherapy and radiotherapy have shown improvement in local control and a reduction in recurrences[7-9].

Neoadjuvant chemoradiotherapy (NCRT), particularly neoadjuvant radiotherapy and sphincter-sparing surgeries, has been criticized for causing complaints such as bowel discomfort, urgency, and fecal incontinence[10-12].These functional disorders have negative affect on the patient's quality of life[13, 14].

With the development of technology, the use of three dimensional conformal radiotherapy (3DCRT) has

become more advanced, intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) have begun to be used routinely in cancer treatment techniques. The definition of this conformity also includes tomographic images necessary for treatment planning.

The utilisation of contrast agent in tomography is beneficial in the determination of the target volume and obtaining more accurate results in critical organ identification[15].It is recommended that computed tomography (CT) images with intravenous contrast (IV) be used for staging purposes in regions from the liver to the rectum[16].

The objective of this study was to assess the impact of contrast agent used for imaging purposes in the treatment of neoadjuvant rectal cancer patients on dose calculations in 3DCRT using four field box technique and helical therapy (HT) treatment techniques. HU changes in tomography images when contrast is used in the study will also be investigated.

2. Materials and Methods

2.1. Patient Selection

A total of eighteen patients with rectal cancer who had undergone neoadjuvant treatment at the Radiation Oncology Department of Necmettin Erbakan University Medicine Hospital (The ethics institutional review board of this retrospective study was approved by the ethics committee of Necmettin Erbakan University Medicine School with approval number 2024/4948) between January 2011 to December 2023 were randomly selected. All patients with appropriate renal function and creatine resistance underwent contrast and non-contrast imaging before planning. Especially elderly patients were hydrated after imaging. The study included eleven male and seven female patients, all of whom were over the 18 years of age. The mean age of the patients selected for the study was 64. All patients were diagnosed with T3 stage. None of the patients had metastatic disease. All patients received concurrent chemotherapy.

2.2. Simulation

All patients were subjected to CT scan (Siemens Emotion Duo, Germany) in the supine position. Before planning, all patients underwent tomography with and without contrast. The patients were initially scanned without contrast enhancement and followed by a second scan with contrast enhancement, both performed with the 5 mm slice thickness, same fixation position and same coordinates. A solution of 300 mg/100 ml non-ionic contrast agent (Omnipaqe) was used as IV contrast. Oral contrast was administrated in the form of 20 to 40 millilitres of gastrografin in 1.5 litres of water. After the first non-contrast imaging was performed, the patients were given 1.5 litres of oral contrast. Then, the second shot was taken approximately 1 minute after IV contrast was administered via an automated injector.

2.3. Treatment Planning

The data obtained from CT scan was transferred via the Digital Imaging and Communication in Medicine (DICOM) protocol to Eclipse™ treatment planning system (TPS), (version 8.9.08, Eclipse, Varian Medical Systems, Palo Alto, CA, USA).The transferred CT images used to delineate critical organs (small bowel, bladder, right femur, and left femur) and planning target volume (PTV) by a radiation oncologist in accordance with the framework of RTOG (Radiation Therapy Oncology Group) protocol and clinical approaches. The contours were delineated on a non-contrast CT images (CT Set-1) with the help of image fusion with contrast CT images (CT Set-2). Then, the contours drawn on the CT Set-1 were copied to the contrast-enhanced CT with the help of fusion to be used in CT Set-2 plans for our retrospective study. Subsequently, all plans were generated by a medical physicist utilising the Pencil Beam Algorithm and 18 MV photon energy in Eclipse TPS, where the Siemens Primus Plus therapy device defined.

Four field box techniques were used in the planning process (anterior, posterior, right, and left). The prescribed dose for patient was 50 Gy in 25 fraction with a dose of 2 Gy/daily. During the planning, it was ensured that the PTV would receive at least 95% of the prescribed dose, while maximum dose allowed in the plan was set to 110%. Additionally, plans were also created using contrast-enhanced CT images under the same conditions. Then, the contours delineated in Eclipse TPS were transferred via DICOM to Accuray Precision version 2.0.1.1 (Accuray Incorporated, Madison, Wisconsin, USA) TPS, which employs the superposition/convolution planning algorithm of the Tomotherapy device. In this helical planning, a dose of 50 Gy was delivered with a field opening of 2.5 cm, a pitch of 0.287, and a modulator factor of 3.0. During the planning process, the same medical physicist made sure that the volume of the PTV received at least 95% of the prescribed dose, while the critical organ doses were kept as low as possible. These helical tomotherapy plans were repeated on contrast-enhanced CT under the identical conditions.

3. Results

A total of 18 patients who had undergone radiotherapy for rectal cancer were included in the study. The radiotherapy plans were calculated using two different algorithms; the pencil beam algorithm in 3DCRT with Eclipse TPS and the superposition/convolution algorithm with Accuray Precision TPS for tomotherapy plans. Figure 1 and Figure 2 shows the 95% of the prescribed dose distribution for 3DCRT and Tomotherapy plans respectively. Table 1 presents Hounsfield Units (HU) at

the same coordinates in both non-contrast and contrast-enhanced tomography images. We measured the changes in HU values with and without contrast in Eclipse TPS from ten points, trying to have the same coordinates for both images. We made HU readings by creating circular regions in TPS in sections that contain mostly vessels of PTV and where contrast changes in the bladder are more visible. While the minimum HU value before contrast was 14, this value reached 33 after contrast, and the maximum HU value before contrast was 62, but it reached 173 after contrast for PTV. With the addition of contrast resulted in average increase in HU in the PTV and bladder. The average increase in HU in the PTV was found to be statistically significant (p = 0.028).

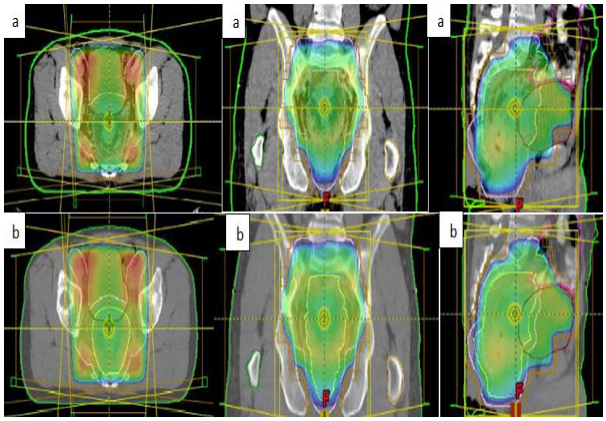

Figure 1. The 95% dose distribution of a patient for 3DCRT plans in axial, coronal, and sagittal planes; a) for contrast plan, b) for non-contrast plan.

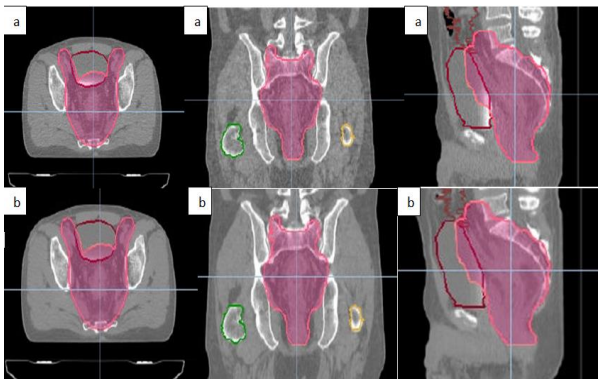

Figure 2. The 95% dose distribution of a patient for tomotherapy plans in axial, coronal, and sagittal planes; a) for contrast plan, b) for non-contrast plan.

The mean doses and standard deviations obtained for PTV and critical organs from TPS calculations made with 3DCRT and HT plans before and after contrast are compared in Tables 2 and 3 respectively. A comparison of the pre-contrast and post-contrast dose calculations was conducted using the SPSS independent t-test. When 3DCRT plans were compared for contrast and non-contrast images, no significant differences were observed in either the target tissue-PTV or the maximum and mean values of critical organs. It was observed that the average post-contrast doses increased significantly for small bowel only in helical therapy (p = 0.019).
Conversely, while the average maximum doses for PTV, small bowel, and bladder in helical planes increased after contrast (p values: 0.208; 0.083 and 0.560, respectively), these values decreased for the right femur and left femur (p values: 0.705 and 0.168, respectively). In HT plans, while the average post-contrast PTV, small bowel, right femur and, left femur doses increased (p values: 0.218; 0.019; 0.137 and 0.166, respectively), the bladder average dose value decreased (p = 0.812). For 3DCRT plans, while the average maximum doses decreased for the post-contrast PTV, bladder right femur and, left femur (p values: 0.646; 0.241; 0.481 and 0.577, respectively), they increased for the small bowel (p=0.241). While the average dose values decreased only for the target PTV after contrast (p = 0.270); It is high for the bladder, small bowel, right femur and, left femur (p values: 0.367; 0.089; 0.175 and 0.079, respectively). With regard to MU required for treatment, no difference was found before and after contrast for both planning techniques.

Table 1. Hounsfield Units (HU) differences due to contrast agent

Site	Min./Max. Range, Mean values (SD) in Hounsfield Units						
	CT Set-1 Min. Range	**CT Set-1 Max. Range**	**CT Set-2 Min. Range**	**CT Set-2 Max. Range**	**CT Set-1 Mean±SD**	**CT Set-2 Mean±SD**	**p-value**
PTV	14	62	33	173	37.4±18.35	70.4±38.30	0.028*
Bladder	-39	35	-16	117	-1±22.34	21.4±46.50	0.144

PTV, planning target volume; SD, standart deviation; Mean, mean HU values of structure; * significant value at $p<0.05$

Table 2. Mean differences in PTV and organ at risk due to contrast agent in 3DCRT plans

	Dose (cGy) mean values ± SD		
	CT Set-1	**CT Set-2**	**p-Value**
PTV			
Dmax(cGy)	5298,00±42, 30	5294,90±54,32	0,646
Dmean(cGy)	5069,00±46,93	5066,20±49,96	0,270
Bladder			
Dmax(cGy)	5267,30±66,22	5265,10±76,29	0,708
Dmean(cGy)	5014,60±85,14	5106,70±322,54	0,367
Small bowel			
Dmax(cGy)	5235,20±77,18	5240,60±84,60	0,241
Dmean(cGy)	1114,60±543,83	1202,70±543,84	0,089
Right femur			
Dmax(cGy)	5109,50±90,79	5107,20±95,96	0,481
Dmean(cGy)	2474,20±314,81	2480,70±319,47	0,175
Left femur			
Dmax(cGy)	5030,70±124,04	5027,80±129,80	0,577
Dmean(cGy)	2276,40±276,78	2290,20±285,78	0,079
MU	222,60±2,95	224,40±2,50	0,555

PTV, planning target volume; SD, standart deviation; 3DCRT, 3 dimensional conformal radiation therapy; Dmax, maximum dose of plan; Dmean, mean dose of structure

Table 3. Mean differences in PTV and organ at risk due to contrast agent in Helical Tomotherapy plans

	Dose (cGy) mean values ± SD		
	CT Set-1	**CT Set-2**	**p-Value**
PTV			
Dmax(cGy)	5302,20±36,11	5312,20±48,38	0,208
Dmean(cGy)	5067,30±40,50	5074,90±12,23	0,218
Bladder			
Dmax(cGy)	5286,70±66,79	5290,40±77,90	0,560
Dmean(cGy)	5006,40±96,44	5005,10±101,35	0,812

Small bowel			
Dmax(cGy)	5250,00±80,92	5258,90±89,01	0,083
Dmean(cGy)	995,43±461,48	1137,30±520,55	0,019*
Right femur			
Dmax(cGy)	5107,50±101,77	5106,00±107,28	0,705
Dmean(cGy)	2495,90±291,42	2504,60±297,48	0,137
Left femur			
Dmax(cGy)	5030,00±140,50	5028,90±147,08	0,168
Dmean(cGy)	2313,00±276,12	2323,80±283,66	0,166
MU	5362,60±71,76	5358,20±74,34	0,771

PTV, planning target volume; SD, standart deviation; 3DCRT, three dimensional conformal radiation therapy; Dmax, maximum dose of plan; Dmean, mean dose of structure; * significant value at $p<0.05$

4. Discussion

In the simulation phase of radiotherapy for pelvic diseases such as the rectum, IV contrast agents are frequently used for the purpose of delineation PTV and oral contrast agents are used to calculate the dose received by the intestines. In this study, we investigated the effects of these contrast agent on the dose distributions for two commercial TPSs using different calculation algorithms and connected to different treatment devices. Our findings revealed that there was no significant difference before and after contrast planning in almost any dosimetric parameter. This inability to find a difference is also applicable when comparing the MU values obtained for both techniques. There may be uncertainties in our study due to the fusion of two different CT scans. In addition, since there is optimization in the helical treatment plan, the results may be affected, but when we look at the literature, the differences in the dosimetric parameters of the treatment plans made with CT Set-2 and CT Set-1 are generally not significant. This may be due to the contrast used not being at a level that will affect the calculations of the algorithms.

In a study conducted by Heydarheydari, Farshchian and Haghparast [17], analysed the plans with CT Set-2 and CT Set-1 images of 11 pelvic cancer patients. Treatment plans created using Collapsed Cone and Superposition algorithms in DosiSoft ISOgray TPS. The researchers found no significant difference in target tissue PTV and critical organs, with the exception of the bladder in both CT situations. Similarly, in our study, while we did not find any significant difference in the target tissue PTV or critical organ doses between contrast and non-contrast plans in the 3DCRT technique, we found that in the Helical Therapy technique, the average dose value increased significantly only for the small bowel. The reason why there was a significant difference only in the bladder may be due to the planning algorithm used and the fact that contrast agents affect the bladder more.

Manindra Bhushan and his colleagues produced a contrast phantom. By assigning different HUs to this phantom, they obtained a non-contrast phantom. IMRT and VMAT plans were created for these phantoms using Eclipse TPS, which is compatible with the True-Beam linear accelerator. The plans created with both phantoms demonstrated comparable dose coverage for the PTV prostate for all photon energies, with exception of the VMAT plan created with the original phantom. As a result, they found target overdose meaningless for the planning made with both techniques[15].In our study, no significant dosimetric differences were observed in the PTV as a result of 3DCRT plans. We only found that the average doses for the small bowel in helical plans increased significantly after contrast.

Jabbari Nasrollah and colleagues created 3DCRT plans with and without IV contrast for 12 rectal patients and compared the doses. As a consequences, no significant difference was identified between contrast-enhanced and non-contrast 3DCRT plans. It was concluded that contrast-enhanced and non-contrast treatment plans were within tolerance limits for the clinic[16]. The results of this study did not reveal any significant differences between the contrast-enhanced and non-contrast for 3DCRT plans similar to their study.

Nadia Montero-Oleas and colleagues performed CT with and without oral contrast on rectal patients. Subsequently, 3DCRT and IMRT plans were created Eclipse TPS using the Acuros XB calculation algorithm with contrast-enhanced CT. These plans were than recreated with contrast-enhanced CT under the same conditions. Ultimately, they found no clinical differences in the majority of dose measurements. The greatest discrepancy was observed in the volume of the small intestine receiving 45 Gy. They interpreted that this difference may be lower due to contrast-enhanced CT. As a result, authors concluded that the use of oral contrast did not significantly impact dose calculations and may not affect the acceptance of plans, provided that the aforementioned limitations are taken into

account[18].According to the results we obtained from contrast-enhanced and non-contrast plans in our study, there were no differences that would affect clinical plan acceptance.

Yuta Shibamoto and his colleagues create two contrast-enhanced and non-contrast plans using Eclipse TPS for 5 pelvic cancer patients. They first made the plans on contrast-enhanced CT scans and then copied the plans to non-contrast images and recalculated. They found the average difference in MUs to be below 1% for both conditions. Consequently, they reported that there was no significant difference in dose calculations between contrast and non-contrast in treatment planning[19]. In our study, parallel to this study, the increase in MUs in 3DCRT contrast-enhanced plans was below 1%.

5. Conclusion

In our study, we compared 3DCRT and helical therapy plans using CT Set-2 and CT Set-1s to be used for the definition of PTV and critical organs in rectum cancer treatments. As a result, no significant difference was observed in terms of PTV and critical organs in the comparison of 3DCRT plans. In the comparison of helical plans, there was only a significant difference in the bladder. Based on these results, we suggest that planning can be done with a single CT Set-2 for 3DCRT treatments, both to avoid further discomfort for the patient and to prevent additional tomography doses. On the other hand, for helical therapy, we believe that it can be clinically evaluated whether the treatment will be performed with CT Set-2 depending on the patient's condition.

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Author's Contributions

Hikmettin Demir: Drafted and wrote the manuscript, supervised the experiment's progress, performed the experiment and result analysis.

Gül Kanyılmaz: Assisted in analytical analysis on the structure, supervised the experiment's progress, result interpretation and helped in manuscript preparation.

Osman Vefa Gül: Assisted in analytical analysis on the structure, supervised the experiment's progress, result interpretation and helped in manuscript preparation.

Ethics

There are no ethical issues after the publication of this manuscript.

References

[1]. H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA: a cancer journal for clinicians 71(3) (2021) 209-249.

[2]. Z. Yu, Y. Hao, Y. Huang, L. Ling, X. Hu, S. Qiao, Radiotherapy in the preoperative neoadjuvant treatment of locally advanced rectal cancer, Frontiers in Oncology 13 (2023).

[3]. R. Glynne-Jones, L. Wyrwicz, E. Tiret, G. Brown, C.d. Rödel, A. Cervantes, D. Arnold, Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, Annals of Oncology 28 (2017) iv22-iv40.

[4]. A.B. Benson, A.P. Venook, M.M. Al-Hawary, L. Cederquist, Y.-J. Chen, K.K. Ciombor, S. Cohen, H.S. Cooper, D. Deming, P.F. Engstrom, Rectal cancer, version 2.2018, NCCN clinical practice guidelines in oncology, Journal of the National Comprehensive Cancer Network 16(7) (2018) 874-901.

[5]. M.J. van der Valk, C.A. Marijnen, B. van Etten, E.A. Dijkstra, D.E. Hilling, E.M.-K. Kranenbarg, H. Putter, A.G. Roodvoets, R.R. Bahadoer, T. Fokstuen, Compliance and tolerability of short-course radiotherapy followed by preoperative chemotherapy and surgery for high-risk rectal cancer–Results of the international randomized RAPIDO-trial, Radiotherapy and Oncology 147 (2020) 75-83.

[6]. T. Conroy, N. Lamfichekh, P.-L. Etienne, E. Rio, E. Francois, N. Mesgouez-Nebout, V. Vendrely, X. Artignan, O. Bouché, D. Gargot, Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: final results of PRODIGE 23 phase III trial, a UNICANCER GI trial, American Society of Clinical Oncology, 2020.

[7]. K.C. Peeters, C.A. Marijnen, I.D. Nagtegaal, E.K. Kranenbarg, H. Putter, T. Wiggers, H. Rutten, L. Pahlman, B. Glimelius, J.W. Leer, The TME trial after a median follow-up of 6 years: increased local control but no survival benefit in irradiated patients with resectable rectal carcinoma, Annals of surgery 246(5) (2007) 693-701.

[8]. M. Zoccali, A. Fichera, Role of radiation in intermediate-risk rectal cancer, Annals of surgical oncology 19 (2012) 126-130.

[9]. J.-P. Gérard, T. Conroy, F. Bonnetain, O. Bouché, O. Chapet, M.-T. Closon-Dejardin, M. Untereiner, B. Leduc, É. Francois, J. Maurel, Preoperative radiotherapy with or without concurrent fluorouracil and leucovorin in T3-4 rectal cancers: results of FFCD 9203, Journal of clinical oncology 24(28) (2006) 4620-4625.

[10]. A. Sipaviciute, E. Sileika, A. Burneckis, A. Dulskas, Late gastrointestinal toxicity after radiotherapy for rectal cancer: a systematic review, International Journal of Colorectal Disease 35 (2020) 977-983.

[11]. A. Dulskas, P. Kavaliauskas, L. Pilipavicius, M. Jodinskas, M. Mikalonis, N.E. Samalavicius, Long-term bowel dysfunction following low anterior resection, Scientific reports 10(1) (2020) 11882.

[12]. N.P. McKenna, K.A. Bews, K.J. Yost, R.R. Cima, E.B. Habermann, Bowel dysfunction after low anterior resection for colorectal cancer: a frequent late effect of surgery infrequently treated, Journal of the American College of Surgeons 234(4) (2022) 529-537.

[13]. E. Pape, P. Pattyn, A. Van Hecke, N. Somers, D. Van De Putte, W. Ceelen, E. van Daele, W. Willaert, Y. Van Nieuwenhove, Rectal cancer survivorship: the struggle of the low anterior resection syndrome (LARS), Annals of Oncology 29 (2018) viii698.

[14]. B. Celerier, Q. Denost, B. Van Geluwe, A. Pontallier, E. Rullier, The risk of definitive stoma formation at 10 years after low and ultralow anterior resection for rectal cancer, Colorectal disease 18(1) (2016) 59-66.

[15]. M. Bhushan, D. Tripathi, G. Yadav, L. Kumar, A. Dewan, S. Tandon, G. Kumar, I.K. Wahi, M. Gairola, Effect of contrast medium on treatment modalities planned with different photon beam energies: a planning study, reports of practical Oncology and radiotherapy 26(5) (2021) 688-711.

[16]. J. Nasrollah, M. Mikaeil, E. Omid, S.S. Mojtaba, Z. Ahad, Influence of the intravenous contrast media on treatment planning dose calculations of lower esophageal and rectal cancers, Journal of cancer research and therapeutics 10(1) (2014) 147-152.

[17]. S. Heydarheydari, N. Farshchian, A. Haghparast, Influence of the contrast agents on treatment planning dose calculations of prostate and rectal cancers, Reports of Practical Oncology & Radiotherapy 21(5) (2016) 441-446.

[18]. N. Montero-Oleas, A. Imbaquingo-Cabrera, A. Coloma-Espin, V. Collantes-Cruz, C. Molineros, C. Núñez-Silva, Dosimetric effects of oral contrast in the planning of conventional radiotherapy and IMRT, for rectal cancer treatment, Journal of Radiotherapy in Practice 22 (2023) e54.

[19]. Y. Shibamoto, A. Naruse, H. Fukuma, S. Ayakawa, C. Sugie, N. Tomita, Influence of contrast materials on dose calculation in radiotherapy planning using computed tomography for tumors at various anatomical regions: a prospective study, Radiotherapy and oncology 84(1) (2007) 52-55.