oncology and radiotherapy

# Calculation of planning target volume margins using the van Herk, Stroom and ICRU methods in patients with gastric cancer

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**Summary**
*The aim.* The aim of this paper was to compare the methods of specifying margins in patients with gastric cancer.
*Material and methods.* The material included 57 patients with gastric cancer during chemoradiotherapy in whom the positioning in the therapeutic system was verified using 2 kV images prior to each radiotherapy fraction. Subsequently, shifts in three axes were assessed. Based on the shifts obtained, systematic and random errors were calculated in given axes and margins were specified using the van Herk, Stroom and ICRU 62 formulae.
*Results.* The margins resulting from the interfraction motion based of the van Herk, Stroom and ICRU formulae were as follows: 9 mm, 7 mm and 6 mm in the lateral axis, 16 mm, 14 mm and 11 mm in the craniocaudal axis as well as 8 mm, 7 mm and 5 mm in the anteroposterior axis, respectively for each formula. The lowest percentage of shifts that were greater than the calculated margin was observed in the van Herk method (1.5% in the lateral axis, 3.3% in the craniocaudal axis and 1.9% in the anteroposterior axis).
*Conclusions.* Based on the material investigated, the margin recommended for centers in which daily patient position verification is not possible is the one calculated with the use of the van Herk formula.
**Key words:** PTV margin, interfraction motion, gastric carcinoma, radiotherapy

## INTRODUCTION

According to the Polish National Cancer Registry, gastric carcinoma still remains the fourth most common cancer and the second cause of death due to neoplasms. In 2011, gastric cancer accounted for 5% and 3% of all malignant cancers in men and women, respectively. Surgical treatment is the standard management in patients with this neoplasm (1, 2). The INT 0116 study has revealed that the usage of adjuvant chemoradiotherapy reduces the risk of local recurrences and contributes to longer survival (3). Radiotherapy in a neoplasm of such a location requires particular precision due to the position of critical organs (the kidneys, spinal cord, liver, bowel and heart) in the vicinity of the target volume. At the same time, radiotherapy must take into account the motion of the stomach and a degree to which it is filled as well as the accurate position of the patient in the therapeutic system. That is why, it is necessary to determine safety margins around the clinical target volume (CTV), as recommended in Report 62 of the International Commission on Radiation Units and Measurements (ICRU) (4). The internal margin (IM) results from the respiratory motion of internal organs, changes in the CTV due to tumor regression and, in the case of gastric carcinoma, a degree of filling the organ in the subsequent days of treatment. Also, setup errors require safety margins (setup margin, SM). Unfortunately, Report 83 of the ICRU does not unambiguously indicate the method to calculate SMs and, at the same time, suggests that they should be determined individually for a center in which radiotherapy is executed (5). The report states that numerous authors base their margin calculations on systematic and random errors. It also indicates examples of calculations according to Bel, Antolak and Rosen, Stroom, Van Herk, Mc Kenzie, Parker, Ten Haken and Engelsman (6–13). Despite so many suggestions concerning SM calculation methods, the question which of them is the most appropriate is still not answered. In the case of gastric carcinoma, there are only few papers that present statistical data concerning the specification of margins for interfraction motion. So far, the margins proposed have been based only on clinical experience (14–16). The author's own calculations indicate that in order to eliminate interfraction motion, there is a need to apply a 9 margin in the lateral axis, a 16 mm margin in the craniocaudal axis and an 8 mm margin in the anteroposterior axis (17). The selection of a method to specify PTV margins is a significant issue in radiotherapy. Numerous radiotherapy centers use the van Herk method. The aim of this paper was to compare various methods of specifying margins in patients with gastric cancer.

## MATERIAL AND METHODS

The investigated material included 57 patients with gastric carcinoma treated in the Department of Radiotherapy of Maria Skłodowska-Curie Institute of Oncology in Gliwice, Poland. The material encompassed both patients after surgery who were receiving adjuvant treatment (48 patients) and those treated with neoadjuvant chemoradiotherapy (9 patients). Combined chemoradiotherapy was applied in patients at various stages of the disease (T2–4N0M0 and T1–4N1–3M0). The patients were irradiated to the stomach bed or stomach including a margin and the regional lymphatic system, i.e. perigastric, pyloric and peripancreatic lymph nodes as well as the nodes of the celiac trunk, splenic hilum, hepatic hilum and pancreaticoduodenal nodes, with a fractional dose of 1.8 Gy to the total dose of 45 Gy. During radiotherapy, 2 chemotherapy cycles were administered based on 5-fluorouracil with or without leucovorin. The treatment was described in detail in the previous publications (17, 18, 19, 20).

All patients were immobilized with the use of a thermoplatic mask (Orfit, Belgium) and underwent planning contrast-enhanced computed tomography scans every 3 mm, at both resting inspiration and expiration. Subsequently, these images were matched and, irradiation sites were determined: internal margin for ITV (internal target volume) and PRV (planning organ at volume). Prior to radiotherapy, the position was verified using 2 kV images at 0° and 90° before each radiotherapy fraction. Subsequently, the portal images were matched with digital reconstruction radiographs (DRR) in order to assess the position of bony structures (spine, ribs, wing of the ilium). Shifts were assessed in craniocaudal (CC) plane (axis Y), lateral (LL) plane (axis X) and anteroposterior (AP) plane (axis Z). Next, the shifts in the aforementioned axes were corrected. The kV images were archived in the database of the Soma Vision system. Based on the shifts obtained, systematic and random errors were calculated in given axes, and margins were specified using the van Herk formula ($2.5\Sigma+0.7\sigma$), the method recommended by ICRU 62 ($\Sigma+0.7\sigma$) and the Stroom formula ($2\Sigma+0.7\sigma$), where $\Sigma$ denotes squared standard deviation for systematic errors and $\sigma$ – for random errors (4, 8, 9). The calculations were conducted in the platform R (21).

## RESULTS

The material included 57 patients with gastric cancer. In total, 1,284 2D kV images were obtained. PTV margins resulting from setup errors in the therapeutic system were calculated with the use of the van Herk, Stroom and ICRU formulae. The margins were: 9 mm, 7 mm and 6 mm in axis X, 16 mm, 14 mm and 11 mm in axis Y as well as 8 mm, 7 mm and 5 mm in axis Z, respectively for each formula (Table 1). Figures 1 and 2 present relationships of the PTV margins and shifts detected in accelerators for each of the three methods in the individual axes. The lowest number of shifts beyond the specified margin was observed in the van Herk method (1.5% in the lateral axis, 3.3% in the craniocaudal axis and 1.9% in the anteroposterior axis). When using the Stroom and ICRU formulae, the following results were obtained: 3.5% and 6.7% in axis X, 4.9% and 9.4% in axis Y as well as 4.1% and 10.6% in axis Z. The results are presented in Table 2.

## DISCUSSION

Most authors base their margin calculations on the Van Herk formula, and the greatest number of statistical data concern prostate cancer (22–24). Also, in Report 83 of the International Commission on Radiation Units and Measurements, the PTV margin is based on the literature data concerning prostate cancer (5). The report does not unambiguously specify which of the methods is the best, but merely indicates authors who have performed such calculations, i.e.: Bel, Antolak, Stroom, van Herk, Mc Kenzie and Parker. Currently, the literature provides little information about statistical calculations concerning interfraction setup errors in the therapeutic system in patients with gastric cancer (7). In the study above, this margin was calculated with the use of the van Herk formula (2.5?+0.7ó). Considering Report 83 of ICRU, a question arises whether other calculation methods could

**Tab. 1.** Margins calculated using the van Herk, Stroom and ICRU formulae in axes X, Y and Z [cm]

| Axis | van Herk | Stroom | ICRU |
|---|---|---|---|
| X | 0,9 | 0,7 | 0,6 |
| Y | 1,6 | 1,4 | 1,1 |
| Z | 0,8 | 0,7 | 0,5 |

**Tab. 2.** Percentage of shifts beyond the margins calculated using the van Herk, Stroom and ICRU formulae in axes X, Y and Z

| Axis | van Herk | Stroom | ICRU |
|---|---|---|---|
| X | 1,5% | 3,5% | 6,7% |
| Y | 3,3% | 4,9% | 9,4% |
| Z | 1,9% | 4,1% | 10,6% |

be better. In the material investigated, the formula proposed by Bel et al. was not used since it is based only on random errors ($0.7\sigma$) (6). According to the Stroom formula, this margin should equal $2\Sigma+0.7\sigma$, and the authors claim that 99% of the CTV is exposed to 95% of the dose. Report 62 of ICRU indicates that the margin of $\Sigma+0.7\Sigma$ should be sufficient. In the material investigated, the margin based on the van Herk formula should equal: 9 mm in the lateral axis, 16 mm in the craniocaudal axis and 8 mm in the anteroposterior axis. According to the Stroom method, margins are smaller by 1–2 mm. As for the ICRU recommendations, margins are smaller by approximately 30% in individual axes. Seemingly, a lower margin is more beneficial since it reduces the risk of both acute and late radiation reactions in the critical organs. However, narrower margins can increase the risk of geographical errors and insufficient PTV irradiation. Margins should be sufficient. It means that 95% of shifts should be included within the margin. The lowest percentage of shifts beyond the specified margin was obtained when margins were calculated with the use of the van Herk method. However, margins obtained with the use of the Stroom formula also seem to be sufficient. As for the ICRU method, the results obtained are neg-

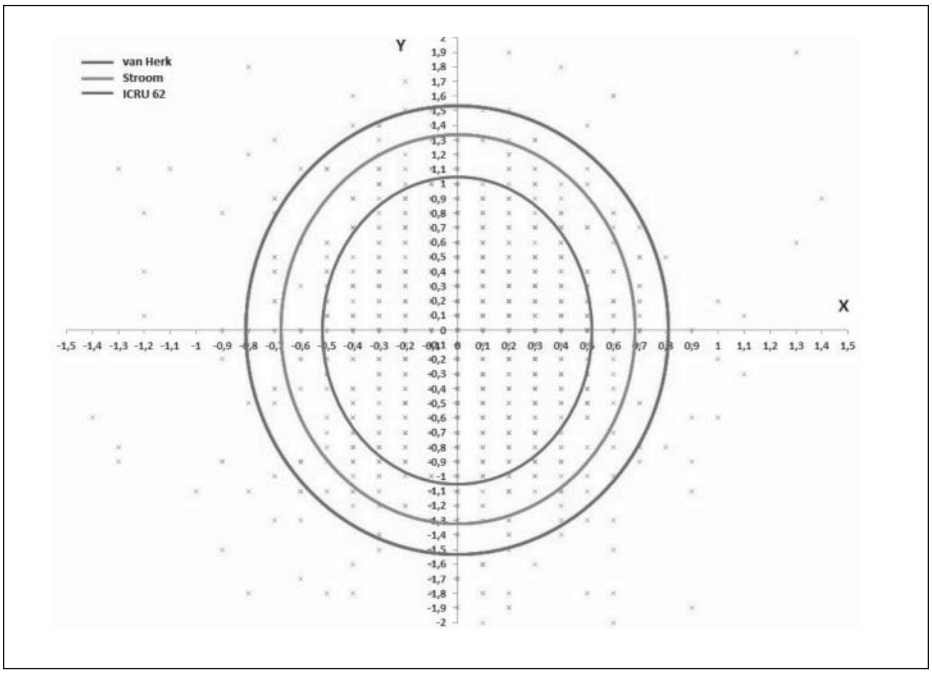


**Fig. 1.** Relationships between shifts in axes X and Y and margins calculated with the use of the van Herk, Stroom and ICRU formulae [cm]

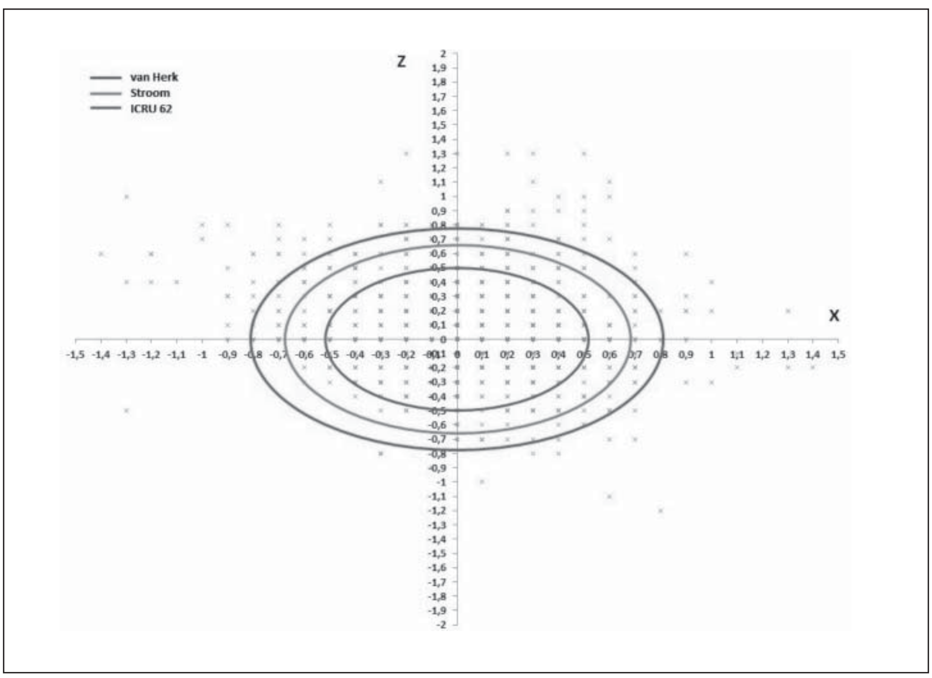


**Fig. 2.** Graphical representation of the relationships between shifts in axes X and Z and margins calculated with the use of the van Herk, Stroom and ICRU formulae [cm]

ative. In the craniocaudal axis, as many as 9.4% of shifts were found to be beyond the margin, and this value amounted to 10.6% in the anteroposterior axis. Based on the material investigated, it can be stated that in radiotherapy centers in which daily verification is not used, the van Herk or Stroom formulae seem to be good calculation methods to be used in gastric cancer patients. The percentage of shifts beyond the margin is below 5%.

## CONCLUSION

Both the van Herk and Stroom formulae are satisfactory methods in determining margins for the planning target volume. However, based on the center's own experience, the recommended margin is the one determined with the use of the van Herk formula ($2.5\Sigma+0.7\sigma$) owing to the low percentage of setup errors beyond the calculated margins.

References:


1. Munson JL, O'Mahony R. Radical gastrectomy for cancer of the stomach. Surg Clin North Am 2005; 85: 1021–32.
2. McCulloch P. The role of surgery in patients with advanced gastric cancer. Best Pract Res Clin Gastroenterol 2006; 20: 767–87.
3. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001; 345:725–30.
4. ICRU Report 62. International Commission on Radiation Units and Measurements. Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50). ICRU Report 62 (International Commission on Radiation Units and Measurements, Bethesda, MD); 1999.
5. ICRU Report 83. Prescribing, Recording, and Reporting Photon-Beam Intensity Modulated Radiation Therapy (IMRT). Journal of the ICRU. 2010; 10(1):1-111.
6. Bel, A., van Herk, M., and Lebesque, J. V. Target margins for random geometrical treatment uncertainties in conformal radiotherapy. Med. Phys. 1996; 23, 1537–1545.
7. Antolak, J. A., and Rosen, I. I. Planning target volumes for radiotherapy: How much margin is needed? Int. J. Radiat. Oncol. Biol. Phys. 1999; 44, 1165–1170.
8. Stroom JC, de Boer HC, Huizenga H, Visser AG. Inclusion of geometrical uncertainties in radiotherapy treatment planning by means of coverage probability. Int J Radiat Oncol Biol Phys 1999; 43:905–919.
9. van Herk M, Remeijer P, Rasch C, Lebesque JV. The probability of correct target dosage:dose-population histograms for deriving treatment margins in radiotherapy. Int J Radiat Oncol Biol Phys 2000; 47: 1121–35.
10. McKenzie, A. L., van Herk, M., and Mijnheer, B. The width of margins in radiotherapy treatment plans. Phys. Med. Biol. 2000; 45, 3331–3342.
11. Parker, B. C., Shiu, A. S., Maor, M. H., Lang, F. F., Liu, H. H., White, R. A., and Antolak J. A. PTV margin determination in conformal SRT of intracranial lesions. J. Appl. Clin. Med. Phys. 2002; 3, 176–189.
12. Ten Haken, R. K., Balter, J. M., Marsh, L. H., Robertson, J. M., and Lawrence, T. S. Potential benefits of eliminating planning target volume expansions for patient breathing in the treatment of liver tumors. Int. J. Radiat. Oncol. Biol. Phys. 1997; 38, 613–617.
13. Engelsman, M., Damen, E. M., De Jaeger, K., van Ingen, K. M., and Mijnheer, B. J. (2001a). The effect of breathing and set-up errors on the cumulative dose to a lung tumor. Radiother. Oncol. 60, 95–105.
14. Wysocka B, Kassam Z, Lockwood G, Brierley J, Dawson LA, Buckley CA, et al. Interfraction and respiratory organ motion during conformal radiotherapy in gastric cancer. Int J Radiat Oncol Biol Phys 2010; 77: 53–9.
15. Milano MT, Garofalo MC, Chmura SJ, Farrey K, Rash C, Heimann R, et al. Intensity modulated radiation therapy in the treatment of gastric cancer: early clinical outcome and dosimetric comparison with conventional techniques. Br J Radiol 2006; 79: 497–503.
16. Leong T, Willis D, Joon DL, Condron S, Hui A, Ngan SY. 3D conformal radiotherapy for gastric cancer—results of a comparative planning study. Radiother Oncol 2005; 74:301–6.
17. Namysł-Kaletka A, Wydmanski J, Tukiendorf A, Bodusz D, Leszczynski W, Kawczynski R, Grabinska K, Polanowski P. Influence of interfraction motion on margins for radiotherapy of gastric cancer. Br J Radiol. 2015 Apr;88(1048):20140610. doi: 10.1259/bjr.20140610. Epub 2015 Feb 10.
18. Wydmański J, Suwiński R, Półtorak S et al. The tolerance and efficacy of preoperative chemoradiotherapy followed by gastrectomy in operable gastric cancer, a phase II study. Radiother Oncol 2007;82(2):132–6.
19. Wydmański J, Suwiński R, Miszczyk L, Mąka B, Maciejewski B. [Evaluation of tolerance and efficacy of postoperative combined radiotherapy and chemotherapy in locally advanced gastric cancer]. Przegl Lek 2005;62(12):1431–5.
20. Wydmanski J, Mohanti B. An appraisal of radiation therapy techniques for adjuvant and neoadjuvant therapy in gastric cancer. J Radiother Pract 2008; 7(02):67–75.
21. R Core Team. R: A language and environment for statistical computing. R Version 3.0.2. Vienna: R Foundation for Statistical Computing; 2014 «http://cran.r-project.org» Accessed August 29, 2014.
22. Bell L. J., Cox J., Eade T, Rinks M, Herschtal A, Kneebone A. Determining optimal planning target volume and image guidance policy for post-prostatectomy intensity modulated radiotherapy Radiat Oncol. 2015; 10: 151.
23. Shiraishi K, Futaguchi M, Haga A, Sakumi A, Sasaki K, Yamamoto K, Igaki H, Ohtomo K, Yoda K, Nakagawa K. Validation of Planning Target Volume Margins by Analyzing Intrafractional Localization Errors for 14 Prostate Cancer Patients Based on Three-Dimensional Cross-Correlation between the Prostate Images of Planning CT and Intrafraction Cone-Beam CT during Volumetric Modulated Arc Therapy. Biomed Res Int. 2014; 2014: 960928.
24. Glowacki G, Majewski W, Wojcieszek P, Tukiendorf A, Bodusz D, Wozniak G, Miszczyk L.
25. Daily image-guidance in prostate cancer radiotherapy - implications for treatment margins. Neoplasma. 2015; 62(2):326-31. doi: 10.4149/neo_2015_039.