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FULL PAPER

The use of new delineation tool "MIRADA" at the level of regional lymph nodes, step-by-step development and first results for early-stage breast cancer patients

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Objective: To describe the practical procedure of implementation and optimization of delineation using "Mirada" software, as well as evaluation of the automatic segmentation for the daily practice of lymph nodes (LN) and organs at risk (OARs) in early stage breast cancer patients.
Methods: 40 patients' CT scans in treatment position were selected and recontoured according to the European Society of Therapeutic Radiation Oncology guidelines. The atlas of data set was then created for automatic delineation. 30 patients with breast/chest wall and lymph nodes regions irradiated were recruited for evaluation. With the same treatment position, the CT scan images were acquired and then contoured by the MIRADA system automatically as well as by the radiation oncologist manually (as the reference). The conformity index (CI) was used to evaluate the concordance between both of them.
Results: The mean time for manual contour was 24.1 ± 5.1 and 26.4 ± 2.8 min for the LN and the OARs respectively. All the volumes of interest were contoured using the software (including corrections) in 30 min, which reduced the time of delineation of target volumes and OAR by about 40%. Of the 30 cases evaluated, the mean CI of 5 principal OARs showed ≥0.8. While the automatic contour of LN was less satisfactory with mean CI of 0.43 ± 0.1 (0.23–0.52).
Conclusion: For the breast cancer patients, the studied software permitted to save time for delineation with acceptable OAR contours. The improvement of LN regions contour is needed. More cases and further evaluation are needed for the system to realize its routine use.
Advances in knowledge: It's the first description and evaluation of the automatic delineation and segmentation system for the breast cancer.

INTRODUCTION

The delineation of target volumes is one of the key steps in the preparation of a radiotherapy treatment plan of intensity modulated radiotherapy (IMRT, as well as the good quality three-dimensional conformal RT. However, the IMRT needs the strict delineation of the target volumes as well as the organs at risk (OARs) of breast cancer (BC) patients, which is a time-consuming process.[1] On the other hand, major differences in anatomical and radiological delineation for BC RT were observed among the physicians,[2] which is why international recommendations and radioanatomy atlases are regularly updated, reducing this variability.[3]

The development of computer systems and the improvement of the images processing makes it possible to develop software for delineation automatically for radiation therapy. In this study, firstly we tried to optimize the delineation procedure in the population of BC patients with the automatic contouring software Workflow Box (Mirada Medical,Oxford, UK). As the second point, we tried to homogenize practices and improve the reproducibility. The purpose of this work is to report the development of this procedure and its use in the routine clinical practice.

METHODS AND MATERIALS

Atlas data set creation

40 records of consecutive patients with early stage BC irradiated in our department were selected. Among them, 10 patients were treated on the right breast, 10 on the right chest wall, 10 on the left breast and 10 on the left chest wall. And all the lymph node areas were included. Contrast-enhanced CT images acquisition was performed using a large bore CT-scanner (Aquilion™ LB, Toshiba Medical, Puteaux, France) with 2.5 mm slices. The patients were placed on

the immobilization system in supine position with the ipsilateral arm abducted, free breathing.

The target volumes and the OARs were recontoured by two radiation oncologists according to the recommendations of the European Society of Therapeutic Radiation Oncology Guidelines for target volume delineation[4,5] to obtain homogeneous volume definition and delineation. Eight target volumes as shown below have been delineated using Eclipse, Varian, USA. The time spent contouring manually was recorded.

Breast	CTVp_breast
Chest wall	CTVp_thoracicw
Rotter or interpectoral nodes	CTVn_interpec
Internal mammary chain	CTVn_IMN
Lymph node level 1	CTVn_L1
Lymph node level 2	CTVn_L2
Lymph node level 3	CTVn_L3
Lymph node level 4	CTVn_L4

Then, 13 OARs were contoured by 5 radiation oncologists in a data set of previously presented 40 patients with BC, as following: heart, left anterior descending coronary artery, bilateral lungs, esophagus, humeral head, contralateral breast, spinal cord, thyroid, and brachial plexus ipsilateral. OARs as kidney, spleen, and liver are delineated in all patients who underwent rotational IMRT by tomotherapy or volumetric arc therapy.

These data were transferred from Eclipse, Varian, USA to Mirada Software by the team of physics. These cases were then used to create an atlas in the automatic segmentation software Workflow Box (Mirada Medical, Oxford, UK) serving as a model for the future automatic contours.

Atlas-based segmentation

We recruited 30 patients who received whole breast or chest wall irradiation in our department. Patients with very special anatomy such as pectus excavatum and patients with breast prostheses were excluded from the study. The images were acquired from the same CT scan with same treatment position as they were acquired in the atlas data set.

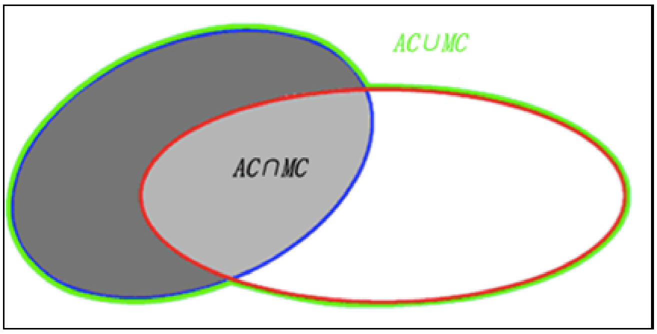
After the images of these patients been imported into the Mirada software, a registration algorithm free form deformation based on Lucas Kanade Optic Flow implementation ($1 \times 1 \times 3$ mm grid size),[4] was used to create the outlines of the lymph nodes target volumes and the risk organs for each of these patients automatically by transforming existing segmentations to the corresponding structures in the current images.

Evaluation

Of the 30 cases for evaluation, 15 cases were irradiated on the left side (10 on the chest wall and 5 on the breast) and 15 cases were on the right side (11 on the chest wall and 4 on the breast). These 30 cases were also contoured by a radiation oncologist according to the recommendations of the European Society of Therapeutic Radiation Oncology.[5,6] The manual contours were acted as a reference for the study. According to our daily practice, the lungs were the only OARs using the semi-automatic contouring tool integrated with Eclipse contouring software (Eclipse 3D v. 13.6, Varian Medical Systems Inc., Palo Alto, CA, USA) which was used to recognize the pulmonary parenchyma instead of manual contouring slice by slice. Then the software Artiview (Aquilab, Loos les Lille, France) analyzed the conformity of the delineation for each patient. The precision of the delineation was evaluated with the conformity index (CI)[7] which represented the ratio of overlapping volume to encompassing delineated volume:

$$CI = \frac{AC \cap MC}{AC \cup MC}$$

CI = Conformity Index
AC = Automatic Contour
MC = Manual Contour



The optimum value of CI is 1, indicating 100% concordance. A CI of 0.50 indicates that the observers agreed on 50% of the encompassing delineated volume, and a CI of 0 indicates no concordance. The variability and differences between the automatic outlines and manual ones were quantified and the standard deviations were calculated.

The volumes evaluated in this preliminary study were the target volumes including lymph nodes regions I, II, III, IV, interpectoral lymph nodes, internal mammary lymph nodes, and the OARs including heart, esophagus, lungs, humeral heads, liver, kidneys, thyroid, spinal cord.

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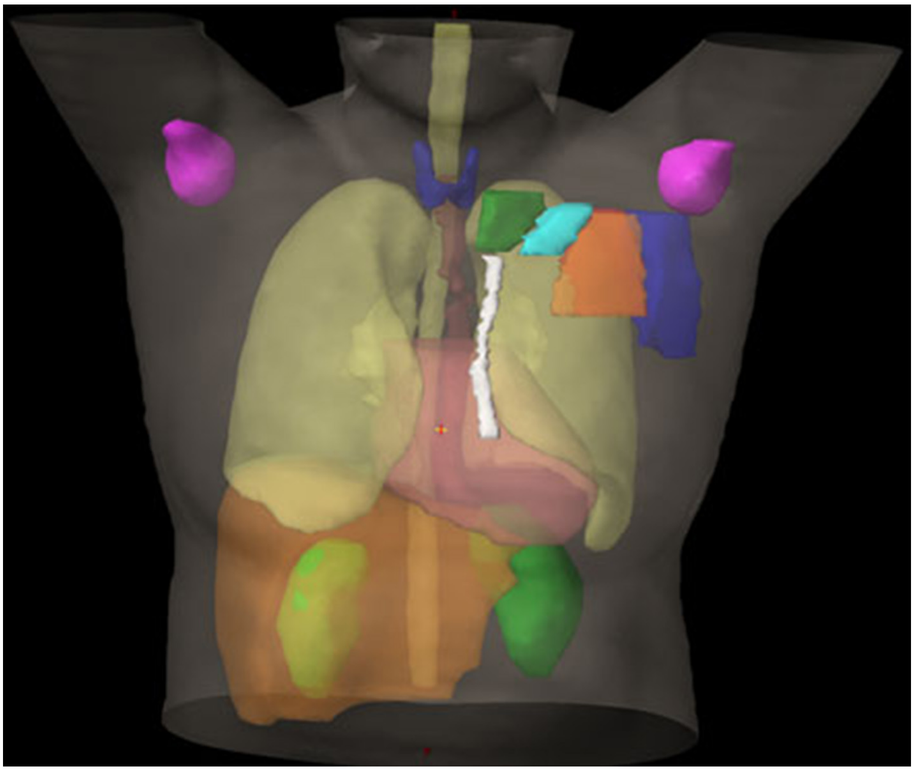
The time that spent on delineation were recorded as well as the time spent on correction.

RESULTS

Eight persons worked in this study, of them four radiation oncologists, two physicists and two were senior dosimetrists. Two radiation oncologists were involved in the delineation of the target volumes. The OARs were contoured by two young radiation oncologists and validated by senior radiation oncologists. Figure 1 showed the three-dimensional reconstruction of the

Figure 1. 3D reconstruction of the volumes of interests: LN—Level I in dark blue, Level II in red, IP in orange, Level III in blue, Level IV in dark green; humeral head in pink, thyroid in violet, esophagus in brown, lungs in yellow, heart in light pink, liver in light brown, kidney left and right in green, spinal cord in yellow. 3D, three-dimensional; IP, interpectoral; LN, lymph nodes.



volumes of interest contoured for this study. The transfer of these data from Eclipse to Mirada Software by the team of physics was realized.

Evaluation of the time

The average time for manual contour was 24.12 ± 5.09 min (mean ± standard deviation) for the ipsilateral lymph nodes regions to obtain satisfaction for the quality and conformity. And the average time for the OARs was 26.44 ± 2.79 min (mean ± standard deviation). While the automatic contour was feasible within 10 min, followed by 20 min corrections and clinical validation. Within 30 min, all the volumes of interest were contoured with the help of the software (including corrections). The automatic contour software has reduced the time spent on delineation of interest volumes (target volumes and OARs) by about 40%.

Evaluation of the OARs

In these 30 cases evaluated, the average CI of these OARs was 0.77 ± 0.17. The lungs were the structure best contoured by the software with the CI of 0.97 ± 0.03, while the thyroid was the worst with the CI of 0.47 ± 0.21. The average CIs in five OARs were greater than or equal to 0.8, while it was less than or equal to 0.5 in only two OARs.

The minimum CI value of the lungs, liver and heart were greater than 0.8, which means that these contours were always consistent with the manual contour. On the other hand, the average CI of the humeral heads was greater than 0.8 but the minimum of which were 0.13 (left) and 0.17 (right). There is, therefore, at least one case of the cohort that was inconsistent with the structure automatically contoured. The CI results for the contours of the risk organs are showed in Table 1.

As for the volumes (cm^3) of the OARs, except the two largest ones (lungs and liver), the software MIRADA tended to contour smaller volumes than those performed by the radiation oncologists. Table 2 compared the volumes (cm^3) of the different contours.

Evaluation of lymph nodes regions

The average CI of lymph nodes regions was 0.43 ± 0.1, with the range from 0.23 ± 0.13 (internal mammary chain, IMN) to 0.52 ± 0.1(lymph node level 1). Except the IMN, other lymph nodes regions were evaluated with the CIs' range from 0.43 to 0.52. Figure 2 shows the difference between the contours of Mirada and those of the radiation oncologists for the lymph nodes regions. The volumes of the lymph nodes regions contoured automatically, same with the OARs, were smaller than those contoured manually (Table 2).

DISCUSSION

In this study, we improved and created our own atlas of delineation for target volumes and OARs in early stage BC patients. And the atlas-based automatic segmentation software—MIRADA, producing an acceptable quality work, allowed a real time-saving work for the radiation oncologists. At the beginning of this work, we selected 13 OARs to create the atlas of delineation in those 40 cases. After that, we found the automatic segmentation software failed in

Table 1. CI of the OARs and the lymph nodes regions

		Mean	SD	Max	Min
OARs	Thyroid	0.47	0.21	0.79	0
	Esophagus	0.51	0.17	0.73	0.23
	Kidney (left)	0.68	0.26	0.92	0
	Kidney (right)	0.71	0.26	0.93	0
	Spinal cord	0.83	0.14	1	0.59
	Humeral head (right)	0.83	0.15	0.98	0.17
	Humeral head (left)	0.85	0.16	1	0.13
	Liver	0.92	0.03	0.99	0.84
	Heart	0.92	0.03	0.99	0.87
	Lungs	0.97	0.03	1	0.9
Lymph nodes regions	IMN	0.23	0.13	0.52	0.04
	I	0.52	0.1	0.67	0.19
	II	0.43	0.11	0.62	0.14
	III	0.45	0.14	0.71	0.13
	IV	0.45	0.11	0.63	0.16
	IP	0.5	0.18	0.77	0

CI, conformity index; IMN, internal mammary chain; IP, interpectoral nodes; LN, lymph nodes; OARs, organs at risk

Table 2.The mean volumes (cm^3) of the automatic contours (Mirada) and the manual contours (references)

		Mirada (mean ± SD)	References (mean ± SD)
OARs	Heart	615 ± 109	622 ± 115
	Liver	1355 ± 316	1282 ± 394
	Kidney (right)	76 ± 45	84 ± 43
	Kidney (left)	97 ± 45	105 ± 42
	Esophagus	21 ± 8	23 ± 4
	Humeral head (right)	50 ± 9	51 ± 7
	Humeral head (left)	49 ± 9	52 ± 7
	Spinal cord	63 ± 14	61 ± 14
	Lungs	1814 ± 769	1764 ± 801
	Thyroid	9 ± 5	11 ± 5
Lymph nodes regions	IMN	5 ± 4	7 ± 3
	I	64 ± 23	72 ± 26
	II	13 ± 5	20 ± 8
	III	11 ± 4	18 ± 5
	IV	10 ± 4	15 ± 5
	IP	10 ± 5	11 ± 5

IMN. internal mammary chain; IP, interpectoral nodes; OARs, organs at risk; SD, standard deviation.

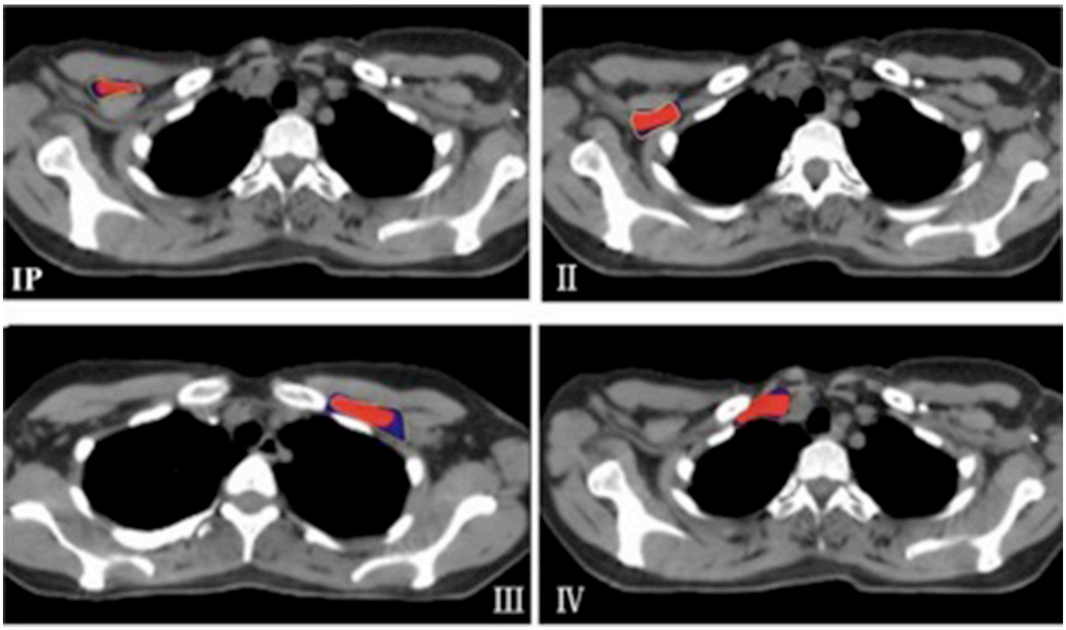
small volumes as the coronaries or brachial plexus. The delineations of them were scattered and only a few slices were contoured. So, we decided to remove these two OARs from our study and to continue to delineate them manually. However, the same problem was then observed in the target volumes as the internal mammary nodes, which was another "small" volume target, with CI of 0.23 ± 0.13. The average volume of IMN in our study was 7 and 5 cm^3 contoured manually and automatically, respectively.

Similar findings were reported by Isambert et al[8] have evaluated an automatic delineation software for cerebral OAR in 11 patients. They reported very similar findings as ours in extremely different localization and they proposed this classification: (i) the "acceptable" region: both the sensitivity and specificity are high. OAR are adequately segmented, thus well-protected, and the number of possibly under irradiated target volume voxels is low, (ii) the "poor" region: the specificity is high and the sensitivity is low. OAR are not sufficiently protected, but the number of under irradiated target volume voxels is low; (iii) the "high risk" region: the sensitivity is high and the specificity is low. The contours of OAR are too large, therefore a neighboring target volume could be under irradiated, (iiii) the "unacceptable" region: both the sensitivity and specificity are low. The automatic segmentation quality is completely unsatisfactory. OARs are not adequately protected and a neighboring target volume could be underirradiated. They found it was a reliable tool for automatic delineation of large structures, the organs that exceeded 7 cm^3. But the smaller structures must continue to be delineated manually by an expert. The important reason we think that may underperform the results in terms of CI level, is the baseline CT slice thickness of 5 mm. It's hard for a software to autodelineate small volume, when we use 5 mm thickness of baseline CT slices.

Many methods exist to compare the automatic segmentation and manual contour. Several indices have been described but their diversity reported makes it difficult to be widely used. The volume index was reported more sensitive in evaluating the errors of overlap.[9] But there is still no consensus on what level of the CI might considered as a threshold for an acceptable conformity between volumes. In this study, the CI levels for most of the OARs were higher than 0.8, which showed a relatively satisfactory concordance. But the CI level for most of the target volumes was around 0.5, which indicated the delineation of lymph nodes volumes was not yet as satisfactory as that of the OARs, and more manual corrections time were needed for the lymph nodes volumes.

The most distinct advantage of the automatic delineation software compare to the manual contour is saving the time. Isambert et al[8] observed that the average time of cerebral OAR delineation was approximately 30–60 min without assistance, while automatic segmentation of OAR was achieved in 7–8 min. Same results were also reported in delineation of pelvic, abdominal and thoracic structures.[10–13] However in these studies, the time spent on the correction of the automatic delineations by the radiation oncologists was not specified. So that the real time saved by the software could not be measured. In this study, we recorded the time spent on the corrections and found 40% of the time was reduced. Moreover, we suspect that the OARs, especially the

Figure 2. Concordance analysis of the contours for some target lymph nodes region realized by the system and the radiation oncologist. In orange: the delineation of reference (manual contour). In red: the overlap between the two contours. In blue: the delineation realized by the system (automatic contour).



big ones, could save more time, although we did not record the correction time for each structure.

With the improvement in the speed of computer calculations and the improvement of algorithms, the automatic delineation tools have grown enormously and have become more and more reliable. They gradually find their place in the radiotherapy treatment, and will most likely be a part of our work tools. However, these tools now are not so efficient to become standard in our daily practice. Since we use a not so large cohort of patients to build the atlas in our study, a multicenter and multiobserver evaluation of these tools is necessary with a sufficient number of patients to evaluate their efficacy, reproducibility and their concordance with recommendations. Currently, large prospective trial is running with 200 prospectively delineated patients in our department to understand better and explain these findings. More importantly, the automatic contour software cannot replace the work of the radiation oncologists. It still needs their review and corrections referring to different clinical situations.

SUMMARY

This study showed that the creation of the contouring atlas is a thorough time-consuming process. The Workflow Box Software (Mirada) is an automatic contouring software that can save time for the radiation oncologists after developing. However, the software remained insufficiently accurate regarding some LN volumes as IMN, as well as the small structures in OAR in BC delineation process. Further clinical validation is still needed before its use in daily practice.

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REFERENCES

1. Smith RP, Heron DE, Huq MS, Yue NJ. Modern radiation treatment planning and delivery-from Röntgen to real time. *Hematol Oncol Clin North Am* 2006; **20**: 45–62. doi: https://doi.org/10.1016/j.hoc.2006.01.006
2. Castro Pena P, Kirova YM, Campana F, Dendale R, Bollet MA, Fournier-Bidoz N, et al. Anatomical, clinical and radiological delineation of target volumes in breast cancer radiotherapy planning: individual variability, questions and answers. *Br J Radiol* 2009; **82**: 595–9. doi: https://doi.org/10.1259/bjr/96865511
3. Kirova YM, Castro Pena P, Dendale R, Servois V, Bollet MA, Fournier-Bidoz N, et al. Simplified rules for everyday delineation of lymph node areas for breast cancer radiotherapy. *Br J Radiol* 2010; **83**: 683–6. doi: https://doi.org/10.1259/bjr/28834220
4. Loi G, Fusella M, Lanzi E, Cagni E, Garibaldi C, Iacoviello G, et al. Performance of commercially available deformable image registration platforms for contour propagation using patient-based computational phantoms: a multi-institutional study. *Med Phys* 2018; **45**: 748–57. doi: https://doi.org/10.1002/mp.12737
5. Offersen BV, Boersma LJ, Kirkove C, Hol S, Aznar MC, Biete Sola A, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer. *Radiother Oncol* 2015; **114**: 3–10. doi: https://doi.org/10.1016/j.radonc.2014.11.030
6. Offersen BV, Boersma LJ, Kirkove C, Hol S, Aznar MC, Sola AB, et al. ESTRO consensus guideline on target volume delineation for

elective radiation therapy of early stage breast cancer, version 1.1. *Radiother Oncol* 2016; **118**: 205–8. doi: https://doi.org/10.1016/j.radonc.2015.12.027

7. Struikmans H, Wárlám-Rodenhuis C, Stam T, Stapper G, Tersteeg RJ, Bol GH, et al. Interobserver variability of clinical target volume delineation of glandular breast tissue and of boost volume in tangential breast irradiation. *Radiother Oncol* 2005; **76**: 293–9. doi: https://doi.org/10.1016/j.radonc.2005.03.029
8. Isambert A, Dhermain F, Bidault F, Commowick O, Bondiau PY, Malandain G, et al. Evaluation of an atlas-based automatic segmentation software for the delineation of brain organs at risk in a radiation therapy clinical context. *Radiother Oncol* 2008; **87**: 93–9. doi: https://doi.org/10.1016/j.radonc.2007.11.030
9. Pasquier D, Peyrodie L, Denis F, Pointreau Y, Béra G, Lartigau É.. Segmentation automatique des images pour la planification dosimétrique en radiothérapie. *Cancer/Radiothérapie* 2010; **14**: S6–S13. doi: https://doi.org/10.1016/S1278-3218(10)70003-2
10. Huyskens DP, Maingon P, Vanuytsel L, Remouchamps V, Roques T, Dubray B, et al. A qualitative and a quantitative analysis of an auto-segmentation module for prostate cancer. *Radiother Oncol* 2009; **90**: 337–45. doi: https://doi.org/10.1016/j.radonc.2008.08.007
11. Pekar V, McNutt TR, Kaus MR. Automated model-based organ delineation for radiotherapy planning in prostatic region. *Int J Radiat Oncol Biol Phys* 2004; **60**: 973–80. doi: https://doi.org/10.1016/j.ijrobp.2004.06.004
12. Rao M, Stough J, Chi YY, Muller K, Tracton G, Pizer SM, et al. Comparison of human and automatic segmentations of kidneys from CT images. *Int J Radiat Oncol Biol Phys* 2005; **61**: 954–60. doi: https://doi.org/10.1016/j.ijrobp.2004.11.014
13. Wang H, Garden AS, Zhang L, Wei X, Ahamad A, Kuban DA, et al. Performance evaluation of automatic anatomy segmentation algorithm on repeat or four-dimensional computed tomography images using deformable image registration method. *Int J Radiat Oncol Biol Phys* 2008; **72**: 210–9. doi: https://doi.org/10.1016/j.ijrobp.2008.05.008