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Practical aspects of intensity-modulated radiation therapy implementation in a Radiation Therapy Clinic with limited resources

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Aim. To compare intensity-modulated radiotherapy (IMRT) with optimized three-dimensional conformal radiotherapy (3D-CRT) for the selected treatment sites weighting benefits and additional labour involved in a busy RT department with limited resources.

Materials and Methods. Two representative cases of locally advanced nasopharyngeal and left large breast cancer treated with 3D-CRT were selected for the study. The prescribed total dose to PTV of the nasopharyngeal cancer case was 66–70 Gy and 50 Gy in the breast cancer case. The labour necessary for different steps of treatment planning and delivery processes of dynamic IMRT and best 3D-CRT was estimated and compared.

Results. Careful analysis of the best 3D-CRT plans with inversely planned IMRT shows that the best compromise in terms of PTV coverage and protection of normal tissues was obtained using IMRT treatment plans. Dose conformation with IMRT was significantly better, with better protection of the parotid gland, spinal cord and the heart. Chiasm dose was similar for both plans in the nasopharyngeal cancer case. In addition, the boost PTV could be irradiated simultaneously with IMRT. The lung in the breast cancer case received a slightly higher radiation dose with IMRT compared to 3D-CRT treatment, but achieved reduction of high dose areas within lung, heart and contra lateral breast. The results show that the average time for IMRT planning was longer than 3D-CRT treatment planning.

Conclusions. The IMRT plan with dose constraints assigned to the PTV allows better dose conformation than the 3D-CRT treatment; however, conventional 3D-CRT plans are adequate for many tumour / normal tissue situations. Advances in control systems and planning systems are continuing to make IMRT easier and faster. At present, in a busy clinic environment, IMRT is worth using for selective patients who can benefit the most from the technology.

Key words: conformal radiotherapy, IMRT, nasopharyngeal cancer, breast cancer

BACKGROUND

Radiation therapy is one of three principle cancer treatment methods which rely strongly on the technological advances in imaging, planning, and treatment delivery. These technologies are essentially competitive, aiming to improve the treatment precision and ultimately improving cure. This process has resulted in a rapid expansion of new technologies for radiation therapy in the last decade (1–3). IMRT is a new conformal radiotherapy technique that uses computer-generated beams to produce high-dose radiotherapy volumes that can avoid irradiation of normal tissues (2, 4). The aims of the current research programs in IMRT are to evaluate the potential benefits of the inversely planned IMRT compared to current radiotherapy techniques, to maximize the efficiency of IMRT delivery, and to implement clinical trials of IMRT for appropriate tumour sites (2, 3).

The use of IMRT has been rapidly growing internationally. This technology is now being used in a multitude of centres and is being incorporated into the treatment of cancers in most anatomical sites, most commonly in head and neck cancer, central nervous system tumours, and prostate cancer. In addition, current protocols are investigating the use of IMRT for the treatment of breast cancer, lung cancer, abdominal/retroperitoneal malignancies, and gynaecological diseases (1, 2).

In general, IMRT methods can be applied to all tumour sites treated by radiotherapy, however, due to a potentially considerable increase in time and effort compared with the standard 3D-CRT for routine treatment planning, equipment quality control (QC), patient related QC, patient setup and delivery; these steps should be well planned and thereby optimized. Furthermore, the tumour sites and clinical circumstances, in which IMRT methods enable the clinician to arrive at ultimate superior dose distribution in target volume and critical structures, should be identified.

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In this paper the authors compare the IMRT and 3D-CRT techniques in two principal sites: head and neck – locally advanced nasopharyngeal tumour and locally advanced breast cancer – where clinical target volumes are of complex shape and lie in close proximity to sensitive tissue. The issues related to the optimization of treatment planning, pre-treatment QC and patient setup, for IMRT application have been recorded and catalogued for presentation.

MATERIALS AND METHODS

Two representative patients, where IMRT may be beneficial, with locally advanced nasopharyngeal cancer and left large breast cancer, originally treated with optimized 3D-CRT, were selected for this study (Table 1). Contouring and treatment planning were performed within Eclipse (Varian Medical Systems) treatment planning system. The GTV and CTV were determined according to the pre-chemotherapy tumour volume in the nasopharyngeal cancer case and to the postoperative anatomical breast and lymph nodes regions in the breast cancer case. For IMRT and 3D-CRT treatment planning 5–10–15 mm isotropic margin was added to CTV to form the planning target volume. The dose constraints assigned to organs at risk (OAR)s led to unsatisfactory PTV coverage, therefore, virtual volumes (VV)s were designed for each patient to satisfactory protect adjacent OARs. The prescribed total dose to PTV of the nasopharyngeal cancer case was 66 Gy (5% reduction of the total dose was made because of undifferentiated carcinoma and for the effort to spare OARs (re-irradiation) and 50 Gy in the breast cancer case for the 3D-CRT treatment plans, and 70 Gy and 50 Gy, respectively, for the IMRT treatment plans. The prescription was made according to the requirements of International Commission on Radiation Units and Measurements Reports No. 50 and No. 62 (5). The designed IMRT treatment plans were compared with 3D-CRT plans. The prescribed total doses to the clinical target volumes for the IMRT plans are shown in Table 2. Labour necessary for different steps of treatment planning and delivery processes of dynamic IMRT and the best 3D-CRT were estimated and compared.

RESULTS

Clinical case of nasopharyngeal cancer

The patient with locally advanced undifferentiated nasopharyngeal tumour T3N1M0 (G3) was irradiated to the same site for lymphoma treatment 8 years ago. The estimated spinal cord tolerance before RT was about 30 Gy. The prescribed total dose to PTV of the nasopharyngeal cancer case was 66 Gy for 3D-CRT (5% reduction of total doses was made because of undifferentiated carcinoma and for effort to spare OARs) and 70 Gy for IMRT. In addition, the IMRT plan was designed in such a way that all the treatment volumes, including the boost PTV, could be irradiated simultaneously. The field setup and dose distribution for the 3D-CRT (7 fields) and IMRT techniques (7 fields) achieved for these methods are demonstrated in Figs. 1A, 1B and Figs. 2A, 2B. Dose conformation with IMRT was significantly better, with a greater protection of the spinal cord. The maximum dose to the spinal cord (0.5 cc) was 34 Gy for 3D-CRT and 21 Gy for IMRT plans. The chiasm dose was similar for both plans in the nasopharyngeal cancer case. It was impossible to designate the whole parotid gland as the volume to protect as far as about a third of the organ was intersecting PTV. The clinical decision was to minimize the mean dose to the rest of parotid without compromising the PTV dose coverage. A much better protection, below the tolerance of the whole organ (30 Gy of mean dose), was possible to achieve for IMRT technique. The resulting DVH comparison for target volume as well as for OAR is shown in Fig. 3.

Clinical case of left breast cancer

Three types of targets for planning were set: a) large breast with the loge of tumour b) left internal mammarian lymph nodes and c) left supraclavicular and axillary lymph nodes. The case was evaluated using 3DCRT and IMRT planning. The established fields and dose distribution for the 3D-CRT (4 fields) and IMRT techniques (6 fields) are demonstrated in Figs. 4 and 5. The maximum target dose was equal for both techniques. Improvement of dose-homogeneity within PTV and improvement of conformity was shown in the IMRT plan comparable with the 3D-CRT

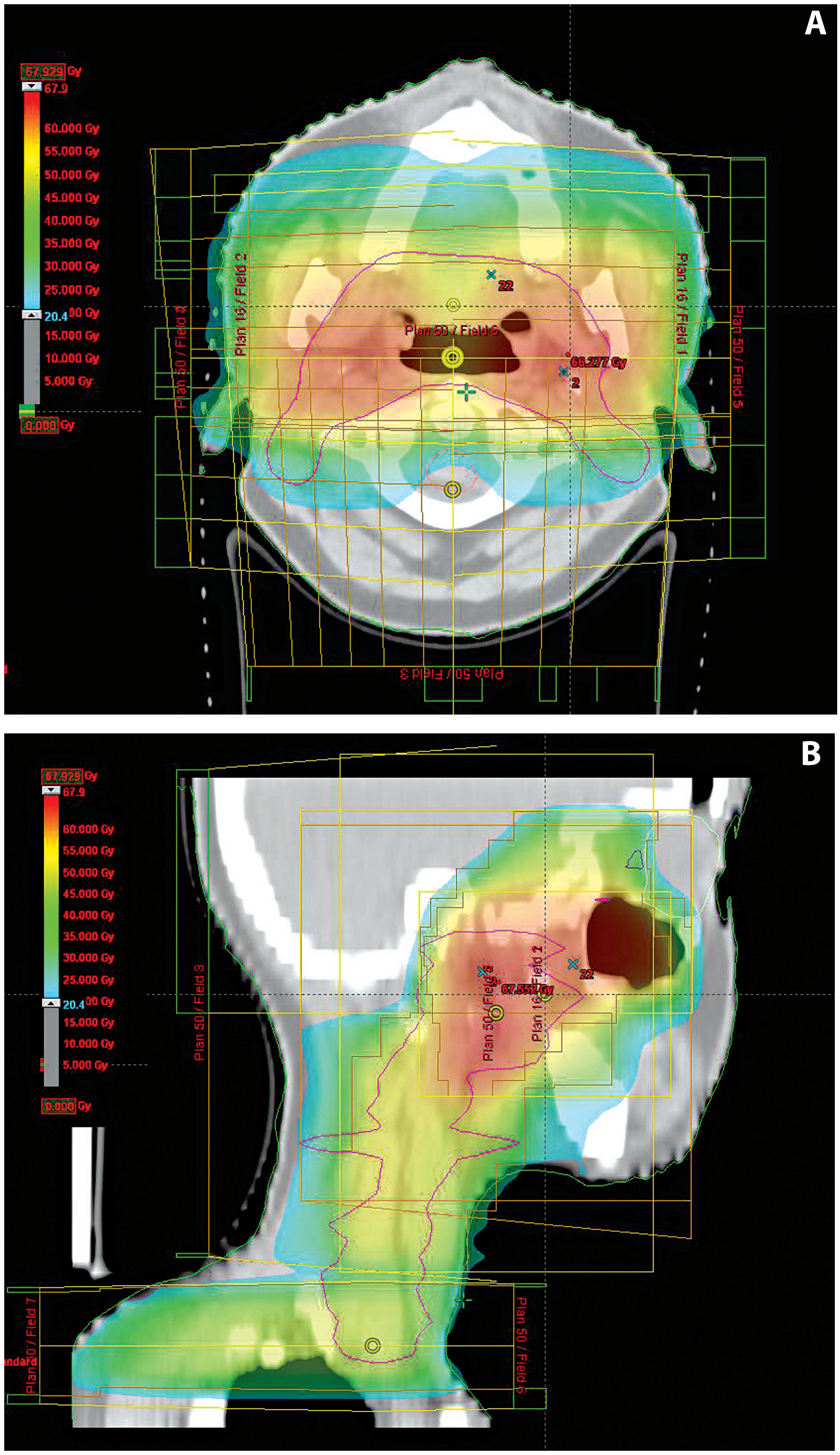
Table 1. **Presentation of clinical cases**

Treatment options	Nasopharyngeal (undifferentiated) cancer cT3N1M0	Breast cancer pT2N2M0 (G3)
Surgery	–	Quadrantectomy with axillary lymphadenectomy
Radiotherapy type	re-irradiation# concurrent with 3 cycles of Cis*	Adjuvant radiotherapy (12 weeks after surgery)
Adjuvant chemotherapy	3 cycles (Cis*)	6 cycles (AC**)

* Cisplatin; ** Adriamycin + Cyclophosphamide; # the patient was irradiated to the same site for lymphoma treatment 8 years ago with 40 Gy (20 fractions)

Table 2. **Dose prescription for IMRT in nasopharyngeal and breast cancer cases**

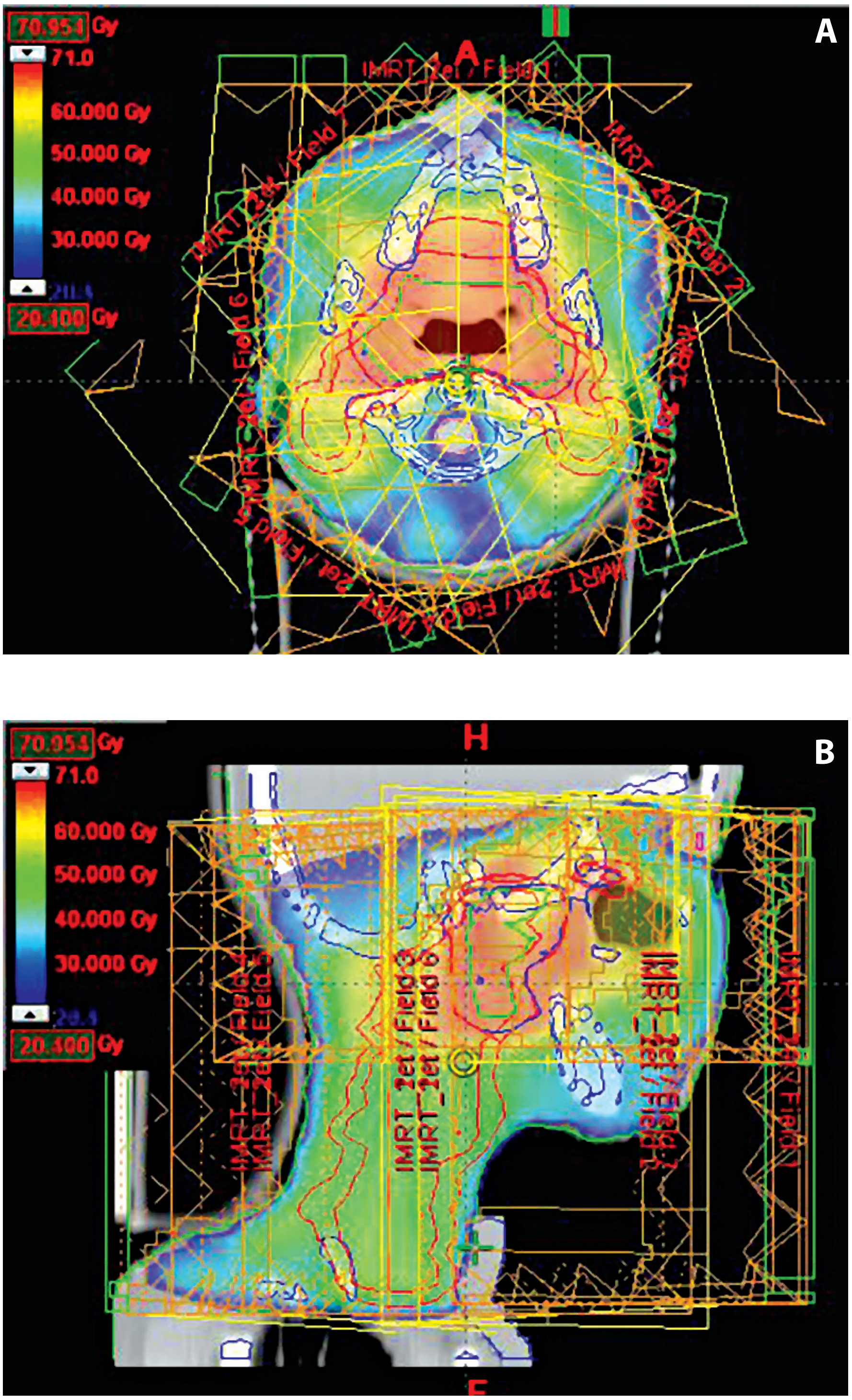
Nasopharyngeal cancer (cT3N1M0(G3))		
Target	Definitive IMRT with chemotherapy (35 fr.)	Dose specification
CTV1	Gross tumor (primary and enlarged nodes) with margin based on clinical and radiological justification	70/2 Gy
CTV2	Soft tissue and nodal regions adjacent to the CTV1	63/1.8 Gy
CTV3	Elective nodal regions	56/1.6 Gy
Breast cancer (pT2N2M0 (G3))		
Target	Postoperative IMRT (25 fr.)	Dose specification
CTV1	Left breast and tumor loge with margin based on radiological justification	50/2 Gy
CTV2	Elective nodal regions	48.6/1.8 Gy



Figs. 1A, B. Field setup and dose distribution for the 3D-CRT plan of nasopharyngeal cancer case (7 fields)

plan; however, a slightly better protection of the heart and coronary arteries was achieved for 3D-CRT plan. Volume of 30 Gy (V30) for the heart was 10% for 3D-CRT and 6% for IMRT plans. The integral dose for the heart as a whole organ at the same time was significantly higher for IMRT plan. The lung in this cancer case received a higher integral radiation dose with IMRT treatment, however, the good indicator of lung complication probability – volume of lung tissue receiving more than 20 Gy (V20) – was only marginally different for two techniques: 20% for 3D-CRT vs. 24% for IMRT. The resulting DVH comparison for target volume as well as for OAR is shown in Fig. 6.

A detailed comparison of the best 3D-CRT plans with inversely planned IMRT indicates that the best compromise in terms of PTV coverage and protection of normal tissue was obtained using the IMRT treatment plans. In addition, we investigated the overall duration of treatment planning, simulation and treatment sessions for both clinical cases realizing the 3D-CRT and IMRT plans. The treatment delivery time for the two representative



Figs. 2A, B. Field setup and dose distribution for the IMRT plan of nasopharyngeal cancer case (7 fields)

Table 3. **Overall duration of treatment planning, simulation and treatment sessions for both clinical cases in the 3D-CRT and IMRT plans:**

Planning	3D-CRT	IMRT
CT + contouring	35 min	50 min
physicist calculation	120 min	150 min
pts. quality assurance	–	50 min
simulation	60 min	25 min
data acquisition	60 min	60 min
	275 min	**335 min**
Treatment		
First session	30 min	20 min
Consequent sessions	15 min	15 min

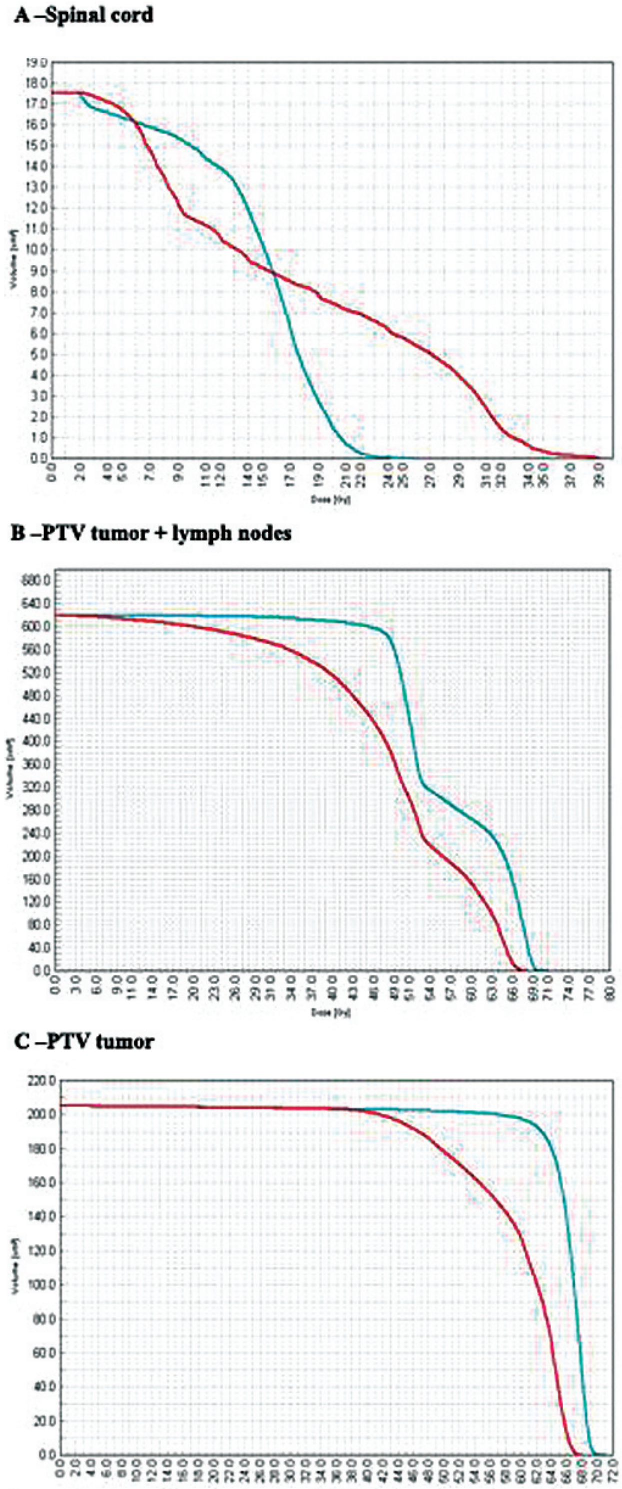


Fig. 3. Comparison of DVHs between IMRT and 3DCRT plans in nasopharyngeal cancer case (curves for IMRT plan marked in blue, and 3DCRT plan in red)

patients with locally advanced nasopharyngeal cancer and left large breast cancer by observing the variations of the planning steps and treatment was evaluated (Table 3).

The results show that the average time necessary for IMRT planning was 1 hour longer than that for 3D-CRT treatment planning, whereas the average time reduction in absolute treatment delivery depends upon the duration of the first session.

DISCUSSION

IMRT represents a significant advance in conformal radiotherapy. IMRT plans for concave shape targets display the greatest improvements compared to conventional and 3D-CRT. The benefits are greatest for tumours where normal tissue structures within the concavity should be spared. For non-concave tumours, dose homogeneity is improved compared to current techniques, and, for all the tumour sites studied to date, a proportion of normal tissue sparing was observed (1, 4, 6).

Head and neck cancer is a suitable tumour site for assessing these technologies since this region can be readily immobilized. Head and neck squamous cell carcinoma displays a clear radiation dose, response relationship, with both the probability of tumour control and the risk of radiation-induced normal tissue damage (increasing with the radiation dose). The OARs include spinal cord, brain stem, optic nerves, oesophagus, and salivary glands that often lie very close to the target volume which commonly has an irregular concave shape. IMRT reduced the dose to the spinal cord by more than 12% and achieved the optimum PTV dose distribution in all the patients tested. IMRT has demonstrated a decrease in acute and late toxicities without compromising tumour control (6–9). Radiation therapy may also lead to sensor neural hearing loss, particularly when radiation is delivered in combination with chemotherapy. Hearing loss occurs more frequently in patients whose cochlea received ≥70 Gy, especially in case of re-irradiation. Unfortunately, the cochleae are often within or adjacent to the high dose target in the nasopharynx and could easily receive doses in excess of 70 Gy (10). Only using IMRT techniques we can adequately spare the cochlea.

We achieved similar results with IMRT plan in nasopharyngeal cancer case with spinal cord and brain stem sparing, and a better protection of parotid gland was also possible. This clinical situation was especially important for sparing OARs, because this case was that of re-irradiation. However, the total dose to the chiasm was similar for both 3D-CRT and IMRT plans.

At present, IMRT is not a standard treatment for head and neck cancers, however, selected patients could benefit from this new technology (7–9, 11).

IMRT is preferable in the treatment of left breast cancer since the target volume is located near the chest wall in close proximity to the heart, lung, and some other OARs or critical dose point, so these critical structures cannot be adequately protected while administrating standard 3D-CRT. IMRT is not routinely used in breast cancer treatment. Current evidence on IMRT usage in breast cancer treatment is limited to descriptive studies, evaluations of technical feasibility, and dosimetric planning studies; there is lack of evidence from clinical outcome studies, and there are no clinical outcome studies that directly compare the effectiveness of IMRT to 3D- CRT for breast cancer (12).

Although dosimetric planning studies have identified differences in uniformity of dose distribution between IMRT and standard 3D-CRT, a number of direct comparative studies have found these differences to be small and of questionable clinical importance (13). In addition, movements in the thorax from respiration and the heart pose special challenges to the application of IMRT for breast cancer cases. Guidelines from the National Cancer Institute (2005) explain that respiratory mo-

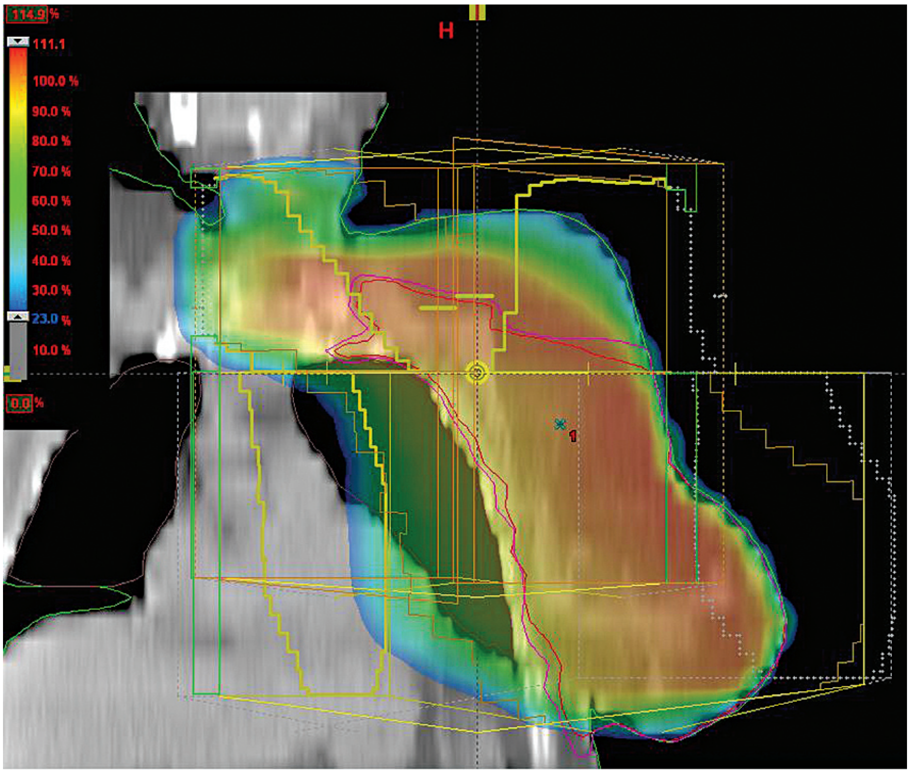


Fig. 4. Field setup and dose distribution for the 3D-CRT plan of left large breast cancer case (4 fields)

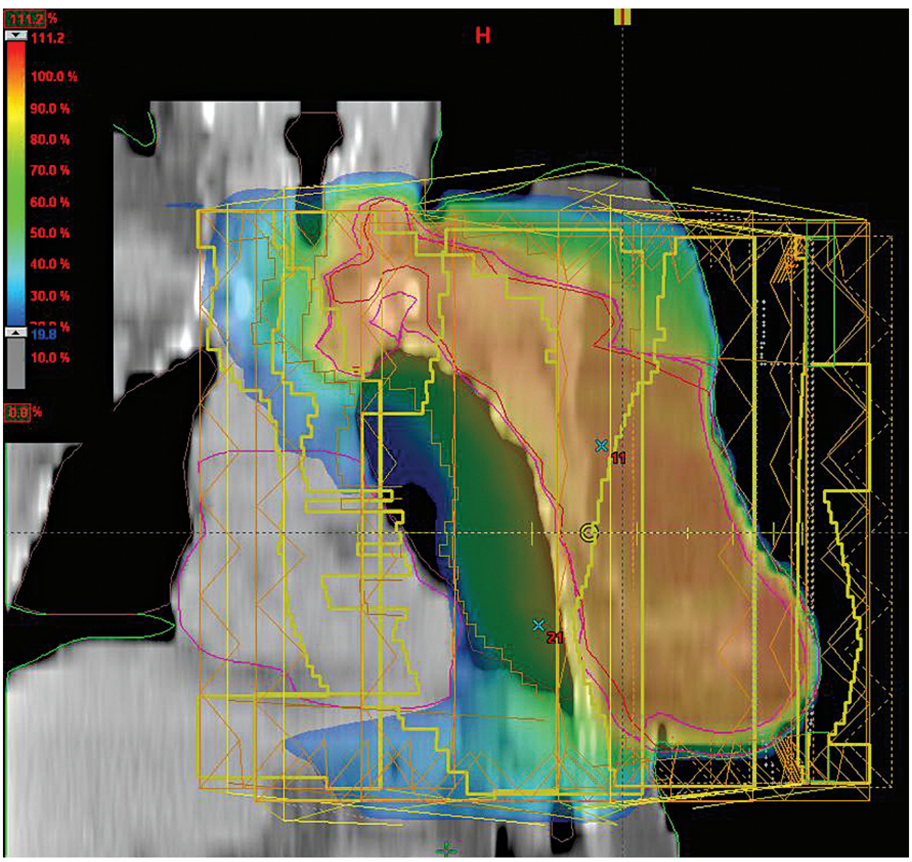


Fig. 5. Field setup and dose distribution for the IMRT plan of left large breast cancer case (6 fields)

tion can cause far more problems for IMRT treatments than for traditional ones. The data available are insufficient to determine whether IMRT is superior to 3D CRT for improving health outcomes of patients with breast cancer (11).

Other authors stated that irradiation of the breast and the regional lymph nodes areas showed a substantial improvement of the dose distribution by inversely planned IMRT compared to 3D-CRT. They noted the benefits of intensity-modulated tangential beams in the irradiation of the intact breast. The authors stated that intensity modulation with a standard tangential beam arrangement significantly reduces the dose to the coronary arteries, ipsilateral lung, contralateral breast, and

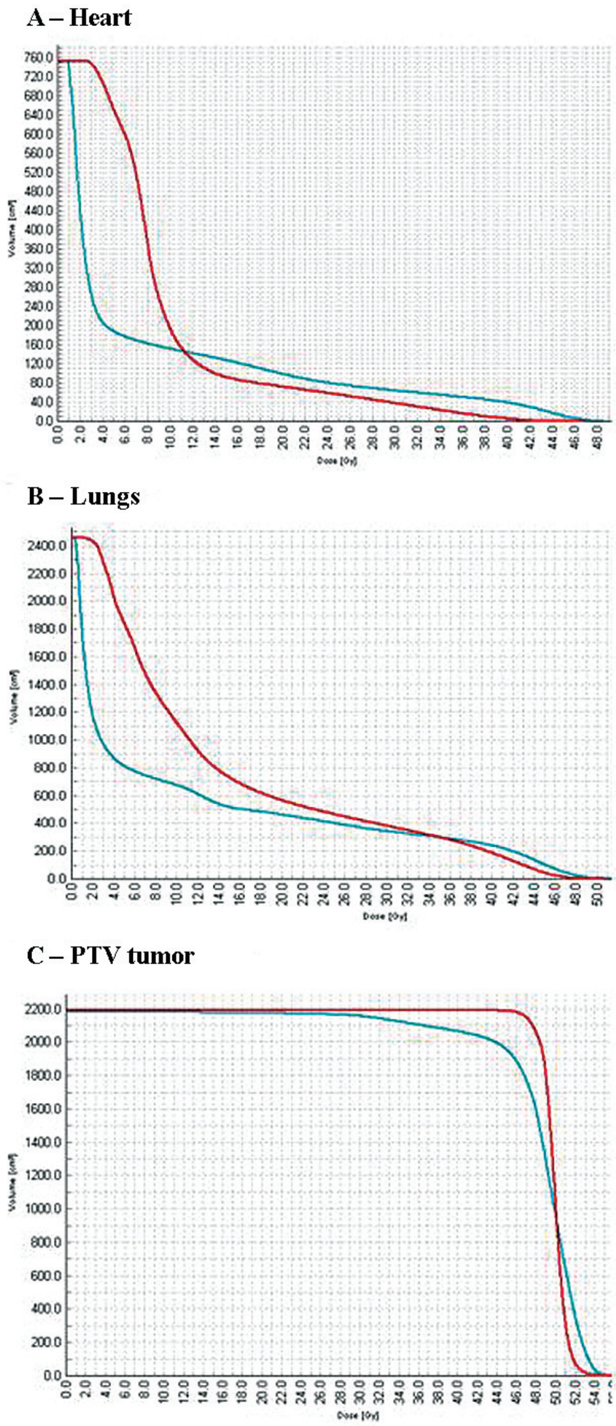


Fig. 6. Comparison of DVHs between IMRT and 3DCRT plans in left breast large cancer case (curves for IMRT plan marked in red, and 3DCRT plan in blue)

surrounding soft tissues. They concluded that despite an increase in integral dose to the entire normal tissue, the application of IMRT might be clinically advantageous in cases where no satisfactory dose distribution can be obtained by 3D-CRT (14–17).

Other clinical data concerning the relationship between the primary breast volume and dose received by the ipsilateral lung, heart (for left-breast cancers) and contralateral breast during primary breast irradiation using IMRT show, that that the primary breast size significantly affects the scatter dose to the contralateral breast but not the ipsilateral lung or heart dose when using IMRT for breast irradiation (18).

In this study employing IMRT planning, improvements in dose homogeneity throughout the target volume were achieved, particularly in the superior and inferior regions of the breast, a better protection of the heart was displayed. However, the lung for investigated cancer case received a slightly higher radiation dose with IMRT compared to 3D-CRT treatment. Only a small reduction of high dose region within lung, heart and contralateral breast was observed using IMRT technique. We hypothesize that the dosimetric improvements achievable with IMRT can potentially lead to significant clinical outcome improvements only when 3D-CRT plans are not satisfactory. To date, there are no evidence-based guidelines concluding that IMRT is the standard of care for radiation therapy of breast cancer as such evidence based on clinical data is insufficient.

Guidelines of the National Cancer Institute (2005) on the use of IMRT in clinical trials summarize that "IMRT is still a nascent technology." Furthermore: "Currently, most published reports on the clinical use of IMRT are single institution studies, and it is either treatment planning studies for a limited number of cases showing the improvement in dose distributions generated by IMRT, or dosimetric studies confirming IMRT treatment". There are not enough prospective randomized clinical studies published concerning the effect of the use of IMRT on the clinical outcomes. Another specific concern is that a widespread use of IMRT could lead to a growing incidence of radiation-therapy-associated carcinomas due to a larger volume of normal tissue exposed to low doses and because of the increase in dose in the whole body as a result of the increased doses of radiation required for the delivery of IMRT (11, 19).

Evaluation of technical and clinical aspects of dynamic IMRT and best 3D-CRT allow us to conclude, that some clinical problems can be appropriately solved by relatively simple (but clever) forward 3D plans, so that IMRT is not required, especially in an RT Clinic with limited resources. Some clinical problems cannot be adequately solved with 3DCRT without compromising tumour coverage or normal tissue constraints – in these cases inversely planned IMRT is a more appropriate approach.

Our results show that the time spent for contouring and patient-related QA during IMRT planning makes this treatment method planning procedure generally longer than that of conventional radiotherapy. A detailed comparison of another labour necessary for different steps of treatment planning and delivery processes of dynamic IMRT and best 3D-CRT shows similar time required for both techniques.

CONCLUSIONS

1. Conventional 3DCRT plans are adequate for many tumour/normal tissue situations.

2. Inversely planned IMRT with conventional multileaf collimators is now a practical and reliable method, which can be implemented even in an RT clinic with limited resources.

3. Complex situations (such as head and neck cancer) can benefit significantly from IMRT.

4. Advances in control systems and planning systems are continuing to make IMRT easier and faster.

5. At present, IMRT is best to use for selective patients who can benefit the most from the technology (re-treatment, difficult head and neck cancer cases).

List of abbreviations

IMRT – intensity-modulated radiotherapy
3D-CRT – three-dimensional conformal radiotherapy
GTV – gross tumor volume
CTV – clinical target volume
PTV – planning target volume
QC – quality control
OAR – organ at risk
VV – virtual volume
DVH – dose volume histogram

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

A. Plieskienė treated the patients, A. Miller and S. Popov performed radiotherapy treatment planning. All the authors performed the clinical analysis as well as wrote and revised the article critically for important intellectual content. All the authors read and approved the final manuscript.

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MODULIUOTO INTENSYVUMO SPINDULINĖS TERAPIJOS PRAKTINIAI ASPEKTAI RIBOTŲ RESURSŲ KLINIKOJE

Santrauka

Darbo tikslas. Palyginti moduliuoto intensyvumo spindulinės terapijos (MIST) metodą su trijų dimensijų konformalios spindulinės terapijos (3D-KST) metodu švitinant galvos-kaklo ir krūties piktybinius navikus ir įvertinti metodų klinikinę naudą bei laiko sąnaudas.

Medžiaga ir metodai. Palyginamajai analizei parinkti vietiškai išplitusio nosiaryklės vėžio ir didelės kairės krūties vėžio klinikiniai atvejai. Parengti MIST planai palyginti su kasdieninėje praktikoje naudojamu 3D-KST metodu. Nustatytos ir palygintos abiejų metodų pagrindinių spindulinės terapijos etapų laiko sąnaudos.

Rezultatai. Išsami rezultatų analizė rodo, kad geresnis dozės homogeniškumas išgaunamas MIST metodu, geriau apsaugomi kritiniai organai – seilių liaukos, širdis, nugaros smegenys, plaučiai. Naudojant šį metodą simultaniškai sustiprinama dozė navike arba jo guolyje.

Gauti rezultatai rodo, kad vidutinės laiko sąnaudos MIST planavimui yra didesnės negu 3D-KST.

Išvados. Naudojant MIST išgaunamas geresnis dozės pasiskirstymas, tačiau 3D-KST yra pakankama daugeliui onkologijos klinikinių atvejų. Spindulinės terapijos klinikoje su limituotais resursais rekomenduojama MIST atlikti kruopščiai atrinktai pacientų grupei, įvertinant šio metodo klinikinę naudą.