UDC: 616-073 : 615.849.114

THE ROLE OF MODERN MEDICAL IMAGING TECHNOLOGIES AT DISTANT RADIATION THERAPY PLANNING

V. P. Starenkiy
State Establishment «Kharkiv S. P. Grigoriev Institute for Medical Radiology of the National Academy of Medical Sciences of Ukraine», Kharkiv, Ukraine

The possibilities of use of modern multimodal imaging technologies during the distant radiation therapy treatment planning are analyzed. The conditions for carrying out of different modality tomography research for needs of treatment planning are determined. The issues of informativity of the hybrid images for target volume finding are considered.

KEY WORDS: distant radiation therapy, radiation treatment planning, target volume, multimodal imaging, image fusion, computed tomography, positron-emission tomography, magnetic resonance tomography

РОЛЬ СУЧАСНИХ ТЕХНОЛОГІЙ МЕДИЧНОЇ ВІЗУАЛІЗАЦІЇ У ПЛАНУВАННІ ДИСТАНЦІЙНОЇ ПРОМЕНЕВОЇ ТЕРАПІЇ

В. П. Старенький
ДУ «Інститут медичної радіології імені С. П. Григор’єва НАМН України», м. Харків, Україна

Проаналізовані особливості застосування сучасних технологій мультимодальної томографічної візуалізації в процесі планування дистанційної променевої терапії. Визначені умови проведення томографічних досліджень різної модальності для цілей планування променевої терапії. Розглянуті питання інформативності гібридних зображень при визначенні об’ємів мішені.

КЛЮЧОВІ СЛОВА: дистанційна променева терапія, планування променевого лікування, об’єм мішені, мультимодальна візуалізація, злиття зображень, комп’ютерна томографія, позитронно-емісійна томографія, магніторезонансна томографія

РОЛЬ СОВРЕМЕННЫХ ТЕХНОЛОГИЙ МЕДИЦИНСКОЙ ВИЗУАЛИЗАЦИИ В ПЛАНИРОВАНИИ ДИСТАНЦИОННОЙ ЛУЧЕВОЙ ТЕРАПИИ

В. П. Старенький
ГУ «Институт медицинской радиологии имени С. П. Григорьева НАМН Украины», г. Харьков, Украина

Проанализированы возможности применения современных технологий мультимодальной томографической визуализации в процессе планирования дистанционной лучевой терапии. Определены условия проведения томографических исследований различной модальности для целей планирования лучевой терапии. Рассмотрены вопросы информативности гибридных изображений при определении объемов мишени.

КЛЮЧЕВЫЕ СЛОВА: дистанционная лучевая терапия, планирование лучевого лечения, объем мишени, мультимодальная визуализация, слияние изображений, компьютерная томография, позитронно-эмиссионная томография, магниторезонансная томография

Modern imaging technologies are playing an increasingly important role in ensuring the quality of radiation therapy preplanning and realization of radiation treatment. Without exaggeration, we can assume that the development of methods of medical imaging has led to fundamental changes in approaches to planning and implementation of modern radiotherapy (RT). The transition from traditional planar medical images to volumetric tomographic imaging of the body structure caused the need to rethink the principles of radiation semiotics, reconsider pathomorphological characteristics of tumor processes, which could not affect at the strategy of modern radiation treatment.

Now three-dimensional (3D) computer tomographic imaging of different modalities is not only the source of anatomical and topological information about the degree of the prevalence of tumor process and its boundaries, but it is a necessary methodological and technological basis of all phases of modern three-dimensional conformal radiotherapy (3D-CRT) [1, 2]. However, the determination of the place of each of the imaging techniques and the prospects for its use for technological improvement of the radiation treatment is always a relevant task. This is primarily due to the permanent development of imaging technologies themselves: they become not only more clinically informative, but also provide new unique methodological and technical capabilities for distant radiation therapy (DRT) and other treatments for which the use of volumetric anatomical imaging is necessary.

The purpose of this work is analytical review of information about the possibilities and limitations of use of the modern medical imaging technologies from viewpoint of improving the quality of distant radiation therapy planning (DRTP).

The use of visual information for DRTP

During the DRTP the anatomical-clinical and topological analysis of previously obtained radiologic diagnostic images is done. These images allow define (fig. 1): Gross Tumor Volume (GTV); Clinical Target Volume (CTV); Planning Target Volume (PTV); Treated Volume (TV); Irradiated Volume (IV). Also the boundaries of Organs at Risk (OAR) are determined [3]. These data are used for DPTP (selection the optimal number of radiation fields; calculation the individual maps of dose distribution; determining the proper area of capture of the target volume and the evaluation of radiation dose in organs at risk). Thus, all the stages of the DPTP process anyway based on the initial data on the topology of the tumor.

Nearly a century the only source of visual information about the topology of the tumors was classic planar radiograph [4]. A limited number of standard two-dimensional projecttions allowed create a very simplified volumetric model of the target volume; there were no objective visual data for the optimal choice of fields and directions of irradiation. Thus, considerable uncertainty in the distribution

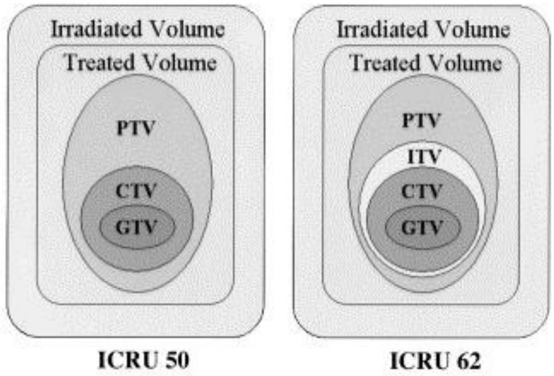


Fig. 1. Schematic illustration of the boundaries of the target volumes defined by ICRU [3]

of doses was formed already at the first stage of treatment planning. In a long time this circumstance restrained the process of improving of DRT equipment. Due to the lack of comprehensive information about the anatomical structure of the patient there was no sense in creation a more effective means of treatment. Patients suffered significant radiation injuries due to excessive irradiation of healthy body parts; it was impossible to simulate accurately the distribution of individual doses of radiation at a given depth and in a given direction. Ideally the shapes of radiation fields has to repeat the outlines of the tumor and dose distribution should provide the most intensive irradiation of the tumor and a sharp decrease of dose in the surrounding tissues. So, for the future there were identified two basic principles of DPT improvement — *conformality* of the radiation fields and *spatial modulation of the radiation intensity* in the therapeutic beam (fig. 2).

The idea of 2D-conformal DPT was realized by applying of standard shielding blocks. Individual dose fields of complex shape created by the beam modifiers — wedge-shaped lead filters and flattening compensators — boluses), which reduced the errors of reproduction of theoretical dose distribution caused by the individuality of the patient's body structure (fig. 3). However, in practice the use of heavy shielding blocks was very uncomfortable, especially for creating of several radiation fields during one treatment session. Boluses were made individually that also required precise anatomical and topographical data and high technological costs. The most difficult was to make correct positioning of all this equipment relative to beam isocentre and ensure its alignment with the target marks on the patient's body. Usually, in practice, irradiation carried out simplistically — by rectangular fields with

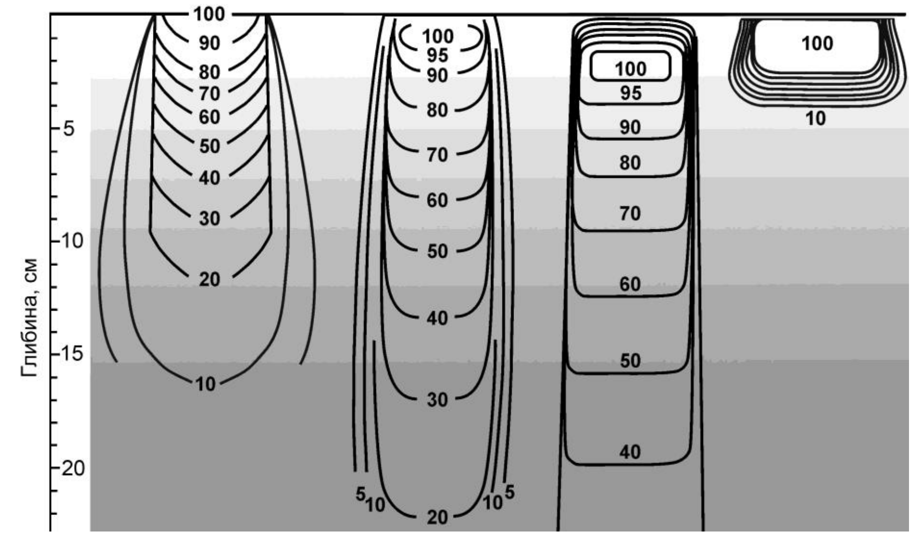
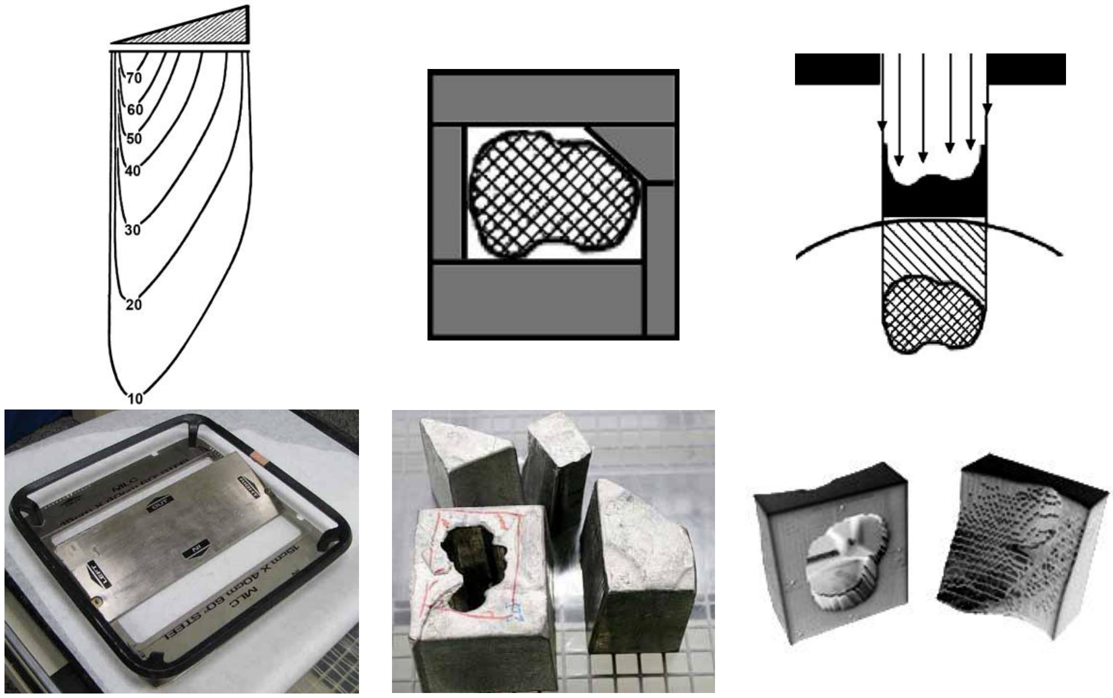


Fig. 2. Charts of depth isodose distribution for photon and electron beams in water:
1 — X-photons 0,2 MeV; 2 — γ-photons ^{60}Co 1,25 MeV; 3 — bremsstrahlung 6 MeV; 4 — electrons 6 MeV



1 2 3

Fig. 3. Means for the forming of individual dose fields:
1 — wedge-shaped filter (http://www-personal.umich.edu);
2 — shielding blocks (http://thestar.com.my/health);
3 — flattening compensators-boluses (http://www.dotdecimal.com)

significant coverage of healthy tissues and non-optimal depth dose distribution. Thus, the development of all technological stages of DRT was constrained primarily due to the lack of comprehensive anatomic imaging.

Computed tomography — an informational basis of modern DRTP technologies

The real breakthrough in the development of radiation therapy was the implementation of a unique method of volumetric anatomical imaging — X-ray computed tomography (CT). Computed tomogram (axial CT scan) is a result of imaging of array of CT numbers (Hounsfield units), calculated after processing of CT scanning data (fig. 4). Computer tomograms are synthesized as digitally reconstructed radiographs (DRRs) which are used to create volumetric (voxel) model of the body — a «virtual patient» (fig. 5). Technology of computed

3D imaging allows synthesizing a virtual cross-section of the body at any given plane [5] (fig. 6). But the most important advantage of CT is the lack of superposition shadows of anatomical structures, their separated imaging (according to CT numbers, computed for them). All these new features allow implementing of previously unavailable technology of 3D-DRTP with calculation of volumetric dose distribution. Generating of patient's anatomical 3D-model allows additional images rendering for each of the selected radiation fields and further use of these images to verify an individual plan of radiation treatment and checkup of patient positioning during irradiation (fig. 6). According to the CT data it is possible to create real volumetric model of tumor. For this purpose up to 100 CT scans can be used, for each of which the contours of the target and outlines of adjacent organs at risk must be marked according to fig. 1. Now, with use the 3D-model of tumor it is possible to accurately identify the boundaries of target for any direction of irradiation. This possibility allowed solving the problem of conformal radiation by another way. The creation of multileaf collimator (MLC) allowed to waive the application of inconvenient protective blocks (fig. 3) and to create technology of automated profiling of therapeutic beam in accordance with the contour of target for each of the planned fields of irradiation (fig. 7, 8). Realization of all the advantages of 3D-DRTP is possible only in case of no less precise technologies of dose delivery which now are based on use of linear electron accelerators. Accelerators deprived of basic disadvantages of cobalt machines (large geometric penumbra of beam, low energy of radiation, non-optimal dose distribution), they are more manageable and easily integrated into a joint hardware-software DRT-complex.

Use of CT technology for DRTP together with the undeniable advantages has several peculiarities which change the standard CT protocol in some aspects [6]:

1. Special flat couch is used for recreate the treatment position of patient, but it is somewhat reduces the CT image quality.

2. It is necessary to use the laser positional indicators which provide coordinate reference marks for reproducible positioning of patient during DRTP verification and radiation treatment.

3. Positioning the patient during CT scanning at once should be the same as for irradiation, if necessary — with use of individual immobilization devices which must be transparent for x-rays.

4. During the scanning shallow breathing is permitted (as during irradiation), but the quality of the CT scans is reduced through the respiratory movements.

5. Quality of 3D-plan for DRT worsens in case of significant changes of volume of patient's fillable organs. It is recommended CT scanning and correction of plan anew.

6. The precise calculation of CT numbers during reconstruction of tomograms significantly affects the accuracy of further calculation of doses. It is important to ensure correct positioning of the patient in the «circle of reconstruction» of CT scanner.

The presence of implants near the target leads to artifacts on CT scans, which worsens the conditions of definition of target volume and dose distribution.

7. Choice of CT slices thickness affects the accuracy of 3D-reconstruction and creation of additional projections (fig. 6).

8. The use of contrast agents in CT scanning makes it easy delineate the tumor and surrounding soft tissues on tomograms, but may affect the accuracy of calculation of doses.

Thus, there are the elements of uncertainty at the use of X-ray CT imaging technology in DRTP, they are caused by the deviation in positioning of patient, target, organs at risk, by features of the CT imaging and its limitations in rendering of the patient's anatomical models. However, CT is the basic technology of data acquisition for adequate dose planning for DRT.Common factor in this process is the use of bremsstrahlung with similar physical nature but with different energy levels. Any other supporting imaging technology which is applied to refine the details of the DRTP should be agreed with the data of CT as the reference method of anatomical and topological visualization and spatial orientation.

Application of tomographic visualization of other modalities for DRTP. Recently, there are actively explored the possibilities of applying tomographic data of other modalities in systems for 3D-CRT planning. Special hopes are assigned to the application of multi-modal and hybrid imaging technologies, which allow co-registration or fusion of medical images of different modalities. Such approach should deepen understanding of metabolic, functional and other factors of the tumor process, which will help improve the algorithms of determining the topology of the tumor and refine DRTP [6, 7].

Development of methods for *emission tomography* and growth of their diagnostic significance in oncology led to review of approaches to the definition of tumor volumes in DRTP. It was proposed the concept of biological target volume — BTV (fig. 8), which provided differentiated dose delivery to the target sub- volumes in accordance with the specifics of their functional state which is detected by diagnostic imaging of other modalities [8]. This is particularly important in determining the boundaries of the CTV (fig. 1), which takes into account the area of subclinical dissemination of tumor that can be visualized by positron emission tomography (PET). Molecular functional imaging with the use of radiopharmaceuticals combined with structural anatomical CT imaging (fig. 10) [9], creates the best conditions for accurate determination of CTV [10]. According to [11] due to the use of hybrid PET/CT technology the following DRTP changes occurred: GTV correction — in 58 % of cases, dose correction — 14 %, configuration of fields — 15 %, choice of other modality of radiation treatment — 5,4 %. Visualization of biological heterogeneities within tumor sub-volumes can be used to adapt the dose according to their local radiosensitivity. PET-technology is prospective not only for the detection of fractions of hypoxic cells, but also to study other specific biological parameters (proliferation, angiogenesis, apoptosis, etc.), which may further modify the existing approaches to defining target volumes and even influence the choice of radiation treatment strategy [12]. Another perspective application of PET is to determine the functional changes in the irradiated volume during radiation treatment and appropriate current adaptation of DRTP. PET study is indispensable in planning DPT for patients after surgery, for which irradiated volume can be adequately estimated only by the result of molecular functional imaging [13]. Peculiarity of emission imaging is that each of radiopharmaceuticals has its own bio-distribution and dynamics of visual characteristics, so the rules of imaging areas of fixing radiopharmaceuticals and contouring of the tumor should be individual for each radiopharmaceutical [14]. Variability of results of determination of the target volume by PET imaging depends on various factors: technical (the dependence of image quality on characteristics of the detecting block of PET scanner, algorithm of visualization), pharmacological (adequately choosing the type of radiopharmaceutical and its activity in a particular clinical case), physiological (features of individual absorption of radiopharmaceutical, uncertainty time limits of studied processes, etc.). With all the unique capabilities of PET imaging there is a physical limit of spatial resolution of these images — about 4 mm in advanced PET systems. Imprecision of the contours of damaged areas, identified on PET images, makes it impossible to make an objective visual estimation of target volume. Only color coding of PET image and its fusion with the appropriate CT scan enables simultaneously compensate deficiencies of PET imaging and limitations of CT in determining the real limits of tumor proliferation. The use of PET imaging in practice gives rise to many questions: how to determine the required PET target volume for DRTP, who can mark the contours of PET target volume: radiologist-oncologist or a physician of nuclear medicine? The experience of radiologists is proved that the use of emission tomography is indisputably an important factor in improvement of radiotherapy. However, experts not in vain called this method is «Pandora's Box»: it is important to achieve a correct interpretation of the obtained information and apply it for the benefit to the aim pursued — improving the quality of DRTP [15].

Method of *magnetic resonance imaging* (MRI) is indispensable for planning radiation treatment of tumors in soft tissues because in such cases CT imaging is uninformative due to small tissue contrast. The rich palette of MRI imaging modes allows you to select the best conditions for imaging of tumor, contours of which are detected due to the difference of nuclear magnetic resonance signals from tumors compared to normal surrounding tissues. MRI visualization of brain structures (fig. 11), chest, abdomen and pelvis in many cases is more informative for determine the PTV, than the corresponding CT images [16].

However, MRI technology has particular warnings to be taken into account when it used for DRTP. Necessary that when laying the patient on MRI in radiotherapy position used immobilization devices did not prevent properly positioning RF coil (fig. 12, 13). On MRI images with a large field of view the geometric distortions can be formed due to the nonli-

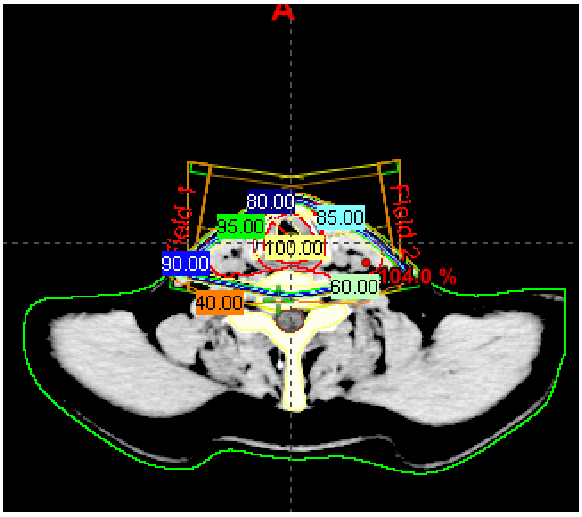


Fig. 4. CT-scan with chart of isodoses

Fig. 5. Voxel CT-anatomical model

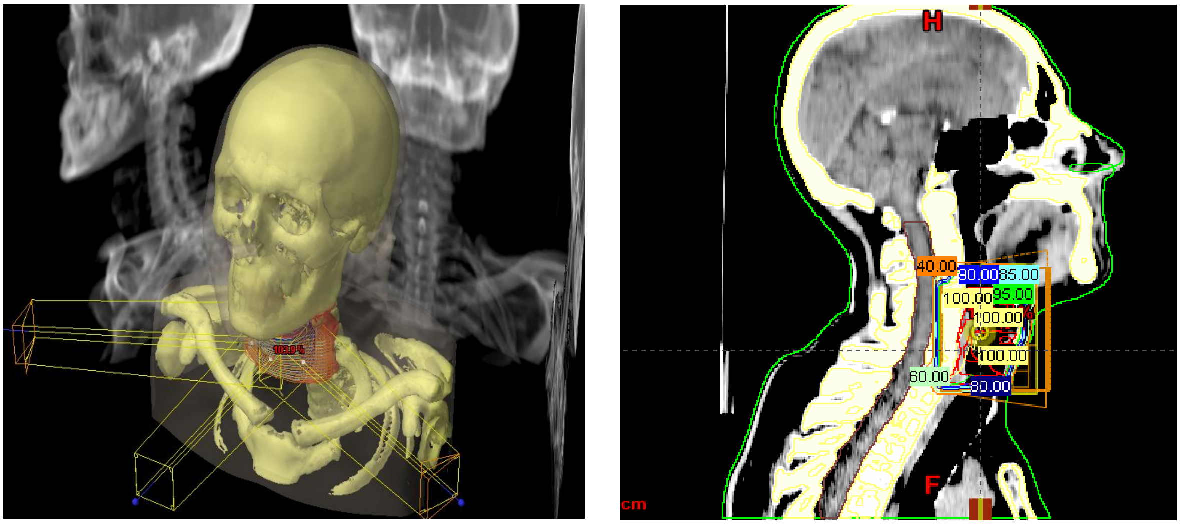


Fig. 6. Simulation of 3D dose distribution and synthesis of additional CT-anatomical projections

Fig. 7. Multileaf collimator (MLC)

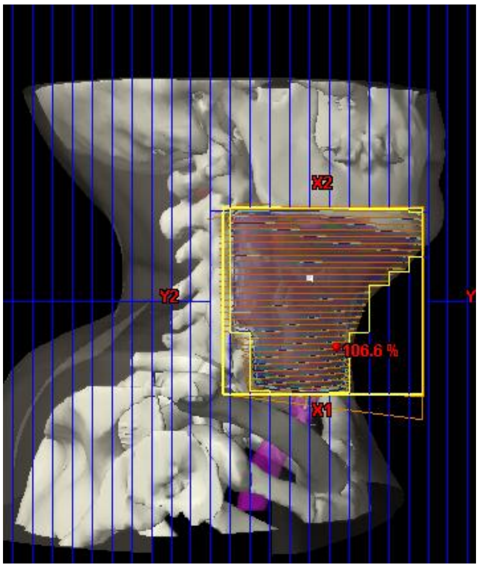


Fig. 8. Programmed positioning of MLC plates according to the target contour

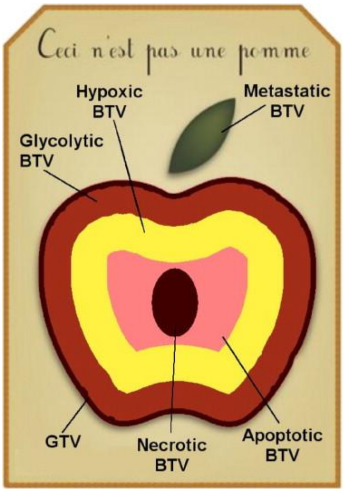
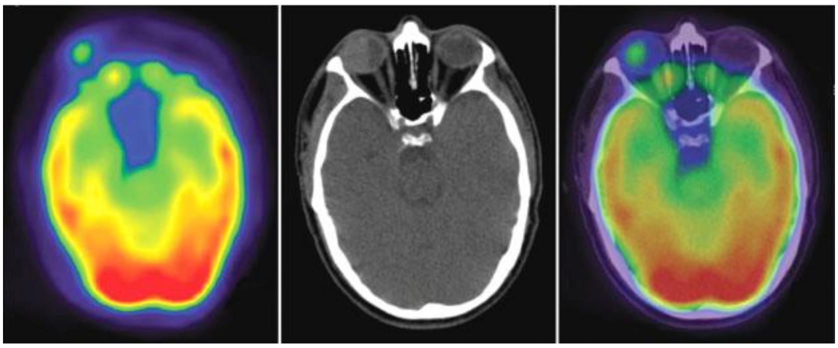


Fig. 9. R. Magritte. BTV mosaic



PET CT PET/CT

Fig. 10. Tomografical visualization of choroidal melanoma [9]. Focus of hypermetabolic activity in the intraocular tumour

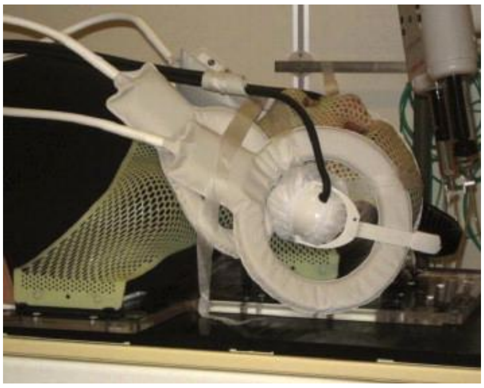
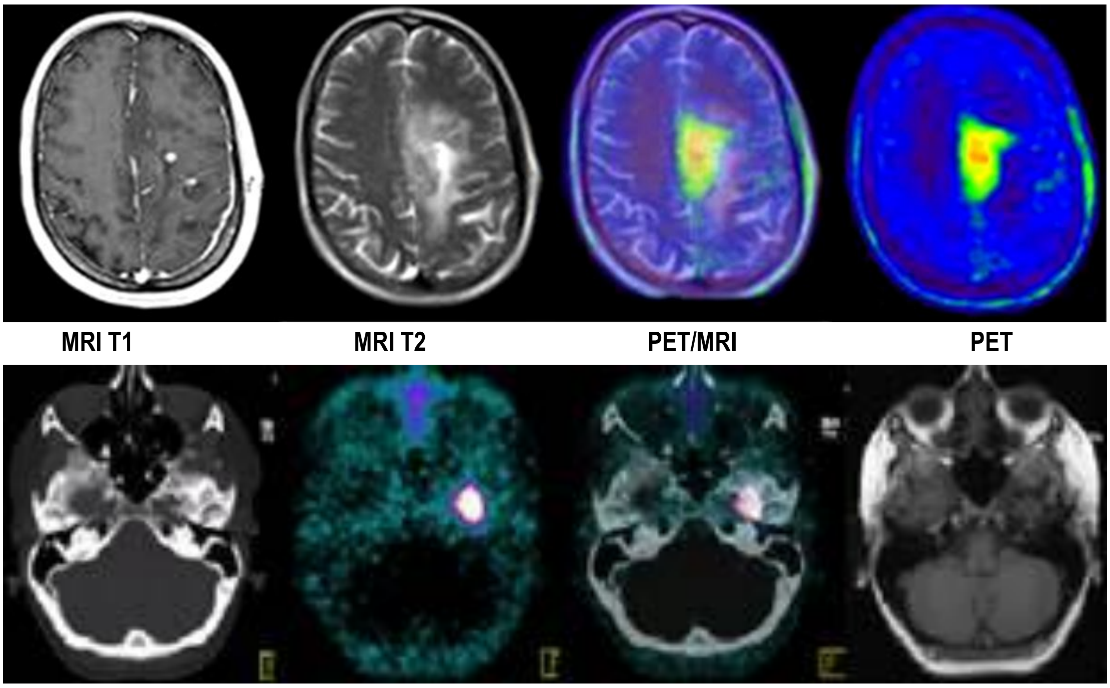


Fig.12. Head coil for MRI, attached to a radiotherapy fixation mask [19]

Fig. 13. MRI Head Coil for DRTP (http://www.hellotrade.com/magmedix)



1

MRI T1 MRI T2 PET/MRI PET

2

CT PET CT/PET MRI

Fig. 15. The results of tumor detection on CT/PET/MRI-scans (http://www.vivantes.de)

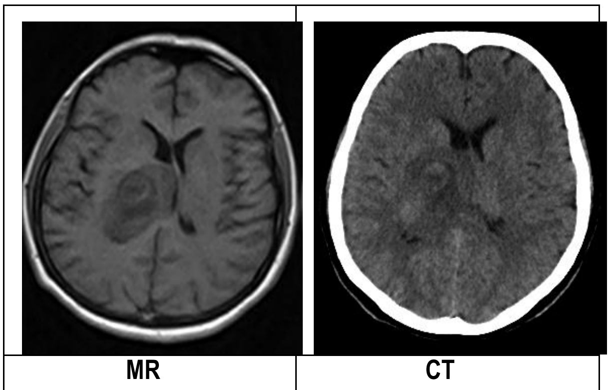


Fig. 11. Brain astrocytoma on MRI and CT-scans [16]

nearity changes the gradients of magnetic field. Unlike CT, MRI studies are lengthy procedure in which it impossible to avoid motion artifacts on MR scans that affect the accuracy of the GTV determining. In radiotherapy MRI mainly used as a duplicate method for anatomical imaging of tumors. But now actively explored the possibility of using MRI instead of CT for DRTP [16]. It is important to remember that there is no match between the intensity of MR signals from protons in tissues and the values of the electron density of the same tissues on CT images. In [17] made an attempt to modify MR images with replacement values of its intensity on CT numbers using the standard data on the density of the tissues [18]. It is proved that this modified MR image can be successfully used instead of CT without losing accuracy of calculation of doses. This avoids excessive radiation load on the patient, systematic errors due to fusion of MR and CT images and reduces the costs for additional CT study. In [19] pointed out that the best option in determining the GTV for DRT of prostate is a fusion of CT and MR images made in radiotherapy position of patient. Are studied the possibilities of use functional MRI (fMRI) with contrast enhancement to estimate radiosensitivity of tumor and identify areas that need more intensive irradiation [20].

Discussion features of applying hybrid tomographic images in DRT

The performed review of modern approaches to determining tumor volume shows that the use of hybrid multi-modal imaging technologies for DRTP doesn't give unequivocal results and requires thorough study [21]. The results of an experiment to determine the GTV using various combinations of tomograms are shown in fig. 14. The results show that in determining the GTV of studied tumor the growth of target volume through the use of PET was low. The added volume through the use of MRI is significantly influenced the result of a common definition of GTV. One can predict that degree of influence each method of tomographic imaging on the result of determining GTV will vary depending on the histopathological type of tumor and clinical estimation the pathological process.

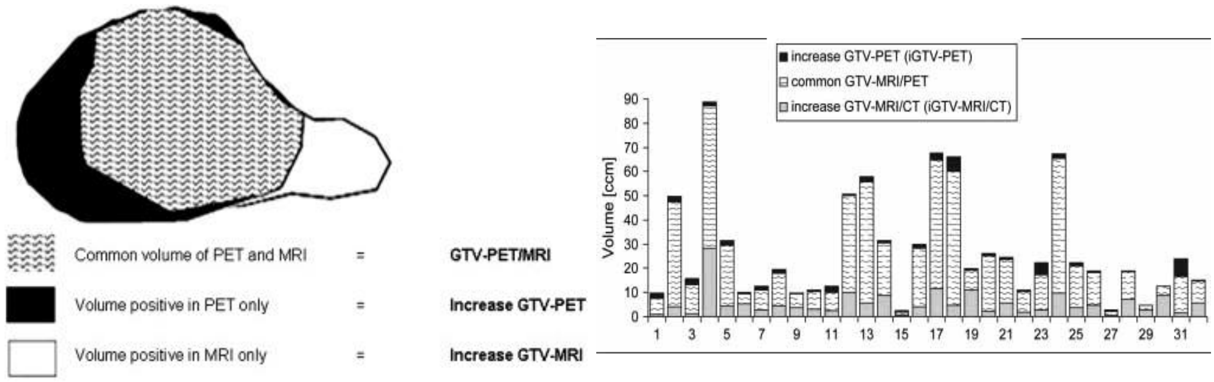


Fig. 14. Illustration of the definition of increase GTV-MRI and GTV-PET [21]

Let's consider specific examples of hybrid tomographic imaging to determine the GTV (Vivantes International Medicine group, http://www. vivantes.de).

Fig. 15-1 shows the results of topological evaluation of tomograms in different modalities when preparing for stereotactic radiotherapy (recurrence of malignant brain tumor). Researches: MRI (T1-weighted with contrast and T2-weighted) and PET tracer F18-FET (tyrosine). Combined PET/MRI images enable to determine the contour of the tumor and separate the areas of necrosis from tumor growth zones. Fig.15-2 shows the results of imaging PET/CT with tracer Ga68-DOTATATE, which showed recurrence of meningioma with infiltration of the bones of the skull base. The tumor is visualized on PET due to the presence of somatostatin receptors and is not determined by MRI.

CONCLUSIONS

The analysis of the opportunities offered by modern technology of topographical imaging in DRTP showed that each one can visualize a predominant property of the tumor, depending on its histopathological variant. Thus, in determining the GTV radiologists should analyze what imaging modality is the most informative for a particular case. Often when planning DRT anatomical CT images are used, but protocol of CT scanning should be coordinated with the technology of planning and realization of radiation treatment. MRI method demonstrates indisputable advantages of anatomical imaging for tumors of brain, chest, abdomen and pelvis in determining the GTV. In perspective can be used the functional MRI imaging to clarify the boundaries of tumor. However, significant duration of MRI study, technical complexity, limited patient positioning and lack of accurate coordinate binding between patient, scanner, simulator and accelerator restrains use of MRI as a basic anatomical imaging modality of the target. The use of PET imaging in some cases allows very accurately differentiate tumor boundaries, but physician must decide exactly which variant of PET image fully corresponds to the nature of the tumor and can be considered as suitable for clarify the boundaries of GTV. Taking into account economical factors and technological features, the most available and necessary in the planning of radiation treatment are technologies of CT and MRI. Actual task for the future is to develop protocols of multi-modal tomographic imaging and topometrical estimation of hybrid images for planning DRT considering histopathological variants of tumors and their morphological and functional features.

REFERENCES

1. Kara Bucci M. Advances in Radiation Therapy: Conventional to 3D, to IMRT, to 4D, and Beyond / M. Kara Bucci, Alison Bevan, Mack Roach III // CA Cancer J Clin. — 2005. — № 55. — P. 117—134.
2. Pylypenko M. I. Selected lectures on radiology / M. I. Pylypenko. — Kharkiv : Grigoriev Institute for Medical Radiology of NAMS of Ukraine, Kharkiv National Medical University, 2012. — 200 p.
3. International Commission on Radiation Units and Measurements : Prescribing, Recording and Reporting Photon Beam Therapy (ICRU Report 50). — Bethesda, MD, International Commission on Radiation Units and Measurements, 1993.
4. Garkusha Yu. The value of modern pre-radiation preparation for conformal radiotherapy / Yu. Garkusha, D. Mechev, V. Ivchuk // Radiol. Visn. — 2010. — № 4 (37). — P. 29—31.
5. Starenkij V. P. The analysis of informational and technical features of up-to-date teleradiotherapy treatment planning systems / [V. P. Starenkij, L. A. Averjanova, L. L.Vasiljev, U. A. Orlova] // Clin. Inform. and Telemed. — 2011. — № 7 (8). — P.79—82.
6. Van Dyk J. The Modern Technology of Radiation Oncology: A Compendium for Medical Physicists and Radiation Oncologists / Jacob Van Dyk, Jake Van Dyk. — Madison : Medical Physics Publishing, 1999. — 1072 p.
7. American Association of Physicists in Medicine Radiation Therapy Committee Task Group 53: Quality assurance for clinical radiotherapy treatment planning // Medical Physics. — 1998. —Vol. 25, № 10. — P. 1773—1788.
8. Ling C. C. Koutcher. Towards multidimensional radiotherapy (MD-CRT): Biological imaging and biological conformality / [C. C. Ling, J. Humm, S. Larson, H. Amols, Z. Fuks, S. Leibel, J. A. Koutcher] // Int. J. Radiat. Oncol. Biol. Phys. — 2000. — № 47. — P. 551—560.
9. Singh A. D. Visualization of primary uveal melanoma with PET/CT scan / A. D. Singh, P. Bhatnagar, B. Bybel // Eye. — 2006. — № 20. — P. 938—940.
10. The role of PET/CT in radiation treatment planning for cancer patient treatment / IAEA. — Vienna, 2008. — http://www-pub.iaea.org/MTCD/publications/PDF/te_1603_web.pdf.
11. Mehta, Minesh P. Coming of age: personalized cancer care, such as using theragnostic radiation oncology to deliver individualized treatment plans, holds promise / Mehta, P. Minesh // Imaging Economics. — 2010.
12. Nestle U. Biological imaging in radiation therapy: role of positron emission tomography / U. Nestle, W. Weber, M. Hentschel, A. L. Grosu // Phys Med Biol. — 2009 Jan 7. — № 54 (1). — P. 1—25.
13. Grosu A. L. C11-methionine PET in radiotherapy planning of glioma / A. L. Grosu, W. A. Weber, R. Lachner [et al.] // Proc Am Soc Clin Oncol. — 2003. — № 22. — (abstr 428).
14. Sean L Kitson. Clinical Applications of Positron Emission Tomography Imaging in Medicine: Oncology, Brain Diseases and Cardiology / Sean L Kitson [et al.] // Current Radiopharmaceuticals. — 2009. — № 2. — P. 224—253.

15. Slobodan Devic. Defining Radiotherapy Target Volumes Using 18F-Fluoro-Deoxy-Glucose Positron Emission Tomography/Computed Tomography: Still a Pandora's Box? / Slobodan Devic [et al.] // Int. J. Radiat. Oncol. Biol. Phys. — Vol. 78, № 5. — December 2010. — P. 1555—1562.
16. Starenkiy V. P. Application of the methods of tomograms contour segmentation for improvement of conformal radiotherapy topometric preparation / V. P. Starenkiy, L. O. Averyanova, L. L. Vasyliev // Herald of the National Technical University «KhPI». Subject issue: Information Science and Modelling. —2012. — № 62 (968). — P. 182—187.
17. Jonsson. Treatment planning using MRI data: an analysis of the dose calculation accuracy for different treatment regions / Jonsson [et al.] // Radiation Oncology. — 2010. — № 5. — P. 62.
18. White GRDR, Wilson I. J. Photon, Electron, Proton and Neutron Interaction Data for Body Tissues / White GRDR, I. J. Wilson // ICRU. — Report 46 Bethesda, Maryland. — 1992.
19. Hanvey S. The influence of MRI scan position on image registration accuracy, target delineation and calculated dose in prostatic radiotherapy / S. Hanvey, A. H. Sadozye, M. McJury [et al.] // Br J Radiol. — 2012. — № 85. — e1256—e1262.
20. Uulke A. van der Heidel. Functional MRI for radiotherapy dose painting / Uulke A. van der Heide [et al.] // Magnetic Resonance Imaging, — 2012. — Vol. 30, № 9. — P. 1216—1223.
21. Sabrina T. Astner. Effect of ^{11}C-Methionine-Positron Emission Tomography on Gross Tumor Volume Delineation in Stereotactic Radiotherapy of Skull Base Meningiomas / Sabrina T. Astner [et al.] // Int. J. Radiat. Oncol. Biol. Phys. — 2008. — № 72. — P. 1161—1167.