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IMAGING

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LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Explain the current status of PET/CT integration to radiation treatment planning.
- Describe how PET/CT fusion can be manually acquired and used for treatment planning.
- List some disease sites where the use of PET/CT for simulation and treatment planning has demonstrated significant benefits in target volume delineation.
- Select cases in which the utilization of PET/CT simulation would be of benefit.

Who will benefit:

Physicians, physician assistants, and radiologic technologists will benefit from the information in this educational activity and can receive Continuing Medical Education credit by completing the post test and evaluation provided.

Clinical Impact of PET/CT on Radiation Treatment Planning

By *Regiane S. de Andrade, M.D., Dwight E. Heron, M.D., and Edward Brandner, Ph.D.*

The use of positron emission tomography (PET) has become increasingly valuable in oncology. With the development of PET imaging combined with computed tomography (CT) scanning, it is now possible to obtain anatomic and biological information in one imaging session with greater diagnostic accuracy. The process of incorporating PET/CT into radiation treatment (RT) planning has created new and exciting possibilities for superior target volume definition.

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This represents one of several major technological advances achieved over the last decade in the field of radiation oncology.

These innovative approaches have evolved into more complex and refined image-based therapeutic radiation techniques, such as intensity-modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT), that more accurately target disease and preserve function of adjacent normal tissues. Radiation oncologists are rapidly embracing functional imaging to augment target volume delineation. Since the success of these highly conformal therapies relies on “dose sculpting” to target tumor volumes and spare surrounding critical structures, accuracy in target volume definition is essential.

PET/CT SIMULATION

Modern RT planning is currently based on 3D conformal radiation therapy, which uses CT—often with contrast enhancement—

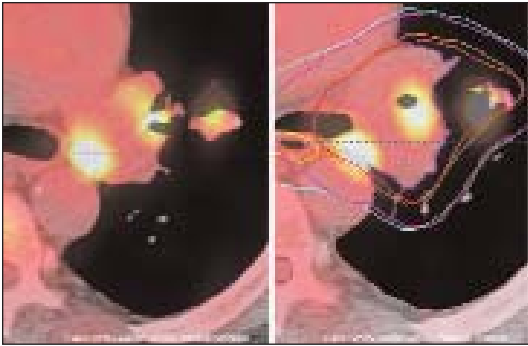


FIGURE 1. Effect of motion on PET/CT imaging. Although PET may cause an increase in GTV, this information may provide a valuable estimation of organ internal motion. A: End of inspiration. B: End of expiration.

the standard imaging method for the treatment planning process. Complementary imaging modalities such as MRI can be fused with simulation CT to aid in target or normal tissue definition. PET alone has been difficult to use for planning purposes due to its lack of the customary anatomic detail necessary for conformal RT planning. The lack of a simple method to fuse the PET data set with the simulation CT data set has further limited the role of stand-alone PET systems in radiation oncology.

Hybrid PET/CT systems, however, avoid the limitations of stand-alone PET systems by acquiring CT (anatomic) and PET (biologic/physiologic) data using the same indexed table without moving the patient. Use of these systems instead of the conventional CT simulation eliminates the need to fuse the PET data set with a CT simulation data set. The CT images from the PET/CT study can serve as the CT simulation for treatment planning. When this option is not available, alternative methods for image acquisition and fusion of the PET/CT data set with the CT simulation have to be developed to guarantee consistent and adequate fused image sets for evaluation and target definition.

PET fusion can provide valuable information when it has been satisfactorily performed (see table). To incorporate PET/CT into the planning process, several parameters must be considered.

First, all of the images must be ac-

quired with proper patient positioning and immobilization. It is important to use the same immobilization for both scans to assure the best possible fusion. Second, to start the fusion process once the images have been acquired, the PET image has to be adjusted to the proper intensity by fine-tuning the window and level. Third, the imaging process of fusing PET and CT can be performed manually. There are many fusion schemes, and available software can even provide automatic fusions, but it is always important

to review nearly all slices in all three planes (sagittal, coronal, and axial) to verify the alignment of the scans, particularly near the target volume. Usually, the brain and spine are recommended anatomic landmarks that can be used in a manual fusing process for aligning a PET scan with a CT image.

It is important to review other anatomic areas in all planes and slices, remembering that PET may show physiological uptake areas that should not be confused with gross disease. CT will help in this distinction. When necessary, it is also recommended that an experienced nuclear medicine physician or radiologist assist in the identification of disease-bearing tissues. There may be small discrepancies between CT and PET that may be the result of volume averaging due to physiologic motion on the PET image (Figure 1).

RADIOLOGICAL EVALUATION AND DISCUSSION

PET has been shown to improve staging of non-small cell lung cancer (NSCLC) for the detection of nodal and distant metastases. Compared with either CT or PET alone, PET/CT can achieve higher diagnostic accuracy, and it has therefore been adopted for the purposes of RT planning. Use of PET/CT for planning faces several technical and clinical issues, however, including PET resolution, tumor edge definition, misregistration due to motion, and PET/CT changes in tar-

get volume delineation.

The visual interpretation of PET/CT scans requires a standardized window setting for the image display. It can be assisted by an experienced nuclear medicine physician or radiologist when necessary.

Investigators have reported various methods for incorporating PET information in the delineation of the gross tumor volume (GTV): visual interpretation of the identified lesion on the PET image, the absolute standardized uptake value (SUV), or the use of a threshold value (percentage of the maximum SUV). An SUV value of 2.5 has been suggested for contouring GTVs on PET images for lung cancer, but this may be an unreliable value.¹ To date, there is no validated standardized method for setting this threshold. Several attempts to define the tumor edge using an arbitrary percentage of the maximum SUV (SUV max such as 40%, 42% or 50%) have been published.²⁻⁵ None of these suggested values has been shown to be reliable in the clinical setting, however. The differences can be mostly associated with tumor inhomogeneity and size. The lack of a single ideal threshold is due to nonuniformity in FDG uptake observed in necrotic and hypoxic tissues present, especially in larger tumors.

Several studies have been published on the impact of FDG-PET for target delineation in NSCLC. Apparently, 30% to 60% of CT-based plans require modifications based on the additional findings of PET. The complementary relationship between CT and FDG-PET is best exploited when these studies are acquired in the treatment position at simulation. A literature review indicates that very few studies have used integrated PET/CT devices for RT planning. Some authors found that introducing PET/CT into RT planning resulted in significant changes (25%) to GTVs. This finding demonstrates that the qualitative target locations were significantly different and that the target plans based on CT only usually underdosed volumes that would have been targeted if a PET scan fusion

had been performed and used.⁶⁻⁸

With regard to the definition of the GTV, the constriction of the GTV or clinical target volume (CTV) based exclusively on PET has yet to be proven. Nonetheless, in carefully selected cases, it may be safe to exclude non-FDG-avid areas from the GTV or CTV to reduce the target volume. More important, the treatment of lung cancer is often complicated by an associated infiltrate and/or atelectasis (Figure 2). In this setting, it is often quite difficult to distinguish these processes from the tumor itself. The combined PET/CT information facilitates differentiating it from tumor and can lead to significant decreases in GTV.^{2,4,8,9}

The ability to spare areas of normal and reactive lung tissue in all patients, especially those with compromised pulmonary function, is very valuable and encouraging. In modern treatment planning, in which routine elective nodal irradiation is usually omitted, it is vital to identify the involved nodal areas that need to be treated. In this setting, PET/CT has played an important role due to its accuracy in detecting involved nodes.¹⁰ The superior diagnostic accuracy of FDG-PET in mediastinal lymph nodes has enabled researchers to selectively irradiate mediastinal nodes with a very low rate of recurrence. They have also been able to escalate therapeutic doses before reaching dose limiting toxicities.^{11,12} Accurate GTV delineation is a fundamental step in dose escalation studies with conformal therapy.

Unfortunately, uniformity in the methods for tumor delineation continues to be lacking in the literature, which makes it difficult to establish guidelines for contouring the GTV using PET information. Without more definitive data, the radiation oncologist should include the metabolic information from PET based on visual criteria with a definite protocol assisted by an experienced nuclear medicine physician or radiologist.

The use of PET/CT for esophageal cancers in the setting of RT planning



FIGURE 2. PET information improving GTV delineation. Metabolic information from PET can aid in exclusion of atelectasis.

remains limited, though fusing an FDG-PET image to a CT simulation potentially appears to have a significant impact on RT planning and management of esophageal carcinoma. Some authors have demonstrated that PET surpassed CT for locoregional lymph node staging, though its sensitivity rates remain quite modest.^{13,14} The incorporation of FDG-PET/CT into RT planning has led to the definition of smaller GTVs in at least one study.¹⁵ The greatest impact of PET/CT is in the identification of locoregional and distant metastatic disease, offering incremental benefit of approximately 20% over CT alone.^{16,17}

Adding PET information to CT-based planning also provides the ability to define the cranial and caudal limits of the primary tumor more accurately, thereby improving GTV definition. PET may reveal metastatic lymph nodes and lead to increases in the target volume that can significantly influence RT management and optimize treatment goals.^{18,19} Its low sensitivity and high specificity limit PET/CT in RT planning to a mainly additive function in target volume delineation. More evidence of prospective data is warranted to ascertain the benefit of PET/CT in RT planning.

Radiation therapy to tumors located in the head and neck area requires careful attention due to the great variety of critical and sensitive structures that can surround the tumor. The radiation dose

given to this area must be carefully planned to take into consideration all adjacent tissue tolerance doses. Highly conformal radiation techniques can be applied, delivering high dose to the target tumor while sparing nearby normal tissues. Precise target definition for this treatment is imperative.

In the diagnosis and staging of head and neck cancers, PET/CT has demonstrated an incremental value over either modality alone. PET/CT outperformed CT and PET in sensitivity, specificity, and accuracy.²⁰⁻²²

Since over 70% of head and neck cancers present as locally advanced disease, it is critical to establish the extent of locoregional and distant disease to assist in the proper selection of therapy and avoidance of unnecessary interventions.

For RT planning, PET/CT has been demonstrated to be exquisitely sensitive and specific in identifying the primary tumor, particularly in infiltrative tumors with poorly defined extension. Many authors have found that GTVs are reduced based on PET/CT (Figure 3).²³ PET/CT can also detect a great number of previously unobserved tumor-bearing nodes and reveal occult metastatic disease.²⁴ Controversy remains, however, regarding PET-based contouring methods. The application of different guidelines for tumor volume delineation and the normalization of PET images may result in a number of variations on the

final target volumes. The appropriate threshold level depends on lesion size and image reconstruction parameters that have to be carefully considered when using PET volume information for RT planning.

There are several suggested methods for PET volume delineation, but many remain under investigation.^{8,25,26} The information provided by PET has demonstrated improvement in conventional target definition in RT planning for head and neck cancers. Although its value is still being investigated, PET/CT has been shown to be superior to current imaging methods in tumor diagnosis. These new biological target volumes can also play a role in target delineation and the definition of boost volumes. Use of PET/CT in RT planning can be valuable for guidance in the assessment of response as well.²⁷

Various tracers have been evaluated in head and neck scans to detect the areas of hypoxia of these tumors and create another opportunity for target therapies. The challenges remain great since no acceptable gold standard exists for measuring the tumor hypoxia often seen in head and neck squamous cell cancers. Further research on tracers is warranted.

The management of lymphomas with radiation has undergone a dramatic evolution in the last decade, moving from first-line comprehensive therapy in some cases to adjuvant therapy after chemotherapy in most stages. Precise anatomic delineation of lymphoma involvement has become increasingly important as use of involved node RT has become the standard approach. In this setting, PET has demonstrated higher accuracy than CT, providing better definition of the involved field.²⁸

The incorporation of PET or PET/CT information into target volume delineation has been evaluated by several authors. FDG-PET and PET/CT have been found to upstage Hodgkin's lym-

phoma patients, often translating into larger RT volumes.²⁸ The improved staging provided by FDG-PET/CT is now being advocated to augment IMRT planning for Hodgkin's lymphoma.²⁹

For patients with cervical cancer, poor prognosis is associated with metastasis to the peri-aortic lymph nodes.³⁰ Extended-field radiation therapy (EFRT) offers a survival advantage for patients with pelvic and para-aortic metastases,³¹ but the toxicities associated with EFRT have limited its use in most centers.³⁰ To minimize

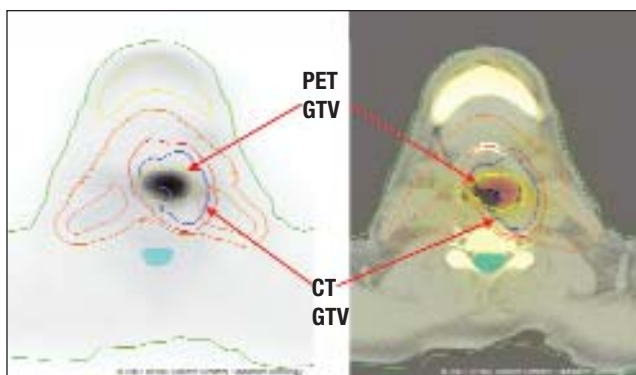


FIGURE 3. PET/CT-based GTV contours. PET information shows smaller GTV when compared with CT-based volume for laryngeal cancer.

these toxicities, IMRT techniques have been introduced with the potential to boost grossly involved para-aortic nodes.^{32,33} PET and PET/CT have been demonstrated to be superior to CT alone and MRI alone in the staging of cervical cancer.³⁴

PET-guided IMRT planning could be used to escalate dose to PET-avid grossly involved para-aortic nodes while maintaining proper dose to the pelvis and limiting dose to adjacent normal tissues.³⁵ Overall, PET/CT offers valuable additional information for diagnosis in cervical cancer, leading to better lesion localization to improve radiation fields.

Colorectal cancer can present locally and be surgically curable in most cases. Advanced rectal tumors have often been treated by preoperative chemoradiation therapy, with reduced recurrence rates and toxicity. Recent studies have demonstrated that PET/CT has been useful in improving primary tumor staging and in

the detection of metastatic lesions.³⁶ This advantage can influence surgical decision making in selection of better candidates and guidance to treatments that are more suitable, such as chemoradiation or even palliation.³⁷

The addition of PET information has demonstrated changes in the GTV in comparison with CT-based volumes, improving target volume definition. This may offer great potential to high-precision radiation treatment modalities.³⁸ A greater uniformity between observers' definitions of the GTVs based on combined PET/CT compared with CT alone has been seen, particularly for nodal disease, and this should result in more accurate target volume delineation. Such an advantage may ultimately lead to improved local tumor control and decreased toxicity.³⁹

Although the picture for PET/CT is not yet fully defined in this setting, data on the improvement obtained from adding PET information to rectal cancer management appear to be promising.

CONCLUSIONS

PET/CT surpasses PET alone and CT alone in accuracy, playing an invaluable role in the diagnosis and staging of cancer patients. Its advantages are of great value in modern RT planning techniques that require a high degree of accurate target delineation to deliver highly conformal radiation.

Although the use of PET/CT in radiation oncology treatment planning is a relatively new phenomenon, we are now beginning to see the impact on planning, assessment of treatment response, and outcome. With the integration of PET/CT into the RT planning process, 25% to 30% of patients will have alterations in their plans as a result of new findings from the hybrid imaging.

The emerging concept of a biologic target volume may become the key for target delineation and therapeutic radiation delivery in this modern radiation

treatment era. It is clear, however, that greater experience and a larger volume of clinical data are needed from the research field to increase this modality's effectiveness in determining the true extent and

STEPS TO FOLLOW FOR ADEQUATE PET FUSION

- Note positioning and immobilization
- Carefully choose window and level
- Do not use target volume for fusing
- Evaluate motion effects
- Align brain or spine on coronal view
- Align brain or spine on sagittal view
- Review other anatomy on both views
- Repeat until good alignment
- Align brain or spine on axial view
- Review anatomy on axial view
- Review all planes and nearly all slices
- Focus near target area
- Diligently evaluate and fine-tune
- Have two people review fusion
- Use PET as additional information for contour based on CT
- Use PET to confirm/identify targets

boundaries of tumor malignancies.

References

1. Paulino AC, Johnstone PA. FDG-PET in radiotherapy treatment planning: Pandora's box? *Int J Radiat Oncol Biol Phys* 2004;59(1):4-5.
2. Giraud P, Grahek D, Montravers F, et al. CT and (18)F-deoxyglucose (FDG) image fusion for optimization of conformal radiotherapy of lung cancers. *Int J Radiat Oncol Biol Phys* 2001;49(5):1249-1257.
3. Erdi YE, Rosenczweig K, Erdi AK, et al. Radiotherapy treatment

- planning for patients with non-small cell lung cancer using positron emission tomography (PET). *Radiother Oncol* 2002;62(1):51-60.
4. Deniaud-Alexandre E, Touboul E, Lerouge D, et al. Impact of computed tomography and 18F-deoxyglucose coincidence detection emission tomography image fusion for optimization of conformal radiotherapy in non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2005;63(5):1432-1441.
5. Nestle U, Schaefer-Schuler A, Kremp S, et al. Target volume definition for 18F-FDG PET-positive lymph nodes in radiotherapy of patients with non-small cell lung cancer. *Eur J Nucl Med Mol Imaging* 2007;34(4):453-462.
6. Ashamalla H, Rafta S, Parikh K, et al. The contribution of integrated PET/CT to the evolving definition of treatment volumes in radiation treatment planning in lung cancer. *Int J Radiat Oncol Biol Phys* 2005;63(4):1016-1023.
7. Grills IS, Yan D, Black QC, et al. Clinical implications of defining the gross tumor volume with combination of CT and 18FDG-positron emission tomography in non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2007;67(3):709-719.
8. Ciernik IF, Dizendorf E, Baumert BG, et al. Radiation treatment planning with an integrated positron emission and computer tomography (PET/CT): a feasibility study. *Int J Radiat Oncol Biol Phys* 2003;57(3):853-863.
9. Nestle U, Walter K, Schmidt S, et al. 18F-deoxyglucose positron emission tomography (FDG-PET) for the planning of radiotherapy in lung cancer: high impact in patients with atelectasis. *Int J Radiat Oncol Biol Phys* 1999;44(3):593-597.
10. Lardinois D, Weder W, Hany TF, et al. Staging of non-small-cell lung cancer with integrated positron-emission tomography and computed tomography. *NEJM* 2003;348(25):2500-2507.
11. De Ruysscher D, Wanders S, van Haren E, et al. Selective mediastinal node irradiation based on FDG-PET scan data in patients with non-small-cell lung cancer: a prospective clinical study. *Int J Radiat Oncol Biol Phys* 2005;62(4):988-994.
12. Belderbos JS, Heemsbergen WD, De Jaeger K, et al. Final results of a Phase I/II dose escalation trial in non-small-cell lung cancer using three-dimensional conformal radiotherapy. *Int J Radiat Oncol Biol Phys* 2006;66(1):126-134.
13. van Westreenen HL, Westertep M, Bossuyt PM, et al. Systematic review of the staging performance of 18F-fluorodeoxyglucose positron emission tomography in esophageal cancer. *J Clin Oncol* 2004;22(18):3805-3812.
14. Meltzer CC, Luketich JD, Friedman D, et al. Whole-body FDG positron emission tomographic imaging for staging esophageal cancer comparison with computed tomography. *Clin Nucl Med* 2000;25(11):882-887.
15. Gondi V, Bradley K, Mehta M, et al. Impact of hybrid fluorodeoxyglucose positron-emission tomography/computed tomography on radiotherapy planning in esophageal and non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2007;67(1):187-195.
16. Kato H, Miyazaki T, Nakajima M, et al. The incremental effect of positron emission tomography on diagnostic accuracy in the initial staging of esophageal carcinoma. *Cancer* 2005;103(1):148-

- 1456.
17. Bar-Shalom R, Guralnik L, Tsalic M, et al. The additional value of PET/CT over PET in FDG imaging of esophageal cancer. *Eur J Nucl Med Mol Imaging* 2005;32(8):918-924.
18. Moureau-Zabotto L, Touboul E, Lerouge D, et al. Impact of CT and 18F-deoxyglucose positron emission tomography image fusion for conformal radiotherapy in esophageal carcinoma. *Int J Radiat Oncol Biol Phys* 2005;63(2):340-345.
19. Leong T, Everitt C, Yuen K, et al. A prospective study to evaluate the impact of FDG-PET on CT-based radiotherapy treatment planning for oesophageal cancer. *Radiother Oncol* 2006;78(3):254-261.
20. Branstetter BF, Blodgett TM, Zimmer LA, et al. Head and neck malignancy: is PET/CT more accurate than PET or CT alone? *Radiology* 2005;235(2):580-586.
21. Menda Y, Graham MM. Update on 18F-fluorodeoxyglucose/positron emission tomography and positron emission tomography/computed tomography imaging of squamous head and neck cancers. *Semin Nucl Med* 2005;35(4):214-219.
22. Yao M, Smith RB, Graham MM, et al. The role of FDG pet in management of neck metastasis from head-and-neck cancer after definitive radiation treatment. *Int J Radiat Oncol Biol Phys* 2005;63(4):991-999.
23. Heron DE, Andrade RS, Flickinger J, et al. Hybrid PET-CT simulation for radiation treatment planning in head-and-neck cancers: a brief technical report. *Int J Radiat Oncol Biol Phys* 2004;60(5):1419-1424.
24. Paulino AC, Koshy M, Howell R, et al. Comparison of CT- and FDG-PET-defined gross tumor volume in intensity-modulated radiotherapy for head-and-neck cancer. *Int J Radiat Oncol Biol Phys* 2005;61(5):1385-1392.
25. Koshy M, Paulino AC, Howell R, et al. F-18 FDG PET-CT fusion in radiotherapy treatment planning for head and neck cancer. *Head Neck* 2005;27(6):494-502.
26. Ashamalla H, Guirgius A, Bieniek E, et al. The impact of positron emission tomography/computed tomography in edge delineation of gross tumor volume for head and neck cancers. *Int J Radiat Oncol Biol Phys* 2007;68(2):388-395.
27. Andrade RS, Heron DE, Degirmenci B, et al. Posttreatment assessment of response using FDG-PET/CT for patients treated with definitive radiation therapy for head and neck cancers. *Int J Radiat Oncol Biol Phys* 2006;65(5):1315-1322.
28. Hutchings M, Loft A, Hansen M, et al. Clinical impact of FDG-PET/CT in the planning of radiotherapy for early-stage Hodgkin lymphoma. *Eur J Haematol* 2007;78(3):206-212.
29. Yahalom J. Transformation in the use of radiation therapy of Hodgkin lymphoma: new concepts and indications lead to modern field design and are assisted by PET imaging and intensity modulated radiation therapy (IMRT). *Eur J Haematol Suppl* 2005;(66):90-97.
30. Grigsby PW, Perez CA, Chan KS, et al. Radiation therapy for carcinoma of the cervix with biopsy-proven positive para-aortic lymph nodes. *Int J Radiat Oncol Biol Phys*, 2001;49(3):733-738.
31. Eifel PJ, Winter K, Morris M, et al. Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation

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for high-risk cervical cancer: an update of radiation therapy oncology group trial (RTOG) 90-01. *J Clin Oncol* 2004;22(5):872-880.

32. Esthappan J, Mutic S, Malyapa RS, et al. Treatment planning guidelines regarding the use of CT/PET-guided IMRT for cervical carcinoma with positive paraaortic lymph nodes. *Int J Radiat Oncol Biol Phys* 2004;58(4):1289-1297.

33. Beriwal S, Gan GN, Heron DE, et al. Early clinical outcome with concurrent chemotherapy and extended-field, intensity-modulated radiotherapy for cervical cancer. *Int J Radiat Oncol Biol Phys* 2007;68(1):166-171.

34. Grigsby PW, Siegel BA, Dehdashti F, et al. Posttherapy [¹⁸F] fluorodeoxyglucose positron emission tomography in carcinoma of the cervix: response and outcome. *J Clin Oncol* 2004;22(11):2167-2171.

35. Mutic S, Malyapa RS, Grigsby PW, et al. PET-guided IMRT for cervical carcinoma with positive para-aortic lymph nodes—a dose-escalation treatment planning study. *Int J Radiat Oncol Biol Phys* 2003;55(1):28-35.

36. Nakamoto Y, Sakamoto S, Okada T, et al. Clinical value of manual fusion of PET and CT images in patients with suspected recurrent colorectal cancer. *AJR* 2007;188(1):257-267.

37. Kantorová I, Lipska L, Bělohávek O, et al. Routine (18)F-FDG PET preoperative staging of colorectal cancer: comparison with conventional staging and its impact on treatment decision making. *J Nucl Med* 2003;44(11):1784-1788.

38. Ciernik IF, Huser M, Burger C, et al. Automated functional image-guided radiation treatment planning for rectal cancer. *Int J Radiat Oncol Biol Phys* 2005;62(3):893-900.

39. Patel DA, Chang ST, Goodman KA, et al. Impact of integrated PET/CT on variability of target volume delineation in rectal cancer. *Technol Cancer Res Treat* 2007;6(1):31-36.