October 14, 2009

Tamara Syrek Jensen, J.D.
Acting Director, Coverage and Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Blvd., Mail Stop C1-09-06
Baltimore, MD 21244

Re: Request for a Limited-Scope Reconsideration of CAG-00181R Regarding Certain Restrictions on Coverage of FDG-PET for Initial Treatment Strategy Evaluation

Dear Acting Director Jensen:

We are writing to request that the Centers for Medicare & Medicaid Services (CMS) open a limited-scope reconsideration of NCD CAG-00181R for the purpose of reconsidering the limitation of coverage of FDG-PET to one scan per patient for initial treatment strategy evaluation.

This letter is submitted jointly on behalf of the National Oncologic PET Registry (NOPR) Working Group, the Academy of Molecular Imaging (AMI), the American College of Nuclear Medicine (ACNM), the American College of Radiology (ACR), the American Society for Radiation Oncology (ASTRO), the Institute for Molecular Technologies, and the Society of Nuclear Medicine (SNM). These groups collectively are composed of clinicians, academicians, researchers and nuclear medicine providers utilizing molecular imaging technologies, including integrated positron emission tomography/computed tomography (PET/CT). We represent tens of thousands of physicians, providers, and patients with regard to this technology, and have worked closely with CMS over the past several years to increase beneficiary access to PET/CT through the development of the National Oncologic PET Registry (NOPR).

We believe that there is substantial evidence that, in certain limited clinical circumstances, the limitation of PET coverage to a single scan for initial treatment evaluation is contrary to good clinical practice. A limited-scope reconsideration of NCD CAG-00181R would enable CMS to harmonize the omnibus PET coverage policy and the existing evidence on the clinical value of certain "second initial treatment strategy evaluation" scans.

I. Overview

We collectively and strongly support the approach taken by CMS in CAG-00181R to streamline the FDG-PET coverage framework into "initial" and "subsequent" treatment strategy evaluation, as we believe that this is a positive development for providers, patients, and payors. However, we remain concerned that the failure of CMS to acknowledge the need for clinically necessary "second initial" scans in certain limited clinical situations may hamper good clinical practice. In response to comments encouraging coverage for second initial scans in such situations, CMS stated that the evidence it had reviewed "addressed the use of single scans," and that "coverage as we have described of only one FDG-PET scan to guide initial antitumor treatment is consistent with the current evidence base." The new NCD, in section IX(2) (Initial Antitumor Treatment Strategy),articulates the formal policy as follows (emphasis supplied):

> CMS has determined that the evidence is adequate to determine that the results of FDG-PET imaging are useful in determining the appropriate initial treatment strategy for beneficiaries with suspected solid tumors and myeloma and improve health outcomes and thus are reasonable and necessary under §1862(a)(1)(A) of the Social Security Act. Therefore, CMS will cover *only one* FDG-PET study for beneficiaries who have solid tumors that are biopsy proven or strongly suspected based on other diagnostic testing when the beneficiary's treating physician determines that the FDG-PET study is needed to determine the location and/or extent of the tumor for the following therapeutic purposes related to the initial treatment strategy:
>
> - To determine whether or not the beneficiary is an appropriate candidate for an invasive diagnostic or therapeutic procedure; or
> - To determine the optimal anatomic location for an invasive procedure; or
> - To determine the anatomic extent of tumor when the recommended anti-tumor treatment reasonably depends on the extent of the tumor.

Three practical scenarios illustrate our general concern with the bright-line approach taken in CAG-00181R. First, where PET is used for diagnosis or initial staging purposes, the result may indicate that radiation therapy, rather than surgery, is the appropriate method of treatment. In such situations, a second (initial) PET scan, often a limited study done under technically different conditions, may be needed for radiation therapy planning (e.g., for PET-based simulation). Second, in a small fraction of patients, PET used to evaluate a suspicious lesion (e.g., a pulmonary nodule) for cancer diagnosis can produce a false-negative result. If such patients are subsequently diagnosed with cancer, however, the prevailing standard of care is to use PET for initial staging prior to treatment, in order to obviate futile locally directed treatment (surgery or definitive radiation therapy) in those patients who had developed metastatic disease in the interval. Third, in some patients with newly diagnosed cancer staged by an initial PET scan, definitive treatment may be delayed either because of patient reluctance or because of intercurrent medical illness that must first be addressed (e.g., a patient who must undergo coronary artery bypass grafting for multivessel coronary artery disease before a radical cystectomy can be performed for muscle-invasive bladder carcinoma. Again, as in the second example, a second PET scan to document that the disease has not become unresectable may be medically necessary.

Although failure to perform a second scan under the above scenarios is contrary to good clinical practice, CAG-00181R nevertheless prohibits Medicare coverage for a second scan in these circumstances. Moreover, we believe that the existing literature available to CMS (summarized below) provides clinical justification for second initial scans in certain radiation planning and prolonged evaluation situations. We thus believe that the bright-line one-scan limitation cannot be reconciled with either the prevailing standard of care or the existing literature, and therefore request that CAG-00181R be amended to accommodate and cover clinically necessary "second initial" scans in situations such as those described above.

II. Rationale

Current standard-of-care in the United States as dictated by American Association of Physicists in Medicine (AAPM) Task Group Report #53 (Fraass, et al, 1998)[1], and updated for CT-based treatment planning in AAPM Task Group Report #66 (Mutic et al, 2003)[2] requires that imaging for radiation treatment planning must take place with a patient immobilized in the position assumed during treatment to account for the positional dependence of tumor and normal tissue location and motion. Clinical management complexity captured in current HCPCS level I coding for radiotherapy simulation reflects effort and expertise with specialized techniques designed to reduce patient position uncertainty at the time of simulation. No anatomic site is exempt from this standard, although certain disease sites, such as thoracic, head and neck, pelvic, and extremity sites are particularly susceptible to positioning errors which can reduce treatment safety and efficacy. Diagnostic PET/CT imaging is almost universally performed with patients resting on a concave tabletop designed to optimize comfort during protracted image acquisition times. In contrast, all imaging for radiotherapy planning, including PET/CT simulation, takes place with patients immobilized on a flat tabletop for stabilization and reproduction of physical position during administration of treatment. The radiation treatment planning PET scan often involves use of special immobilization devices (e.g., alpha cradle) with laser positioning of patient by radiation therapy technologist and/or radiation oncologist. Incorporation of non-immobilized diagnostic PET/CT imaging into radiotherapy planning is inconsistent with accepted standards for good clinical practice in the United States, and can significantly limit the presumed utility of PET/CT towards radiotherapy patient management.

Specific evidence to support incorporation of treatment-dedicated PET-CT into therapy planning is derived from level II-2/3 evidence collected from a large number of institutional cohort studies across a spectrum of cancer disease sites. A large prospective institutional cohort study was very recently published in early 2009 to complement these data, as were level III expert panel recommendations from Europe. An obvious limitation to the availability of higher quality, matched cohort-controlled evidence is the universal acceptance by American clinicians and medical physicists of simulation imaging in treatment position; in fact, *it is difficult to envision adequate scientific equipoise and provider/patient accrual interest to ethically justify dedication of resources towards clinical trials designed to provide level II-1 or better quality evidence to support PET/CT imaging in treatment position for radiotherapy planning*. Specific evidence from the available body of relevant retrospective and prospective literature will be outlined below.

III. Evidence

Although the most recent data from the National Oncologic PET Registry (NOPR) project pertaining to the limited and clearly delineated clinical necessity for second initial scans were available during the comment period on CAG-00181N, several key manuscripts published in early 2009 were not yet available for review.

First, Kruser et al (2009)[3] published findings from a prospective, blinded institutional trial (level II-2 evidence) enrolling 111 patients with lung, head and neck, breast, cervix, esophageal, or hematologic (lymphoma) cancer undergoing PET/CT imaging in treatment position at the time of radiotherapy planning. Clinicians designed two treatment plans for each patient, one based on CT imaging blinded to PET, the other based on combined PET/CT findings. The two plans were compared prior to the start of therapy. PET/CT imaging resulted in changes in radiotherapy planning in 68% of subjects, about half of whom had a major alteration in treatment dose, field design, or employed treatment modalities. All patients enrolled onto this study underwent PET/CT while immobilized in treatment position. This is the largest such prospective study of its kind in the peer-reviewed literature, and complements a host of smaller prospective series outlined below.

Given the increased availability and procurement of integrated PET/CT scanners over the past 3-5 years, there are fewer contemporaneous data available to critique real world impact of PET/CT on radiotherapy planning quality for patients *not* imaged in treatment position using current generation equipment and software. However, Hwang et al. (2009)[4] recently published data from a carefully conducted 12 patient medical physics investigation to complement earlier literature (Ireland et al. (2007))[5] to show that integrated PET/CT imaging obtained in non-treatment position can significantly degrade quality of treatment planning for head and neck radiotherapy. Although use of advanced deformable image registration algorithms could reduce registration uncertainties for non-treatment position PET/CT, potential localization errors with this approach were large enough (>5 mm) to potentially affect patient safety. Planning accuracy for spinal cord, mandible, and tumor were all significantly improved with the use of immobilized PET/CT imaging in treatment position. The implications for U.S. cancer care are sobering since formal validation of deformable image registration strategies in clinical practice remains difficult, and the time frame for widespread deployment of such software into community practice is difficult to anticipate. Thus, the vast majority of head and neck radiotherapy patients in the United States would potentially be subjected to larger treatment uncertainties with the use of non-treatment position PET/CT for radiotherapy planning than those quoted for this study. This unfortunately suggests that *formal recommendations against the incorporation of non-treatment position PET/CT into radiotherapy planning merit consideration*, representing a significant opportunity cost for cancer patients in this country.

This would quickly disadvantage patients in the United States relative to the international community, despite a clear history of American leadership in the field of PET/CT cancer imaging research. The International Atomic Energy Authority (IAEA) organized two expert panels in July 2006, and charged them with evaluating the available literature on the use of PET for radiotherapy planning. MacManus et al (2009)[6] recently published the final report (level III evidence) on behalf of the IAEA. The panel found "numerous studies to support the routine use

of FDG-PET for radiotherapy target volume determination in non-small cell lung cancer (NSCLC). There was also evidence for utility of PET in head and neck cancers, lymphoma and in esophageal cancers, with promising preliminary data in many other cancers." The panel went on to conclude that *"the best available approach employs integrated PET/CT images, acquired on a dual scanner in the radiotherapy treatment position...PET scans that are not recent or were acquired without proper patient positioning should be repeated for radiotherapy planning."* Lack of HCPCS level I reimbursement coding for a second initial PET/CT scan for radiotherapy planning in situations of clinical need will pressure the United States to abdicate an important role in international cancer care leadership and to absorb potentially greater longitudinal patient and societal costs resulting from inferior treatment outcomes. Below we provide an abridged outline of recent relevant literature, much of which was highlighted by the IAEA Report to support the conclusions above.

A. Lung Cancer

This disease site benefits from the largest amount of literature commenting on the role of PET imaging in radiotherapy planning.

The National Institute for Health and Clinical Evidence (NICE) in the United Kingdom published formal treatment guidelines for lung cancer for the U.K.'s National Health System in 2005, including use of PET imaging. To complement these and other cancer care guidelines, the Health Technology Assessment (HTA) program of the U.K.'s National Institute of Health Research published a follow-up report (Facey et al. (2007))[7] summarizing the effectiveness of PET imaging for lung cancer and many other disease sites. The NICE Guidelines group calculated a 42% pooled weighted average for radiotherapy management changes for non-small cell lung cancer with the incorporation of PET imaging. Interestingly, the subsequent HTA Report questioned the methodology of this particular finding, but did not refute the high quality grade assigned by NICE to the literature supporting this conclusion, and updated the NICE Guidelines with five additional supporting references dated through 2005 to support the clinical utility and cost-effectiveness of the addition of PET to lung cancer radiotherapy planning. Among the strongest of these studies, De Ruysscher et al. (2005),[8] prospectively demonstrated in 21 patients the ability to safely intensify treatment to gross tumor from 55.2 Gy to 68.9 Gy with dedicated PET/CT simulation.

It should be noted that earlier series frequently did study incorporation of separate diagnostic single-modality PET imaging into CT-based treatment planning due to limited availability of integrated PET/CT scanners and dedicated PET simulators. Other studies have documented ambiguous changes in treatment planning due to PET findings, including both improvements and decrements in normal tissue sparing with use of PET/CT-defined tumor target volumes (Deniaud-Alexandre et al. (2005)).[9] However, correction for motion-related uncertainties for planning dose-intensified image-guided lung cancer radiotherapy is a well recognized clinical need and is currently a prioritized topic of investigation. *Given the tight dependence of tumor and at-risk normal tissue movement and location on patient position, use of any imaging obtained in non-treatment position for treatment planning currently cannot be considered to be of adequate quality for either study or practice.* Most recent studies now presume the appropriateness of integrated PET/CT scanner-based simulations with patients in

radiotherapy position, and have retrained their focus towards refinement of the use of PET/CT simulation for lung cancer treatment planning. Accordingly, there are no studies available to directly compare diagnostic PET/CT and simulation PET/CT imaging for lung cancer radiotherapy planning, nor are any future reports making such comparisons anticipated.

Klopp et al. (2007)[10] studied 35 patients undergoing PET/CT simulation in treatment position for non-small cell lung cancer. Primary tumor and nodal regions of interest were identified in each patient, and relative risk for each region was assessed according to disease volume and FDG avidity. Recursive partitioning analysis demonstrated that PET/CT identifies high risk disease which can be exclusively targeted to high dose while excluding low risk nodal stations from elective coverage, improving the therapeutic ratio without untoward risk for out-of-field treatment failure.

Van Loon et al. (2008)[11] demonstrated significant modification in regional nodal coverage in 24% of 21 patients treated for limited-stage small cell lung cancer with PET/CT-guided treatment planning.

Gillham et al. (2008)[12] prospectively studied PET/CT-guided dose escalation for non-small cell lung cancer, with patients serially simulated both at baseline and after 50-60 Gy treatment. Use of mid-treatment PET/CT imaging permitted improvements in dose escalation to gross disease, with 40% of cases able to receive up to 78 Gy with or without repeated PET/CT simulation.

B. Head and Neck Cancer

This disease site has also been well studied for utility of PET/CT-guided treatment planning. Similar to lung cancer, head and neck cancer location is closely associated with patient positioning. PET/CT simulation in treatment position would be the clinical standard to complement the stringent planning criteria currently required for head and neck IMRT planning.

Paulino et al. (2005)[13] retrospectively studied 40 patients undergoing PET/CT simulation in treatment position. PET imaging led to changes in tumor volumes in 92% of cases, and prevented clinically significant underdosing of gross tumor in 25% of cases.

Schwartz et al. (2005)[14] prospectively demonstrated improved regional nodal coverage accuracy with PET/CT imaging in 20 patients with locally advanced disease. Dose could be safely escalated to FDG-avid primary disease in 25% of cases.

Wang et al (2006)[15] prospectively delivered PET/CT simulation-guided IMRT to 28 patients with locally advanced head and neck disease. PET/CT altered disease stage in 57% of cases and changed gross disease target volumes for 14 patients.

Zheng et al. (2007)[16] prospectively enrolled 43 patients with locally recurrent nasopharyngeal carcinoma onto a trial investigating PET/CT simulation-guided salvage radiotherapy. Inadequate target volume coverage with CT imaging guidance alone was seen in 51% cases, leading to clinically significant underdosing of gross disease in 13 patients.

Shintani et al. (2008)[17] evaluated the utility of post-operative PET/CT imaging for planning of adjuvant head and neck radiotherapy in 91 patients with squamous or non-squamous disease. PET found residual gross disease in 11 cases. Radiotherapy management was significantly altered by PET/CT imaging in 14 cases. However, one should be cautioned that false-positive findings with post-operative PET/CT imaging were common (55% of patients with residual FDG-avid foci were biopsy-negative).

Vernon et al. (2008)[18] reported clinical outcomes for 42 head and neck cancer patients treated with PET/CT simulation-guided IMRT. Encouraging disease-free and overall survival rates of 67% and 74%, respectively, were demonstrated at 3 years. The authors noted a favorable toxicity profile for the study cohort.

Soto et al. (2008)[19] retrospectively identified 61 head and neck cancer patients undergoing pre-treatment PET/CT imaging. Eight of 9 disease failures occurred within the original FDG-avid tumor volume, arguing for a role of PET/CT simulation imaging to more optimally define high risk tumor target volumes for treatment planning.

C. Additional Cancer Sites

Beyond the literature cited by the 2009 IAEA Report, additional institutional series have been published since 2007 directly supporting the use of dedicated PET/CT simulation imaging in treatment position for lymphoma ((Hutchings et al. (2007); Girinsky et al. (2007)),[20, 21] cervical (Esthappan et al. (2008); Yildirim et al. (2008)),[22, 23] ovarian (Thrall et al. (2007)),[24] breast (Ford et al. (2008)),[25] esophageal (Vesprini et al. (2008)),[26] anorectal (Patel et al. (2007); Anderson et al. (2007); Nguyen et al. (2008)),[27-29] and pancreatic (Topkan et al. (2008))[30] cancer patients.

D. Evolving Cancer and Delayed Initial Curative-intent Cancer Treatment

We are unable to find prospective studies or case series in the peer-reviewed scientific literature that specifically address the scenarios described in the Overview section of this request letter. However, we nonetheless submit that all experienced physicians who care for cancer patients have encountered such patients in their practices. Although these clinical scenarios are uncommon, the potential clinical impact of a second PET scan is substantial if futile curative-intent therapy, which may have substantial morbidity (and cost) is averted.

IV. Reconsideration Request

On the basis of the evidence presented above, we formally request that CMS initiate a limited-scope reconsideration of NCD CAG-00181R for the specific purpose of reconsidering the limitation of coverage of FDG-PET to one scan per patient for initial treatment evaluation.

We are cognizant of the desire of CMS to avoid situations in which coverage of second initial scans in limited circumstances such as those described above could lead to attempts to obtain reimbursement improperly for second initial scans beyond such circumstances. We

believe that it is possible to extend coverage to certain limited radiation therapy purposes and the other scenarios we describe without allowing the exception to swallow the general rule.

We look forward to working closely with CMS throughout this limited-scope reconsideration process, and to providing any additional information that CMS may require.

Sincerely,

Timothy J. McCarthy, PhD
President, AMI

Jay A. Harolds, MD, FACNP
President, ACNM

Harvey L. Neiman, MD, FACR
Executive Director, ACR

Michael M. Graham, PhD, MD
President, SNM

Laura I. Thevenot, CAE
Chief Executive Officer, ASTRO

References

1. Fraass B, Doppke K, Hunt M, *et al.* American Association of Physicists in Medicine Radiation Therapy Committee Task Group 53: quality assurance for clinical radiotherapy treatment planning. *Med Phys* 1998;25:1773-1829.

2. Mutic S, Palta JR, Butker EK, *et al.* Quality assurance for computed-tomography simulators and the computed-tomography-simulation process: report of the AAPM Radiation Therapy Committee Task Group No. 66. *Med Phys* 2003;30:2762-2792.

3. Kruser TJ, Bradley KA, Bentzen SM, *et al.* The Impact of Hybrid PET-CT Scan on Overall Oncologic Management, with a Focus on Radiotherapy Planning: A Prospective, Blinded Study. *Technol Cancer Res Treat* 2009;8:149-158.

4. Hwang AB, Bacharach SL, Yom SS, *et al.* Can positron emission tomography (PET) or PET/Computed Tomography (CT) acquired in a nontreatment position be accurately registered to a head-and-neck radiotherapy planning CT? *Int J Radiat Oncol Biol Phys* 2009;73:578-584.

5. Ireland RH, Dyker KE, Barber DC, *et al.* Nonrigid image registration for head and neck cancer radiotherapy treatment planning with PET/CT. *Int J Radiat Oncol Biol Phys* 2007;68:952-957.

6. Macmanus M, Nestle U, Rosenzweig KE, *et al.* Use of PET and PET/CT for Radiation Therapy Planning: IAEA expert report 2006-2007. *Radiother Oncol* 2009;91:85-94.

7. Facey K, Bradbury I, Laking G, *et al.* Overview of the clinical effectiveness of positron emission tomography imaging in selected cancers. *Health Technol Assess* 2007;11:iii-iv, xi-267.

8. De Ruysscher D, Wanders S, Minken A, *et al.* Effects of radiotherapy planning with a dedicated combined PET-CT-simulator of patients with non-small cell lung cancer on dose limiting normal tissues and radiation dose-escalation: a planning study. *Radiother Oncol* 2005;77:5-10.

9. 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;63:1432-1441.

10. Klopp AH, Chang JY, Tucker SL, *et al.* Intrathoracic patterns of failure for non-small-cell lung cancer with positron-emission tomography/computed tomography-defined target delineation. *Int J Radiat Oncol Biol Phys* 2007;69:1409-1416.

11. van Loon J, Offermann C, Bosmans G, *et al.* 18FDG-PET based radiation planning of mediastinal lymph nodes in limited disease small cell lung cancer changes radiotherapy fields: a planning study. *Radiother Oncol* 2008;87:49-54.

12. Gillham C, Zips D, Ponisch F, *et al.* Additional PET/CT in week 5-6 of radiotherapy for patients with stage III non-small cell lung cancer as a means of dose escalation planning? *Radiother Oncol* 2008;88:335-341.

13. 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;61:1385-1392.

14. Schwartz DL, Ford EC, Rajendran J, *et al.* FDG-PET/CT-guided intensity modulated head and neck radiotherapy: a pilot investigation. *Head Neck* 2005;27:478-487.

15. Wang D, Schultz CJ, Jursinic PA, *et al.* Initial experience of FDG-PET/CT guided IMRT of head-and-neck carcinoma. *Int J Radiat Oncol Biol Phys* 2006;65:143-151.

16. Zheng XK, Chen LH, Wang QS, *et al.* Influence of FDG-PET on computed tomography-based radiotherapy planning for locally recurrent nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys* 2007;69:1381-1388.

17. Shintani SA, Foote RL, Lowe VJ, *et al.* Utility of PET/CT imaging performed early after surgical resection in the adjuvant treatment planning for head and neck cancer. *Int J Radiat Oncol Biol Phys* 2008;70:322-329.

18. Vernon MR, Maheshwari M, Schultz CJ, *et al.* Clinical outcomes of patients receiving integrated PET/CT-guided radiotherapy for head and neck carcinoma. *Int J Radiat Oncol Biol Phys* 2008;70:678-684.

19. Soto DE, Kessler ML, Piert M, *et al.* Correlation between pretreatment FDG-PET biological target volume and anatomical location of failure after radiation therapy for head and neck cancers. *Radiother Oncol* 2008;89:13-18.

20. 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;78:206-212.

21. Girinsky T, Ghalibafian M, Bonniaud G, *et al.* Is FDG-PET scan in patients with early stage Hodgkin lymphoma of any value in the implementation of the involved-node radiotherapy concept and dose painting? *Radiother Oncol* 2007;85:178-186.

22. Esthappan J, Chaudhari S, Santanam L, *et al.* Prospective clinical trial of positron emission tomography/computed tomography image-guided intensity-

modulated radiation therapy for cervical carcinoma with positive para-aortic lymph nodes. *Int J Radiat Oncol Biol Phys* 2008;72:1134-1139.

23. Yildirim Y, Sehirali S, Avci ME, *et al.* Integrated PET/CT for the evaluation of para-aortic nodal metastasis in locally advanced cervical cancer patients with negative conventional CT findings. *Gynecol Oncol* 2008;108:154-159.

24. Thrall MM, DeLoia JA, Gallion H, *et al.* Clinical use of combined positron emission tomography and computed tomography (FDG-PET/CT) in recurrent ovarian cancer. *Gynecol Oncol* 2007;105:17-22.

25. Ford EC, Lavely WC, Frassica DA, *et al.* Comparison of FDG-PET/CT and CT for delineation of lumpectomy cavity for partial breast irradiation. *Int J Radiat Oncol Biol Phys* 2008;71:595-602.

26. Vesprini D, Ung Y, Dinniwell R, *et al.* Improving observer variability in target delineation for gastro-oesophageal cancer--the role of (18F)fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography. *Clin Oncol (R Coll Radiol)* 2008;20:631-638.

27. 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;6:31-36.

28. Anderson C, Koshy M, Staley C, *et al.* PET-CT fusion in radiation management of patients with anorectal tumors. *Int J Radiat Oncol Biol Phys* 2007;69:155-162.

29. Nguyen BT, Joon DL, Khoo V, *et al.* Assessing the impact of FDG-PET in the management of anal cancer. *Radiother Oncol* 2008;87:376-382.

30. Topkan E, Yavuz AA, Aydin M, *et al.* Comparison of CT and PET-CT based planning of radiation therapy in locally advanced pancreatic carcinoma. *J Exp Clin Cancer Res* 2008;27:41.