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ORIGINAL ARTICLE

Role of SPECT-CT in radiotherapy

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Summary

Purpose: *The role of fusion imaging methods SPECT-CT and PET-CT is currently being investigated in radiotherapy (RT) treatment planning. SPECT and PET provide extra information for gross tumor volume (GTV) delineation. The purpose of this study was to evaluate the role of SPECT-CT in RT.*

Methods: *SPECT-CT studies were performed in 55 patients with ^{99m}Tc-MIBI/Tetrofosmin (TF), with 99mTc-Nanoco, with 99mTc-MDP and with 185 MBq ^{131}I scan. All studies were performed with SPECT-CT camera, using low dose CT (130KeV, 30 mA, 3-5 mm step). Corresponding slices on SPECT-CT were compared to the diagnostic CT projections from the simulator. Diagnostic CT scans were performed using 3-5 mm slices both to aid volume definition and to create high quality digitally reconstructed radiographs (DRRs) to aid verification. The volumetric CT data were sent to the treatment planning system.*

Results: *Application of SPECT-CT with ^{99m}Tc-MIBI/TF allowed to diagnose residual malignant mass or a recurrent tumor after combined (surgery and chemotherapy/hormonotherapy) therapy in studied patients with breast cancer, thymomas and lung cancer. SPECT-CT ^{99m}Tc-MIBI/TF contributed to the definition of clinical target volume (CTV). SPECT-CT imaging of sentinel lymph nodes (SLNs) in medially located breast cancer was important for correct topography of intercostal space in cases with parasternal drainage. Irradiation of this subgroup of patients in conjunction with the chest wall and the supraclavicular region should be considered electively for each patient. The combined application of baseline whole body bone scintigraphy, followed by SPECT-CT fusion gave the possibility for correct radiotherapy planning of the GTV in tumor-induced bone disease. SPECT-CT is useful for diagnosis of recently discovered non-responsive to ^{131}I treatment patients with differentiated thyroid cancer. SPECT-CT data are important to avoid prescribed ^{131}I therapy and to define CTV for external beam RT (EBRT).*

Conclusion: *SPECT-CT images could be applicable in RT planning to precisely delinate tumor volume.*

Key words: *gamma-emitters, radiotherapy planning, SPECT-CT*

Introduction

For precise and accurate dose placement, imaging of the tumor at the time of RT is crucial. The role of fusion imaging methods (SPECT-CT and PET-CT) is currently being investigated in RT planning [1]. Up to date image-guided RT extensively involves CT and MRI image data. The quality of targeting RT depends directly on the precise determination of [1,2]:

1. GTV: macroscopic tumor tissue based on imaging and histopathology.
2. Clinical target volume (CTV): this volume includes GTV with a margin accounting for subclinical microscopic invasion, e.g. CTV=GTV+0.5 cm. CTV is anatomical-clinical volume.
3. GTV and CTV are purely oncological concepts independent from any technology. The corresponding RT term is planning risk volume (PRV).
4. Planning Target Volume (PTV): this volume includes CTV with a safety margin from organ motion, daily patient setup, radiation technique, and intra treatment variation. PTV

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is geometrical term.

5. Volume of the organ at risk (OAR): OAR has a tolerance dose that depends on the dose per fraction, and the dose must be kept as low as possible.

SPECT and PET provide extra information for GTV delineation [1,3,4]. SPECT-CT modality is useful to visualize tumor tissues using different gamma-emitted radiopharmaceuticals. SPECT-CT allows correct localization of "hot" scintigraphic spots, differential diagnosis of physiological from pathological uptake, benign from malignant lesions, and residual or recurrent tumor masses from the fibrous tissue after treatment [5-7].

Several useful SPECT-CT clinical applications in RT planning, including SLN mapping, tumor imaging with ^{99m}Tc-MIBI/TF in breast cancer, thymoma, lung cancer, bone scintigraphy and ^{131}I thyroid scintigraphy are considered.

The purpose of this study was to evaluate the role of SPECT-CT in RT.

Methods

SPECT-CT studies were performed in 55 patients:

1. SPECT-CT imaging with ^{99m}Tc-MIBI/TF was carried out in 25 patients: 5 with lung cancer, 15 with breast cancer (3 after neoadjuvant chemotherapy and 12 after combined treatment [surgery and chemotherapy/hormonotherapy] suspicious for relapse) and 5 with thymomas.
2. SPECT-CT SLN imaging with ^{99m}Tc-Nanocol was carried out in 5 patients with medially or centrally located breast cancer.
3. SPECT-CT bone scintigraphy with ^{99m}Tc-MDP was carried out in 20 patients.
4. SPECT-CT with 185 MBq ^{131}I scan was carried out in 10 thyroid cancer patients in order to detect non-iodineavid residual tumor tissue, lung lesions and/or cervical lymphadenopathy.

All studies were performed with SPECT-CT camera (Siemens Symbia T2), using low dose CT (130KeV, 30 mA, 3-5 mm step).

The corresponding slices on SPECT-CT were compared with the diagnostic CT projections from the simulator. Diagnostic CT scans were performed using 3-5 mm slices both to aid volume definition and to create high quality DRRs to aid verification. The volumetric CT data were sent to the treatment planning system.

The RT tools used in our study were:

1. Linear accelerator – Primus HE (Siemens, Germany) and Varian ix Clinac with OBI (Varian, USA).
2. Simulator and source projectors. The simulation of irradiation was done on Simview simulator (Siemens, Germany).
3. The treatment planning of RT was done on the planning system "Oncentra" by Nucletron and Eclipse, v.8.9 (Nucletron, the Netherlands). Multi-leaf collimators allowed the intensity modulation of the beam taking into account the heterogeneity of the tissues, the shape of the body and the shape of the PTV.
4. Portal imaging systems allowed verification of the treatment field accuracy produced by the treatment machine at the time of treatment.

Most of the patients were followed up after RT.

Results

SPECT-CT scintigraphy with ^{99m}Tc-MIBI/TF was positive for residual tumor tissue in 3 cases with locally advanced breast cancer after neoadjuvant chemotherapy. In 3 women local relapse in the breast was identified after quadrantectomy of the primary tumor, in 6 patients local relapse on the chest wall was diagnosed after radical mastectomy and in 3 cases metastatic disease in the ipsilateral internal mammary lymph node chain was discovered. In 4 out of these 12 patients supraclavicular and axillary I and II level metastatic lymph nodes were depicted. SPECT-CT showed exact location of "hot" pathological spots corresponding to the diagnostic CT projections of the treatment planning system. In patients with locally advanced lung cancer and thymomas, residual tumor tissue and/or locoregional mediastinal and hilar enlarged lymph nodes with intensive tracer uptake were imaged after surgery. SPECT-CT data were very important in these cases for correct tumor delineation (Figure 1).

Our results showed that SPECT-CT imaging of SLNs increased the sensitivity and diagnostic accuracy of lymphoscintigraphy in 5 patients with medial and central breast cancer by detecting additional "hot" regional axillary nodes in 1 of them, imaging of lymph node drainage to the ipsilateral internal mammary lymph nodes in 3 and discovering SLNs in 1 case with negative planar lymphoscintigraphy. Three women with medial localization of the primary tumor were patients with high-risk breast cancer and visualized internal parasternal lymph nodes were added to the RT planning as GTV (Figure 2).

Patients with positive internal mammary nodes (INM) and negative axilla (pN2b), ipsilateral parasternal and axillary lymph nodes, level III

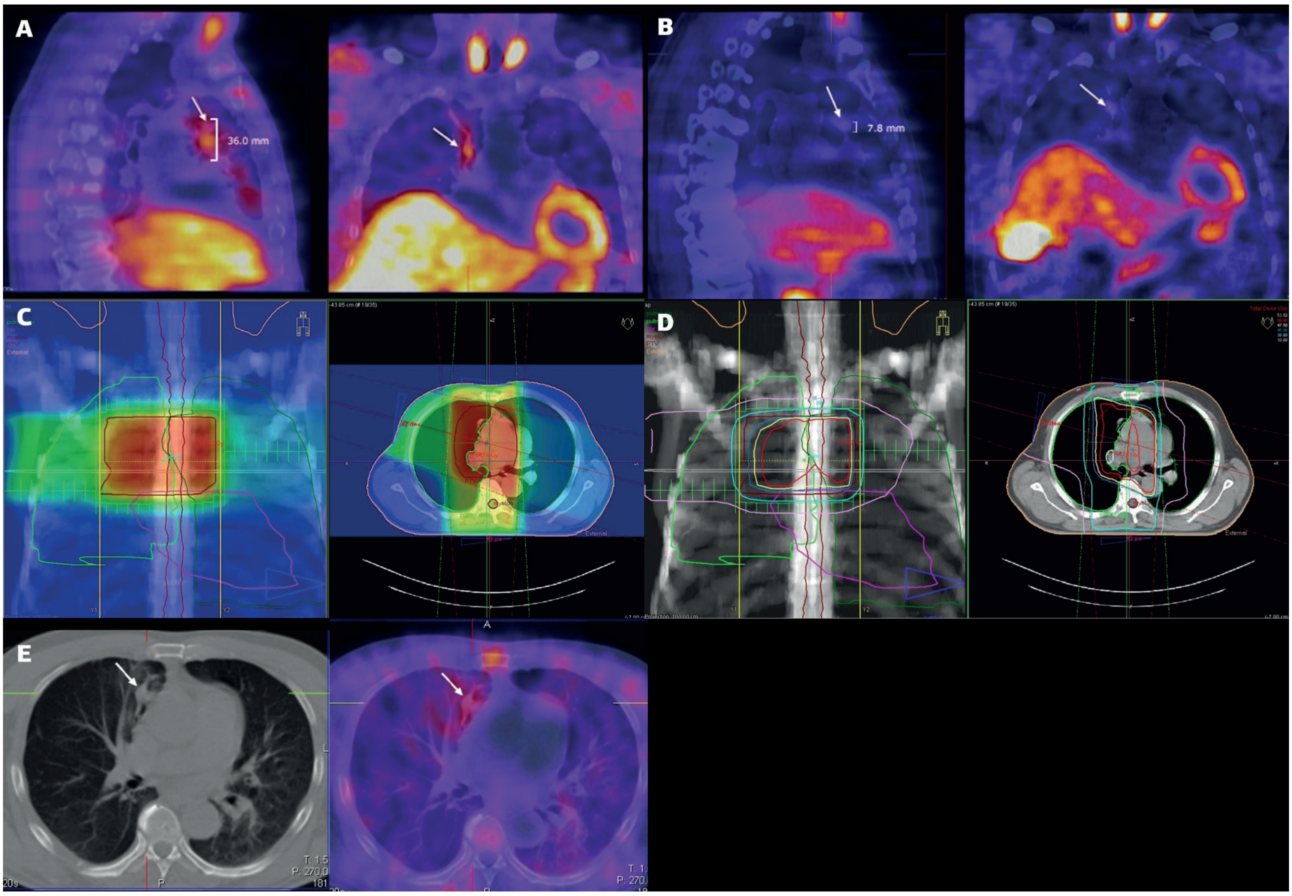

Figure 1. A: A patient with thymoma and infiltration of the right lung after surgery. SPECT-CT 99mTc-MIBI showed residual tumor mass with intensive tracer uptake in the region of the right mediastinal pleura and anterior mediastinum with sagittal size of 36 mm (arrow). **B:** Control study after EBRT showed reduced size (7.8 mm) (arrow) with decreased tracer uptake. **C:** Dose plan - coronal and transaxial CT images. **D:** Coronal and transaxial images showing the PTV (red line) and dose distribution. **E:** Diagnostic SPECT-CT can change treatment volumes by identifying involved mediastinal pleura (arrow) and mediastinal lymph nodes. Contrast-enhanced CT showing a right paratracheal node 10 mm in short axis diameter (arrow). The corresponding slice on SPEC-CT shows intensive uptake. This node should be contoured as CPTV. CT scans are obtained from the cricoid cartilage to the superior aspect of the L2 vertebra to allow the lung DVH to be calculated. A co-registered SPECT scan can be used to aid volume definition. Defining volumes on a SPECT-CT image may help distinguish residual tumor and lymph nodes from other structures.

(paraclavicular and supraclavicular) without level I and level II, were indicated for external beam radiotherapy (EBRT) to a total dose 46-50 Gy (Figure 3).

INM recurrence was identified as a chest wall recurrence (parasternal) or as isolated bone metastases (sternal). (Figure 2).

The CT part of the fusion images in 20 cases with skeletal lesions allowed to detect direct infiltration of bone structures as a result of proximity to the neoplastic recurrent or metastatic process localized in the surrounding soft tissues and to determine the volume of the cortical destruction and spongious infiltration and to differentiate painful degenerative bone changes from secondary lesions. The volume of locally advanced metastatic disease with expansion of preexisting soft-tissue metastatic lesions could be described. These results gave the possibility for correct planning of the GTV in palliative RT of painful osseous metastases (Figure 2).

The precise localization of the ^{131}I uptake used for the management of patients with differentiated thyroid cancer was difficult due to lack of anatomical landmarks in the whole body (WB) scan. SPECT-CT was useful for the diagnosis of 10 cases, clinically discovered non-responsive to ^{131}I treatment. SPECT-CT data were important to avoid prescribing ^{131}I therapy and to defining GTV for EBRT.

Discussion

The clinical roles of ^{99m}Tc-MIBI/TF are well

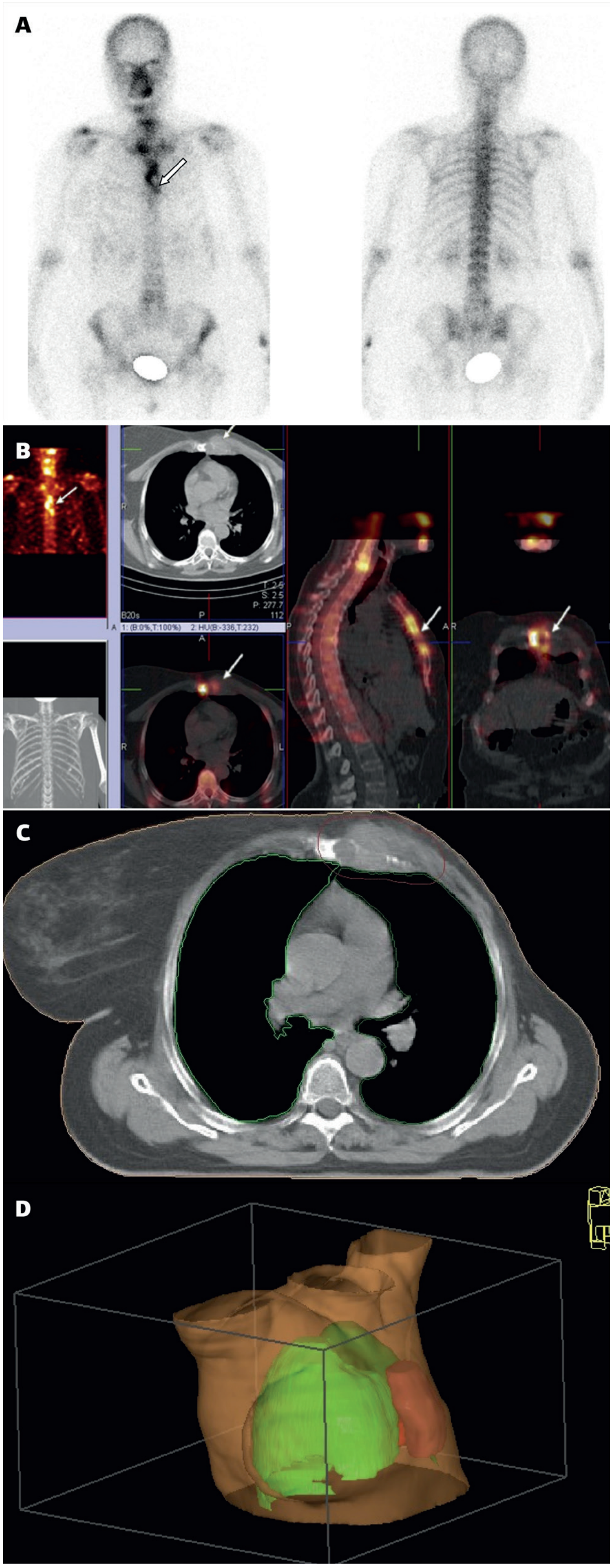

Figure 2. A: A patient with breast cancer localized in the inner quadrant on the left. Whole body bone scan showed a solitary metastatic bone lesion in the sternum (arrow). **B:** SPECT-CT revealed soft tissue formation in the ipsilateral parasternal space directly infiltrating the sternum (arrow). PTV **(C)** and radiation dose distribution **(D)**.

known as tracers of cellular metabolism used for visualization of higher uptake in proliferating tumor cells [8]. The uptake of these two radiotracers is favored by the increased blood flow, capillary permeability and elevated metabolic activity of neoplastic cells [9,10]. It is strictly depended on cell membrane and mitochondrial potential and also on the expression of p-glycoprotein. ^{99m}Tc-TF predominantly accumulates in the cytosol and mitochondria, while ^{99m}Tc-Sestamibi accumulates only in the mitochondria in proliferative malignant cells [11].

SPECT-CT has proved more sensitive and specific than SPECT imaging in various clinical settings because of better spatial resolution, in particular in the detection of smaller lesions [12].

Applications of SPECT-CT with ^{99m}Tc-MIBI/TF allow to diagnose residual malignant masses or a recurrent tumor after complex therapy (surgical intervention, radio/chemotherapy) and to evaluate the response to the neoadjuvant treatment in locally advanced breast carcinomas in patients with breast cancer, thymomas and lung cancer. SPECT-CT ^{99m}Tc-MIBI/TF contributes to the definition of GTV.

SPECT-CT visualised the exact topographic location of all SLNs for radio-guided biopsy and had a clinically potential role for RT planning in patients with medial and central localization of breast cancer [13,14].

According to the “IEO Breast Cancer Treatment Recommendations 2010” [15] “patients with breast cancer in the inner quadrants should have a biopsy of the internal mammary chain lymph nodes. Biopsy should be performed during breast surgery with minimum increase in the operating time. The IMNs are easily accessed through the intercostal space. Fatty tissue containing the node should be examined and carefully freed from blood vessels, taking care also to avoid damaging the underlying pleura. If an involved internal mammary chain (IMC) node is found (even if the axilla is disease free) the disease is upstaged so that adjuvant treatments (chemo or radiation therapy) must be given”.

SPECT-CT imaging of SLNs in patients with medial location of breast cancer is important for correct topography of intercostal space in cases with parasternal drainage [13,14].

Visualization of internal mammary lymph nodes is often ignored by surgeons. Treatment of this group of lymph nodes is a problem that has created much controversy. Irradiation of this subgroup of patients in conjunction with the chest wall and supraclavicular region should be considered electively for each patient [16].

The combined application of baseline whole body bone scintigraphy, followed by more specific techniques such as SPECT-CT fusion, is an advanced approach for diagnosis, differential diagnosis and staging of osseous metastases [5]. SPECT-CT data are very important to establish the exact structure of painful bones, the volume of metastatic destruction and the infiltration of the surrounding soft tissues.

Conclusion

The integration of modern multiple modalities such as SPECT-CT, PET-CT, PET-MRI may allow identification of target and non-target structures using morphological, functional and biological information better than applying each single imaging modality. SPECT-CT images could be applicable for RT planning to achieve precise tumor volume delineation.

References

1. Paulino A, Thorstad W, Fox T. Role of Fusion in Radiotherapy Treatment Planning. Semin Nucl Med 2003;33:238-243.
2. Armstrong J, Raben A, Zelesky M et al. Promising survival with three-dimensional conformal radiation therapy for non-small cell lung cancer. Radiother Oncol 1997; 44:17-22.
3. Grosu AL, Feldmann HJ, Disk S et al. Implications of IMT-SPECT for postoperative radiotherapy planning in patients with gliomas. Int J Radiat Oncol Biol Phys 2002;54:842-854.
4. Berthelsen AK, Loft A. Use of PET/CT in radiotherapy planning. In: Federspiel MK, Hogg P (Eds): PET/CT in radiotherapy planning. EANM Brochures-part 3. EANM vereint: Association & Conference Management LTD, Vienna 2012, pp 61-67.
5. Mariani G, Bruselli L, Kuwert T et al. A review on the clinical uses of SPECT/CT. Eur J Nucl Mol Imaging 2010;37:1959-1985.
6. Sergieva S, Alexandrova E, Baichev G, Parvanova V. SPECT-CT in breast cancer. Arch Oncol 2012;20:127-131.
7. Van der Ploeg IM, Valdes Olmos RA, Kroon BBR, Nieweg OE. The hybrid SPECT/CT as an additional lymphatic mapping tool in patients with breast cancer. World J Surg 2008;32:1930-1934.
8. Schillaci O, Buscombe JR. Breast scintigraphy today: indications and limitations. Eur J Nucl Med Mol Imaging 2004;31(Suppl 1):S35–S45.
9. Moretti JL, Azaloux H, Boisseron D. Primary breast cancer imaging with technetium-99m sestamibi and its relation with P-glycoprotein overexpression. Eur J Nucl Med 1996;23:980-986.
10. Sergieva BS, Timcheva KV, Hadjiolov ND. 99mTc -MIBI scintigraphy as a functional method for Multi Drug, Resistance (MDR) evaluation in breast cancer patients. JBUON 2006;11:61–68.
11. Madeddu G, Spanu A. Use of tomographic nuclear medicine procedures, SPECT and pinhole SPECT, with cationic lipophilic radiotracers for evaluation of axillary lymph node status in breast cancer patients. Eur J Nucl Med Imaging 2004;31(Suppl 1):S23-S34.
12. Van der Ploeg IM, Nieweng OE, Kroon BB et al. The yield of SPECT-CT for anatomical mapping in patients with breast cancer. Eur J Nucl Med Mol Imaging 2009;36:903-906.
13. Gang Cheng G, Kurita S, Torigian DA, Alavi A. Current status of sentinel lymph node biopsy in patients with breast cancer. Eur J Nucl Med Mol Imaging 2011;38:562–575.
14. Benda RK, Cendan JC, Copeland EM et al. Should decisions on internal mammary lymph node irradiation be based on current lymphoscintigraphy techniques for sentinel lymph node identification? Cancer 2004;100:518-523.
15. IEO Breast Cancer Treatment Recommendations 2010. In: Goldhirsch A, Veronesi U, Orecchia R (Eds). Istituto Europeo di Oncologia, Milano, Italia, 2010, p17.
16. Bourre JC, Payan R, Collomb D et al Can the sentinel lymph node technique affect decisions to offer internal mammary chain irradiation. Eur J Nucl Med Mol Imaging 2009;36:758-764.