PET/CT-Based Dose Planning in Radiation Therapy

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Introduction

Approximately 50% of cancer patients are estimated to receive radiation therapy as part of their total treatment regimen. External-beam treatment methods most commonly used at the Department of Radiation Oncology at Copenhagen University Hospital include 3D conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), intensity-modulated arc therapy (IMAT), and stereotactic radiation therapy (SRT). Radiation therapy can either cure patients of malignant disease or palliate symptoms caused by malignant disease. Radiation therapy is an inexpensive treatment method compared with, for example, surgery, chemotherapy, and immunotherapy [1]. One of the most pronounced disadvantages of radiation therapy is the acute side effects in normal tissue, e.g., mucous membranes occurring during and after the treatment. Correctly identifying and including all tumor cells in the target volume and avoiding as much normal tissue as possible is the challenge of curative radiation therapy, especially when the new treatment methods, such as 3D-CRT, IMRT, IMAT, and SRT, are used.

Positron emission tomography (PET) with the tracer [^{18}F]-fluorodeoxyglucose (FDG) uses the fact that malignant cells have an increased metabolism and up-regulated membrane-bound glucose transporters [2]; therefore, they have a higher FDG uptake than normal tissue. PET is a functional imaging method without the precise anatomical resolution of computed tomography (CT) and magnetic resonance imaging (MRI). PET/CT scanners combine functional information from PET with anatomical information from CT, and the use of this imaging modality in cancer patients has increased very rapidly since it was introduce in 2001. PET/CT is increasingly used for radiation therapy dose planning.

PET/CT-Based Dose-Planning Process

The planning process is carried out with utmost precision within the short time period between the scan and the treatment initiation. It is done by a team of qualified staff, including mould technicians, nuclear technologists, radiation technologists, nuclear physicians, radiologists, radiation oncologists, physicists, and dosimetrists.

It is of great importance that the PET/CT scan is carried out in the precise treatment position. For this reason, laser lights should be installed in the scanner, a flat tabletop should be placed on the scanner bed, and the patient must be positioned in the immobilization device precisely as for the treatment.

The scan is performed according to routine procedures; however, it is of great importance that the scan is performed with contrast enhancement and diagnostic quality, as the scan is used for radiotherapy-dose planning. We always perform the PET/CT scan as a whole-body examination, thereby allowing detection of possible unknown distant metastases, which typically would have an impact on further treatment planning.

After the scan patient setup marks are tattooed or marked on the immobilization device so the exact position can be reproduced during daily treatment.

Radiation Therapy Dose-Planning Process

The dose planning process starts with the nuclear medicine physician the radiologist in consensus interpreting the PET/CT scan and depicting any malignant foci. The nuclear medicine physician then delineates the PET-positive tumor(s), gross tumor volume defined by PET, hereafter named gross tumor volume (GTV)-PET. CT scan and GTV-PET volumes are transferred to the dose planning system in the radiotherapy department.

On the CT scan, radiologist and radiation oncologist define the GTV-CT, which can include, for example, enlarged, necrotic lymph nodes that were non-FDG avid and therefore were not included in the GTV-PET. A final GTV including information from the GTV-PET and GTV-CT is then defined, a process also involving clinical information gained by physical examination, previous imaging studies (e.g., CT, MRI, US), and information from invasive diagnostic methods, including surgery.

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The radiation oncologist then defines the clinical target volume (CTV), including the GTV and any areas of suspected microscopic disease. There could be several CTVs receiving different doses, as is common in, for example, the head and neck area.

Hereafter, the dosimetrist continues the planning process by delineating the planning target volume (PTV), allowing a margin around the CTV for setup uncertainties, possible CTV movement due to respiration, or inter- and intratreatment variations. The organs at risk (OARs) are defined on the dose-planning computer system. These might be the spinal cord, kidneys, or any radiosensitive organ in the treatment area.

A treatment plan will be generated using a dose-planning system with the best technique available in the department for the individual patient. This could be 3D-conformal RT, 4D-conformal RT using gating (respiratory control during radiotherapy), IMRT, SRT, IMAT, or proton therapy. This process involves appropriate dose distribution to the CTV and OARs. The final plan will be checked at a conference with several radiotherapy experts, radiation oncologists, and physicists, before being digitally sent to the treatment machines.

Results

It is our opinion that target definition is strongly facilitated by using PET/CT in the dose-planning process. We also believe that the working method we use for defining target, involving nuclear physicist, radiologist, and radiation oncologist, is a safer method that the one previously used by a single radiation oncologist. It is also our feeling that this working method allows more energy for the radiation oncologist to focus on the definition of proper CTV/CTVs.

The use of PET/CT frequently changes previously known tumor size and stage, including both presence of lymph node and distant metastases. These facts sometimes lead to changes in treatment modality with, for example, addition of concomitant chemotherapy or surgery and even to another treatment intention. In concordance with what others also have experienced, synchronous cancers are also detected when whole-body PET/CT is used for dose planning [3, 4].

Side effects most commonly seen are those of acute systemic allergic reactions due to iodine-containing contrast (not related to PET but to CT) and claustrophobic reactions during scanning, when the patient is immobilized and going through the gantry opening.

Discussion

In our work to improve imaging techniques for radiation-therapy dose planning, we are using intravenous (IV) and orally applied contrast for CT scanning, our slice thickness is 3 mm, we have our own MRI scanner in our department. We also have a dedicated PET/CT scanner for whole-body PET/CT before dose planning, which has led to findings that change the intended treatment in approximately 30% of patients. This is confirmed by others using the same method [5]. One possible reason for this is that we not only use the older CT criteria for pathologic lymph node definition but also include increased metabolism in lymph nodes <10 mm in diameter [6]. Several studies [7-10] have shown increased conformity in target definition when using PET/CT instead of CT alone.

We find that the method we use for target definition in which a nuclear physicist and a radiologist work together and (often, but not always) the same radiologist works with a radiation therapist, is working very well. The radiation oncologist experiences a lot more energy and security when defining CTVs after GTV definitions together with the radiologist, compared with doing the entire procedure alone. We also experience that the teamwork makes the target definition more pleasant.

The effect of PET/CT has shown that the treated volume can either be smaller or larger, depending on additional information gained [5, 7]. We also believe that using PET/CT for radiotherapy dose planning is necessary if the patient is to have any gain from the new treatment techniques, such as IMRT, IMAT, IMPT, and SRT.

We strongly recommend the use of [^{18}F]-FDG-PET/CT in radiotherapy dose planning. In the future, we expect an increased use of PET/CT with tracers other than FDG for known prognostic factors such as hypoxia and tumor cell proliferation [11, 12]. It is of greatest importance to find tracers for genetically determined intrinsic tumor radiosensitivity, a significant prognostic factor for local control. These factors are all important for delivering radiotherapy with the so-called dose-painting technique [13, 14].

Conclusion

In conclusion, we find whole-body PET/CT scanning for radiation-therapy dose planning a very useful tool in upfront radiation therapy and we believe it will be used even more in the future. We strongly believe in our working method involving different specialists in modern imaging techniques and specialists in radiation therapy, as described. The potential effects for patient outcome need to be observed in the future.

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