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Original Article

Functional Imaging in Radiotherapy in the Netherlands: Availability and Impact on Clinical Practice

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Abstract

Aims: Functional imaging with positron emission tomography/computed tomography (PET/CT) and multiparametric magnetic resonance (mpMR) is increasingly applied for radiotherapy purposes. However, evidence and experience are still limited, and this may lead to clinically relevant differences in accessibility, interpretation and decision making. We investigated the current patterns of care in functional imaging for radiotherapy in the Netherlands in a care evaluation study.

Materials and methods: The availability of functional imaging in radiotherapy centres in the Netherlands was evaluated; features available in >80% of academic and >80% of non-academic centres were considered standard of care. The impact of functional imaging on clinical decision making was evaluated using case questionnaires on lung, head/neck, breast and prostate cancer, with multiple-choice questions on primary tumour delineation, nodal involvement, distant metastasis and incidental findings. Radiation oncologists were allowed to discuss cases in a multidisciplinary approach. Ordinal answers were evaluated by median and interquartile range (IQR) to identify the extent and variability of clinical impact; additional patterns were evaluated descriptively.

Results: Information was collected from 18 radiotherapy centres in the Netherlands (all except two). PET/CT was available for radiotherapy purposes to 94% of centres; 67% in the treatment position and 61% with integrated planning CT. mpMR was available to all centres; 61% in the treatment position. Technologists collaborated between departments to acquire PET/CT or mpMR for radiotherapy in 89%. All sites could carry out image registration for target definition. Functional imaging generally showed a high clinical impact (average median 4.3, scale 1–6) and good observer agreement (average IQR 1.1, scale 0–6). However, several issues resulted in ignoring functional imaging (e.g. positional discrepancies, central necrosis) or poor observer agreement (atelectasis, diagnostic discrepancies, conformation strategies).

Conclusions: Access to functional imaging with PET/CT and mpMR for radiotherapy purposes, with collaborating technologists and multimodal delineation, can be considered standard of care in the Netherlands. For several specific clinical situations, the interpretation of images may benefit from further standardisation.

Key words: Care evaluation; functional imaging; MR; patterns of care; PET/CT; radiotherapy

Introduction

External beam radiotherapy increasingly relies on imaging for patient selection and target definition [1]. The desired imaging accuracy to depict tumour lesions and their borders has increased since the introduction of intensity-modulated radiotherapy, where dose can be delivered more conformal, with steep gradients and high spatial modulation [2], and it will further increase with the introduction of new tools for real-time position verification and adaptive re-planning during dose delivery, such as magnetic resonance (MR)-linac systems [3].

Computed tomography (CT) is currently the cornerstone of imaging for radiotherapy, as it provides anatomical orientation, visualisation of many tumours and organs at risk, and the electron density map required to calculate

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dose distribution [4]. In addition, anatomical MR sequences can contribute to target definition for many tumour types [5,6]. However, in many situations CT and anatomical MR are insufficient for the discrimination of tumour and normal tissues [7–9]. This contributed to the application of functional imaging in radiotherapy to incorporate biological tissue characteristics, with proven impact on staging, treatment selection, target definition and treatment adaptation for various tumour types [10,11]. Applied functional imaging modalities include positron emission tomography (PET) and advanced MR sequences, each with their own characteristics and levels of supporting evidence.

Molecular imaging with PET(/CT) and radiolabelled tracer molecules can be applied to visualise and quantify metabolic pathways *in vivo*, reflecting functional tissue characteristics, including metabolism, proliferation and hypoxia [12]. The most applied tracer is fluor-18-labelled deoxyglucose (FDG) used to visualise glucose metabolism, for lesion characterisation and staging of various tumour types and with implications for patient selection and treatment outcome for radiotherapy [13]. In addition, FDG-PET can contribute to better and more consistent target definition [14,15], potentially allowing lower toxicity and higher tumour doses [16]. Another increasingly applied tracer is fluor-18-labelled choline, for (re)staging of prostate cancer. PET/CT has the advantage of straightforward signal quantification, and its applications for radiotherapy are increasingly supported by technical guidelines [17,18]. Disadvantages include the limited spatial resolution, relatively high costs and radiation exposure.

Functional imaging with MR is also able to depict various tissue characteristics that have relevance for lesion recognition and characterisation [19]. Two broadly available sequences are dynamic contrast-enhanced (DCE) MR for visualisation and quantification of perfusion and vascular permeability parameters, and diffusion-weighted imaging (DWI) for evaluation of cellular density. For prostate cancer, DCE and DWI are standard of care for the detection of a primary tumour [20] and are used for tumour delineation with improved observer agreement in several tumour types [21,22]. Advantages of functional MR are the ability to acquire DCE and DWI in a single session with anatomical MR, and no exposure to radiation. Disadvantages include, particularly for DCE, non-straightforward signal quantification, limited reproducibility across scanners and centres, and positioning issues related to limited gantry size and the use of coils.

PET and multiparametric MR (mpMR) each have clear value and potential for patient selection and target definition in radiotherapy [10,23], both offer imaging in the treatment position for many tumour sites as required for target delineation, and they are increasingly supported by technical guidelines on image acquisition and image registration [18]. Efforts to combine both modalities together in radiotherapy strategies are increasing [24–26].

However, at this moment, there is still a relative lack of validated interpretation criteria and accepted guidelines for clinical management based on functional imaging [21]. Thus, current implementations of functional imaging for radiotherapy may largely depend on personal preference and expert opinion. This can lead to differences between centres and observers, including in, for example, availability of equipment, options for imaging in the treatment position, interpretation of images, management of discrepancies on multiple imaging modalities and the translation of imaging findings to medical decisions. This can subsequently result in differences in verification strategies, costs, patient burden and treatment outcome.

Efforts to evaluate and improve specific applications of PET/CT and mpMR for radiotherapy need to consider present clinical practice. The aim of this patterns of care evaluation was to determine current patterns of care related to functional imaging in radiation oncology in the Netherlands, focusing on the applications of FDG-PET/CT, choline PET/CT, DCE MRI and DWI MRI for treatment decisions in lung, head/neck, prostate and breast cancer.

Materials and Methods

Access to Functional Imaging

A survey was conducted among all 20 independently operating radiotherapy centres in the Netherlands. The local availability and implementations of functional imaging modalities applied for radiotherapy were noted for the year 2015. Only tools in clinical use were noted, thus excluding research tools. An imaging modality was considered available for radiotherapy purposes when radiation oncologists could request imaging with at least some influence on imaging protocols in order to adapt scans to their needs. This also implies access to radiologists or nuclear medicine specialists for image interpretation and protocol development. A modality capable of imaging in the treatment position (PET/CT or mpMR) was defined as being equipped with a flat table top and having access to positioning materials to allow the treatment position for at least some target areas (e.g. support for a customised mask of the head or neck, arm support for treatment of the lungs or breast, or knee support for treatment of the pelvic area). For PET/CT, a planning CT-capable scanner was defined as being equipped with an external laser positioning system and calibrated Hounsfield units, thus validated for clinical radiotherapy planning and obviating the need for a separate planning CT and additional image registration. To determine a possible difference between resources, we carried out subgroup analyses of academic versus non-academic centres. In this study we defined the current standard of care as imaging facilities that were available for radiotherapy purposes in $\geq$80% of academic as well as in $\geq$80% of non-academic centres.

Clinical Impact

The impact of functional imaging on clinical decision making was evaluated using clinical cases that were designed to contain clinically relevant dilemmas encountered in daily practice in the applications of PET/CT and

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