European Journal of Cancer 62 (2016) 18–27

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Individual patient information to select patients for different radiation techniques

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Received 29 January 2016; received in revised form 29 March 2016; accepted 5 April 2016

KEYWORDS
Head and neck cancer;
Patient-level simulation model;
Photon;
Proton;
Comparative effectiveness

Abstract ***Background and purpose:*** Proton therapy is an emerging technique in radiotherapy which results in less dose to the normal tissues with similar target dose than photon therapy, the current standard. Patient-level simulation models support better decision making on which patients would benefit most.

Materials and methods: A simulation model was developed tracking individual patients' status regarding the primary tumour and multiple complications. As a proof of principle, the model was populated based on information from a cohort of 1013 head and neck cancer patients. Dose–volume parameters for photon and proton radiation treatment plans were then fed into the model to compare outcomes in terms of length and quality of life and select patients that would benefit most.

Results: The illustrative model could adequately replicate the outcomes of photon therapy in

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http://dx.doi.org/10.1016/j.ejca.2016.04.008

the cohort. Improvements from proton therapy varied considerably between patients. The model projects medium-term outcomes for specific individuals and determines the benefits of applying proton rather than photon therapy.
Conclusions: While the model needs to be fed with more and especially recent data before being fully ready for use in clinical practice, it could already distinguish between patients with high and low potential benefits from proton therapy. Benefits are highest for patients with both good prognosis and high expected damage to adjacent organs. The model allows for selecting such patients a priori based on patient relevant outcomes.

1. Introduction

Quality of life after cancer treatment is of increasing interest now that overall survival has improved. Consequently, prevention of side-effects by avoiding damage to adjacent organs is pursued in radiotherapy. Although proton therapy can target the tumour more precisely [1], it is more expensive than photon therapy, so it merits careful consideration of which patients would benefit most.

The superior beam properties of protons can be translated into clinical benefits by two strategies. First, protons can deliver higher doses of radiation to the tumour to improve locoregional tumour control without increasing the dose to healthy tissues and, thus, without enhancing radiation-induced side-effects [2]. Second, more precise proton radiation techniques can reduce the exposure of healthy structures surrounding the tumour (organ at risk [OAR]) to radiation, thereby reducing complication risks [3]. Previous research showed that the expected reduction in radiation-induced side-effects may improve quality of life during and after radiotherapy [4].

In head and neck cancer (HNC), many critical organs surround the tumour loci, indicating considerable potential for proton therapy [5]. The relationship between dose distributions in OARs and the risk of complications is usually described by normal tissue complication probability (NTCP) models [1]. These present the risk of a specific complication for combinations of doses on OARs, allowing the risk reduction from different radiotherapy techniques to be calculated by comparing photon and protons treatment plans [3,6].

Patient and tumour characteristics differ substantially and lead to different outcomes regarding prognosis and quality of life after initial radiotherapy. Therefore, it is important to compare individual HNC patients' health gains after radiation. For some, the advantages of proton therapy may be modest for obvious reasons (e.g. short life expectancy). However, more complex situations may exist, such as tumour locations too close to the OARs or even overlapping them. These specificities underline the need to carefully select patients for whom proton therapy would be advantageous.

One could select patients for proton beam therapy based on a certain minimal threshold of NTCP reductions. However, such an approach ignores effects on more than one complication as well as the role of life expectancy. The proposed model in this study allows integration of several NTCPs and life expectancy into an estimate of overall expected gain in quality-adjusted life years (QALYs). To support decision making, the integrated model simulates patient's typical course of life and complications. By integrating the effects of individual NTCP models with a primary tumour prognosis model, it compares the photon to the proton technique based on individual radiation plans. The main objective of this study was to show a proof of principle of such a model.

2. Materials and methods

2.1. Selection and description of patients

Data from an observational patient cohort were used to populate a first draft of the model. The cohort consisted of patients treated with definitive radiation therapy either with or without systemic treatment (concurrent chemotherapy or cetuximab) for HNC between 25th February 1980 and 13th December 2010 at the UMC Groningen (n = 277) and VU Medical Center Amsterdam (n = 736). The patient registry included survival status, demographics, and tumour and treatment characteristics (Table 1). Median follow-up time was 25 months, with a mean of 3 years. Variables were registered at each follow-up visit and when notification of death was received. Details on the registry can be found in previous publications using the same data [7–10].

To determine the expected differences between photons and protons, *in silico* planning comparative studies were performed for 50 recent patients that were actually treated with intensity-modulated photon radiotherapy at UMC Groningen [3,4]. For these patients, a back-up proton treatment plan was made and dose distributions in the relevant OARs were obtained. The current study is mainly interested in whether