Physica Medica 30 (2014) 309–313

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Original paper

Peripheral organ doses from radiotherapy for heterotopic ossification of non-hip joints: Is there a risk for radiation-induced malignancies?

Theocharis Berris [a, 1], Michalis Mazonakis [a, 2], Stefanos Kachris [b, 3], John Damilakis [a, *]

[a] University of Crete, Faculty of Medicine, Department of Medical Physics, P.O. Box 2208, 71003 Heraklion, Crete, Greece
[b] University Hospital of Heraklion, Department of Radiotherapy and Oncology, P.O. Box 1352, 71110 Heraklion, Crete, Greece

ARTICLE INFO

Article history:
Received 23 November 2012
Received in revised form
3 September 2013
Accepted 7 September 2013
Available online 29 September 2013

Keywords:
Cancer risk
Heterotopic ossification
Monte Carlo simulation
Radiotherapy

ABSTRACT

Radiotherapy, used for heterotopic ossification (HO) management, may increase radiation risk to patients. This study aimed to determine the peripheral dose to radiosensitive organs and the associated cancer risks due to radiotherapy of HO in common non-hip joints. A Monte Carlo model of a medical linear accelerator combined with a mathematical phantom representing an average adult patient were employed to simulate radiotherapy for HO with standard AP and PA fields in the regions of shoulder, elbow and knee. Radiation dose to all out-of-field radiosensitive organs defined by the International Commission on Radiological Protection was calculated. Cancer induction risk was estimated using organ-specific risk coefficients. Organ dose change with increased field dimensions was also evaluated. Radiation therapy for HO with a 7 Gy target dose in the sites of shoulder, elbow and knee, resulted in the following equivalent organ dose ranges of 0.85–62 mSv, 0.28–1.6 mSv and 0.04–1.6 mSv, respectively. Respective ranges for cancer risk were 0–5.1, 0–0.6 and 0–1.3 cases per 10^4 persons. Increasing the field size caused an average increase of peripheral doses by 15–20%. Individual organ dose increase depends upon the primary treatment site and the distance between organ of interest and treatment volume. Relatively increased risks of more than 1 case per 10,000 patients were found for skin, breast and thyroid malignancies after treatment in the region of shoulder and for skin cancer following elbow irradiation. The estimated risk for inducing any other malignant disease ranges from negligible to low.

Introduction

Heterotopic ossification (HO) is a complication by which bone formation occurs outside the skeletal structure. Post-traumatic, post-surgical or neurogenic HO frequently affects the large joints of the upper and lower extremities such as hip, knee, elbow and shoulder [1]. This non-malignant condition may cause local pain, swelling and functional deficits leading to a limited motion range or even ankylosis of the involved joint [1]. The surgical removal of HO needs to be followed by prophylactic treatment to prevent a new abnormal bone formation. The adjuvant administration of non-steroidal anti-inflammatory drugs might result in gastrointestinal and renal side effects and in an increased rate of bone nonunion after fracture [2]. Pre- and post-operative single-fraction radiotherapy plays a major role in the prophylaxis of HO. The main concern with this effective treatment is the risk of subsequent carcinogenesis. Jansen et al. estimated the risk magnitude of fatal tumor induction from irradiation for ectopic bone formation [3]. Their study was limited to hip radiotherapy whereas risk assessment was based on the effective dose concept without providing any data about cancer risk to individual organs. HO of non-hip joints usually appears in a young patient population with longer life expectancy than that of patients with this disease in the hip region [4,5]. To our knowledge, no attempts have been made to quantify the cancer risk from radiotherapy for HO of non-hip joints using dosimetric measurements or calculations. Cancer risk data might be solely derived from the short-term follow-up of patients receiving a single irradiation therapeutic dose in sites other than hip [4–10]. However, the mean or median follow-up periods in the above patient series varied from 6.0 to 43.3 months. Reported

* Corresponding author. Tel.: +30 2810 392569; fax: +30 2810 394933.
E-mail addresses: theocharisberris@gmail.com (T. Berris), mazonak@med.uoc.gr (M. Mazonakis), leukisgr@yahoo.com (S. Kachris), John.Damilakis@med.uoc.gr, damilaki@med.uoc.gr (J. Damilakis).
[1] Current address: International Atomic Energy Agency, Department of Nuclear Safety and Security, NSRW, RSM, Radiation Protection of Patients Unit, Vienna International Centre, PO Box 200, A-1400 Vienna, Austria. Tel.: +43 1 2600 21268.
[2] Tel.: +30 2810 392342.
[3] Tel.: +30 2810 392500.

1120-1797/$ – see front matter © 2013 Associazione Italiana di Fisica Medica. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejmp.2013.09.003

experience has suggested that the latent period for radiation-induced leukemia reaches a peak by 7–12 years whereas solid tumors require a longer latency exceeding ten years [11].

The current study was conducted in order to: (a) determine the radiation dose received by all main and remainder organs defined by the International Commission on Radiological Protection (ICRP) [12] and, (b) estimate the associated lifetime organ-specific cancer risk attributable to radiotherapy for HO at the sites of elbow, knee and shoulder.

Materials and methods

Monte Carlo model

The model of a medical linear accelerator (SL 75, Elekta/Philips, The Netherlands) producing 6 MV X-rays has been developed using the general-purpose Monte Carlo N-Particle (MCNP) transport code as previously described [13]. The simulated therapeutic X-ray beam in conjunction with an androgynous phantom (Body Builder software, White Rock Science, Los Alamos, New Mexico, USA) simulating an average adult (with a height of 179 cm and a weight of 73.54 kg) were used to simulate radiotherapy of HO of the shoulder, elbow and knee. The phantom was appropriately modified to include all organs at risk for secondary radiation induced cancer as defined by the ICRP in publication 103 [12]. The validity of the model regarding the in-field and out-of-field dose calculations and details on the phantom modifications have been reported previously [13].

Simulation of radiotherapy techniques

The simulation of radiotherapy setups for HO was realised with the aid of a radiation oncologist experienced in the clinical management of benign diseases. To simulate irradiation at the elbow, a left arm was added to the phantom. The arm included all appropriate cells representing bone, soft tissue and skin tissue. The aforementioned cells represent geometrical volumes with boundaries defined by mathematically described surfaces creating the 3-dimensional geometry of the MCNP models. Furthermore, the adjacent phantom's legs were separated to represent the real patient's irradiation in the knee region. For all non-hip sites considered in this study, AP and PA field irradiations were simulated. Equally weighted field treatments delivering 7 Gy to the target were considered. The source-to-skin distance was 100 cm. Monte Carlo simulations were initially performed with the standard field sizes that may be used during radiotherapy for HO. Additional simulations were performed by applying the maximum field dimensions that could be used in such therapies, in order to obtain the most conservative peripheral organ dose calculations. The standard and maximum field sizes, respectively, employed for the different sites were the following: Shoulder: 10×10 cm^2, 10×12 cm^2, elbow: 9×9 cm^2, 10×10 cm^2, knee: 10×12 cm^2, 11×13 cm^2.

Dose estimation

For each irradiation site under consideration, the peripheral dose to all main and remainder organs as defined by ICRP in publication 103 [12] was calculated using Monte Carlo methodology. For each AP and PA field treatment, the radiation dose to all organs was calculated. Organ dose was calculated as the weighted average value of the radiation doses received by all fractions of each organ under consideration. In the simulation, dose was calculated by using the F6 tally of the MCNP code. This tally calculates the air kerma in the designated cells. The F6 tally has been widely employed for dose calculations around small cavities and material interfaces leading to acceptable results [13–15]. This is mainly because the error in dose estimation is very small but the time of acquisition of statistically meaningful measurements is substantially decreased compared to using the F8* MCNP tally which calculates energy deposition to the corresponding designated cells.

Cancer risk estimation

The estimation of risk was performed for organs outside the primary beam. All organs or parts of organs in the primary beam were excluded from calculations. This method has previously been employed to address the problem of different response of tissues to different intervals of dose received [13,16]. In highly irradiated areas problems arise in the estimation of the risk for cancer by using the factors derived for low dose and low dose rates [17]. In the current study the risk factors published by the ICRP in 2007 were used for estimation of cancer incidence probability to individual organs [12]. These coefficients are called "nominal risk coefficients" and according to ICRP they "are derived by averaging sex and age-at-exposure lifetime risk estimates in representative populations". The ICRP has published risk factors for the following organs: esophagus, stomach, colon, liver, lung, breast, ovary, bladder, thyroid, skin, bone surfaces and red bone marrow (RBM). The rest of the organs at risk for which data are not sufficient to estimate risk individually are pooled under the remainder category. Table 1 shows the risk factors for the various organs.

Results

The organ doses attributable to radiotherapy for HO in the regions of shoulder, elbow and knee are presented in Tables 2–4, respectively. Doses for the typical-sized fields are presented. The prevention of HO at the shoulder using radiation treatment resulted in an organ dose range of 0.85–61.57 mSv depending upon the organ location in respect to primary irradiated area. Organs receiving doses over 30 mSv were the breast, thyroid and esophagus, while the RBM, remainder and stomach received equivalent doses exceeding 10 mSv. The corresponding dose ranges from radiotherapy at the knee and elbow were 0.28–1.60 mSv and 0.04–1.61 mSv, respectively. The effect of field size on the total organ dose is shown in Fig. 1. Radiotherapy in the regions of shoulder, elbow and knee with the maximum field sizes resulted in average organ dose increase by 14.9% (range: 10.0–21.0%), 20.0% (range: 15.9–22.4%) and 15.2% (range: 9.3–36.1%), respectively.

Table 1
Organs for which the ICRP has defined cancer risk coefficients and the respective nominal risks.

Organ	Nominal risk (cases per 10,000 persons per Sv of equivalent dose)
Red bone marrow	41.9
Colon	65.4
Lung	114.2
Stomach	79.1
Breast	112.1
Ovary	10.6
Bladder	43.4
Esophagus	30.2
Liver	60.6
Thyroid	32.5
Skin	1000
Bone surfaces	7.0
Remainder	143.8