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Deep Inspiration Breath-Hold (DIBH) Techniques for Reducing Cardiotoxicity of Breast Cancer Radiotherapy

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ABSTRACT

The aim of this review was to present the 4D-based radiotherapy techniques used to reduce the heart doses given in radiotherapy of breast cancer. Deep Inspiration Breath-Hold (DIBH) technique provides dosimetry benefit for heart in radiotherapy of left breast. Techniques of DIBH may be divided into two types: spirometry-based and image-based techniques. No superiority of one technique over the other has been demonstrated. Its choice depends mainly on the experience of the center and available equipment. The benefits and limitations related to the use of DIBH are discussed.

Keywords: Deep Inspiration Breath-Hold (DIBH); 4D-Radiotherapy; Breast Cancer; Cardiotoxicity

Abbreviations: 4D-RT: Four-Dimensional Radiation Therapy; DIBH: Deep Inspiration Breath-Hold; MHD: Mean Heart Dose; LAD: Left Anterior Descending Artery; FB: Free Breathing; ABC: Active Breathing Coordinator; vDIBH: Voluntary Deep Inspiration Breath Hold; SGRT: Surface-Guided Radiation Therapy

Introduction

One of major advances in contemporary radiotherapy is Four-Dimensional Radiation Therapy (4D-RT). The fourth dimension is time, meant here as a change of the target and organs at risk in time, i.e. during a treatment session and planning. In general, it is a technique in which period motion due to respiration is considered. Management of respiratory motion effects during treatment has different forms, from simple integration of respiratory movements into treatment planning to define more individualized margins, to respiratory gating and tracking techniques. In most cases, the goal of this technology is to reduce the respiratory motion effects. Deep Inspiration Breath-Hold (DIBH) technique used in radiotherapy of breast cancer is 4D-based, because it is a special kind of gating, i.e. the irradiation of patients is carried out only in the phase of deep inspiration, however, its unique goal here is not the reduction of margins but the shift of target away from the heart by increasing the volume of lung between the irradiated breast and heart.

We have gathered a lot of evidences that giving higher doses to heart and a Left Anterior Descending Artery (LAD) increases cardiotoxicity and a risk of major coronary events. A linear relationship has been found between Mean Heart Dose (MHD) and the rate of major coronary events, which was estimated to increase by 7.4% per Gy of the MHD [1]. Additionally, clinical data show that LAD doses might be better predictors of acute cardiac events than MHD [2]. This may be of a special concern in left-sided plans, as with a proximity of the heart and coronary vessels to the target an achievement of recommended by the guidelines MHD as low as 2.0-2.5 Gy is challenging [3,4], especially, in some patients with socalled unfavorable anatomy, i.e. with high body mass index and/or large adherence of the heart to the thoracic wall. DIBH has proved to be effective in reduction of doses given to LAD and heart in leftsided plans compared to plans realized in Free Breathing (FB) [5-7]. It is also a technique that has some pitfalls and its feasibility for all patients has been challenging. In this review, we summarize the technical aspects, dosimetry/clinical benefits, and some limitations of the use of DIBH in breast cancer radiotherapy.

DIBH Techniques in Breast Cancer Radiotherapy

There are different methods of realization of DIBH in practice. However, they all have the same principle. Patient has to inspire to a specified threshold, sufficiently deep to move a target as far as possible away from the heart, but also this should be sufficiently comfortable to allow a hold of this level of inspiration during a specified period of time, in order to deliver irradiation efficiently. This leads to the reduction of doses given to the heart and LAD without compromising coverage of the PTV which is the left breast or chest wall. Techniques of DIBH which are currently in practice may be divided into two types: spirometry-based techniques, in which a main commercially available system is Active Breathing Coordinator (ABC) system (Elekta, Sweden, Stockholm) [8] and image-based techniques, with the most prevalent, the video-based Real-Time Position (RPM) system (Varian Medical Systems, Palo Alto, CA) [9].

The ABC uses a spirometer to track the patient's actual lung volume during a planning and treatment sessions. Patient is breathing through a mouthpiece attached to a spirometer with a pegged nose to assure that a breathing is only through the device. Once the required volume of the inspired air is reached, the pinch valve in the spirometer remotely closes, preventing the patient from exhaling outside the predefined threshold. The device is connected to a computer and a radiation therapist is able to monitor in the treatment room the patient's lung volume and to switch on an irradiation only during a breath-hold. Patient has a button pressed during a breath-hold and has a possibility to release it to stop a procedure. Once the button is released the balloon valve is deflated and the procedure is interrupted. Obviously, an efficient and reproducible conduction of irradiation requires a close cooperation with patient. Thus the organization of some training sessions in holding a deep inspiration level and understanding of the procedure is necessary. In the practice of our center, an efficient training takes usually 1-2 (exceptionally:3) sessions of 20-30 minutes.

The image-based methods do not require the use of spirometer. Patient voluntarily holds an inspiration at the deepest possible for him level during a time of irradiation. In this method, there is no direct measure of the inspired air volume, but a visualization of the expansion of the patient's thorax during breathing is used as a surrogate of the inspiration level. There are different methods of the monitoring of the level of the thorax expansion during a voluntary breath hold and all these methods are described in the literature using the term "Voluntary Deep Inspiration Breath Hold" (vDIBH). The simplest method of the measure of the adequacy of the breath-hold in vDIBH is based on the monitoring of the

distance moved by the laser from the anterior and lateral tattoos in breath-hold. Treatment rooms cameras are zoomed so that the pen marks of the tattooed fields centers are visible on the control rooms monitors. This enables the radiation therapist to monitor breath hold during treatment [10]. Today, more developed systems as the most prevalent the Varian RPM are in use. In this system, a marker box with the reflective dots is placed on the patient (usually near the xiphoid process) and is used as a surrogate to measure the expansion of the patient's thorax during breathing. The system of cameras mounted on the wall of the treatment unit detects the marker box and calculates the position and movement of the thorax. The system is connected with the linear accelerator and automatically interrupts irradiation if the patient's breathing falls outside of the predefined threshold [9].

DIBH may be also monitored by other means than marker box with the reflective dots. One of these is a real-time Surface-Guided Radiation Therapy (SGRT) assuring the patient surface monitoring throughout the whole treatment session. In general, SGRT systems use a combination of the systems of projectors and several cameras' units to register a real time 3D surface of the thorax. A reference surface relative to the treatment isocenter position is used to calculate the necessary correction of the patient position in translational and rotational directions. One of the commercially available systems of SGRT is the AlignRT system (VisionRT, London, UK) that includes a system of cameras combined with projectors to create a 3D surface model of the thorax with the focus on the treated breast by projecting a red light containing a random speckle pattern on the treated area. This projected pattern is the reference image containing thousands of points on the treated skin. The beam can be paused if parts of the patient's surface deviate from the reference position based on the planning CT set-up or if the calculated isocentric deviations exceed a certain threshold [11,12].

To the best of our knowledge, there was only one prospective study that compared spirometer based DIBH (ABC-DIBH) with vDIBH in patients undergoing left breast radiotherapy in terms of heart sparing, positional reproducibility, and patient comfort/Staff satisfaction. Twenty-three patients were recruited and completed a treatment with both techniques. vDIBH and ABC-DIBH were comparable in terms of positional reproducibility and normal tissue sparing, however patients judged vDIBH more comfortable than ABC-DIBH and for radiographers vDIBH was more satisfactory and took less time to deliver [10]. Despite a paucity of data directly comparing spirometer-based and image-based DIBH techniques, case series and dosimetric studies reporting results on the feasibility, reproducibility and dosimetric outcomes of both techniques indicate similar benefits of the use of any method [5,7,10,13,14]. Both described DIBH techniques, spirometer based and vDIBH are able to reproduce the level of required inspiration and are viable method of delivering DIBH treatment. The choice of

method depends on the possessed equipment and experience of the center.

Dosimetric Benefits and Limitations of DIBh

Dosimetric benefit of the use of DIBH over a FB approach for heart and LAD has been demonstrated by numerous studies. In the systematic review of 10 prospective studies, the MHD and maximum dose to LAD were reduced with DIBH use in the range of 1.0-3.4 Gy and 5.5-21.9 Gy, respectively [7]. In the UK multicenter study (HeartSpare Study, Stage II) evaluating a value of DIBH for left breast irradiation in 101 patients, a mean reduction of MHD and maximum dose to LAD were 0.7 Gy and 11.3 Gy, respectively [14]. Despite a demonstrated dosimetric benefit of DIBH, its routine use is challenged by several reasons. This is a demanding technique for patients, which requires an adequate respiratory function to achieve a breath-hold. Some degree of cooperation, effort and engagement from the patient is necessary for the procedure to be performed properly. In the prospective study evaluating various clinical aspects of the use of DIBH, as many as 20% (26 among 130 enrolled) patients were not suitable for this technique [15]. Similar observation was made by Czeremszynska, et al. [5], about 20% of breast cancer patients would not be compliant with the use of this technique. DIBH requires an additional cost for an extra equipment and training of the radiotherapy staff. Its use increases overall planning and treatment time what may reduce a total number of treated patients. For these reasons, some alternative methods of heart protection in the irradiation of left breast are in use, irradiation in the prone position, Multi-Leaf Collimator (MLC) heart and LAD shielding, and proton beam are among them [16].

However, some data indicate that the DIBH use is more efficient in the heart protection than "prone position", or MLC heart/ LAD shielding. The UK HeartSpare study (Stage IB) compared prospectively MHD and LAD doses and positional reproducibility in 34 larger-breasted women receiving left breast radiotherapy using supine DIBH and FB prone techniques. Supine DIBH led to the reduction of MHD and mean LAD doses compared to FB prone technique [17]. FB MLC shielding of the heart and LAD may be envisaged, however with its use, a risk of underdosage of the breast tissue adjacent to the heart exists and it is not recommended in case of the proximity of the tumor bed to the protected area [18]. We have relatively scarce data on the utility of proton beam therapy for breast cancer irradiation. The phase III RadComp study (NCT02603341) comparing proton and photon beam radiotherapy in pN+ breast cancer patients has for a main goal an evaluation of the incidence of major cardiovascular events. This study is still recruiting patients and the study completion is planned for 2032 [19].

Conclusion

DIBH technique revealed to be very effective for a significant heart dose reduction. Its benefit is strictly dosimetric. We have

no data demonstrating its clinical benefit. Nevertheless, a close relationship between heart doses and the risk cardiovascular events has been demonstrated [2,16]. Thus every effort should be done to reduce heart and LAD doses in radiotherapy of breast cancer. There is no evidence that any DIBH technology is superior to another. Thus the choice of DIBH method should be based on the experience of the center and its existing equipment. In the case of radiotherapy of left breast, when DIBH cannot be used, other alternative methods and measures of cardiac dose reduction should be implemented.

Conflict of Interest

No conflict of interest to declare.

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