

Systemic Circulatory Stiffening as a Complication of Stereotactic Ablative Body Radiotherapy Treatment to the Left Lung

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Case Report

A 57-year-old man presented with a three centimetre mass in the superior lobe of the left lung during a routine surveillance CT scan (Figure 1) eighteen months after thoracoscopic wedge resection of a metastatic renal cell carcinoma from the same area. The mass was located on the previous suture line. The patient had no comorbidities and was considered a surgical candidate for open thoracotomy to remove the superior lobe of the left lung. The patient, however, concerned about negative impacts of thoracotomy to his active lifestyle, elected to proceed with stereotactic ablative body radiation therapy (SABR) as an alternative treatment [1, 2]. The patient was treated with 48Gy in four fractions on alternate days dosed to the 74% isodose line using a conformal SABR technique (Figure 2). At 52 weeks post-SABR, the metastatic renal cell carcinoma demonstrated excellent radiological response.

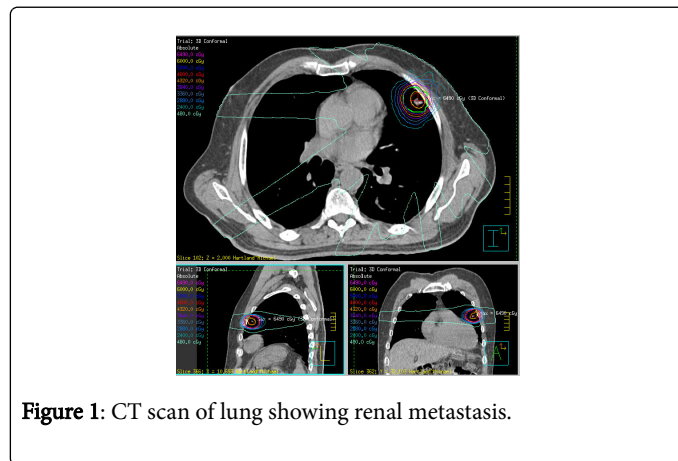


Figure 1: CT scan of lung showing renal metastasis.

The patient maintained his regular exercise regime during and after treatment in accordance with the American College of Sports Medicine guidelines for exercise and cancer which recommends a minimum of 150 minutes of moderate intensity exercise per week [3]. General health and fitness of the patient were monitored at the University of South Australia's clinical exercise physiology laboratory before and for 12 months after SABR. Notably, one marker of cardiovascular health status, the Augmentation Index (AIx), which provides an indication of arterial stiffness, was adversely affected following SABR. AIx is measured using SphygmoCor™ apparatus (AtCor medical Pty. Ltd. Australia) and is a composite marker of both central arterial compliance and peripheral arteriolar resistance. Elevated AIx is a

predictor of future cardiovascular mortality independent of age, diabetes or prior cardiovascular disease [4]. Measures of AIx were taken by a skilled operator in a temperature controlled room (22°C), with the patient rested and lying supine for 15 minutes prior to assessment; tester reliability was at 92.5%. The minimal detectable change (MDC) for AIx was 4.9%.

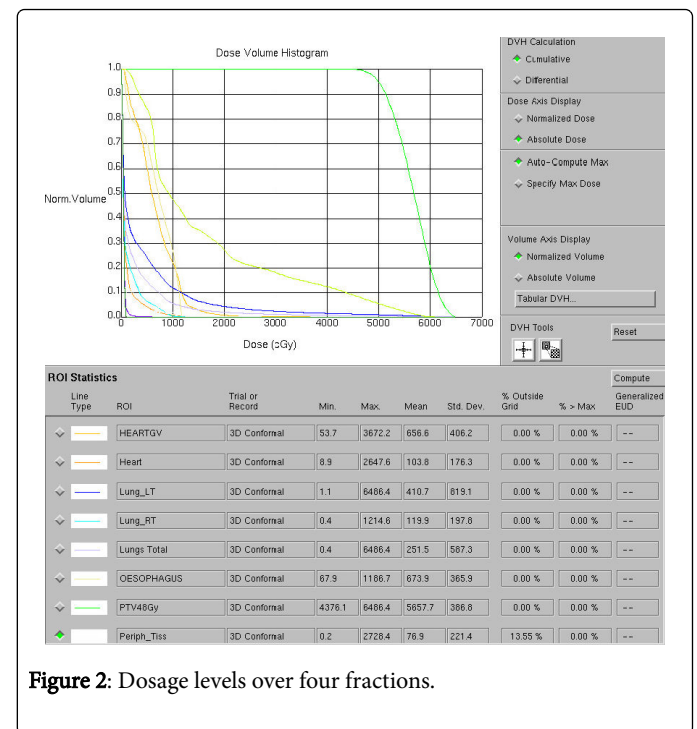


Figure 2: Dosage levels over four fractions.

This MDC was calculated from a previously reported standard deviation (SD) and intraclass correlation coefficient (ICC) [5] and the formula:

$$MDC = 1.96\sqrt{2}(SD\sqrt{1 - ICC})$$

AIx was 3.7% before SABR (Figure 3), which is typical for a healthy 25 year old male. However, by one month after SABR, AIx had increased more than fourfold to 17.1% (Figure 3). This increase in AIx was almost three times the MDC. AIx remained elevated during the second (18.8%), third (20.3%), and six (17.0%) month after SABR (Figure 3). AIx reduced to 10.0% 12 months after SABR (Figure 3).

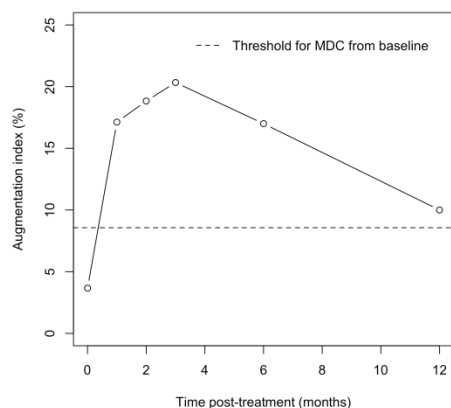


Figure 3: Augmentation index measured before and after stereotactic ablative body radiation therapy. Values are normalised to 75% max heart rate. The SphygmoCor operator index indicated $\geq 93\%$ accuracy for all measurements. MDC, minimum detectable change.

Discussion

This case study is the first investigation of arterial stiffness in lung cancer patients following SABR. It has recently been shown that conventional wide beam radiotherapy is associated with local arterial stiffening and increased cardiovascular risk in breast cancer patients 15 years post treatment [6]. Whilst this breast cancer study suggests long term stiffening after radiotherapy to the thoracic area, nothing is known about potential acute or short term effects on arterial stiffness following SABR. The side effects of SABR are generally regarded as more limited than traditional wide beam radiotherapy, but it appears there may still be adverse effects on cardiovascular health, at least when treating the superior lobe of the left lung. The AIx was increased from 3.7% at baseline to $\geq 17.0\%$ for the first 6 months following treatment (i.e. 14.3% increase). Increases of 10% have been shown to increase the relative risk of cardiovascular mortality by 30% and all-cause mortality by 40% [7]. It is unknown whether the effects seen here are due to direct radiation of cardiovascular structures or an indirect consequence of systemic exposure. It can be assumed they are biological as opposed to age induced changes as they become elevated during treatment and then began to decrease six months later.

This provides some evidence that any adverse effects on cardiovascular health after SABR can begin recovery in the first 12 months following treatment. Additionally, the patient was continuously engaged in over of 435 minutes of gym-based moderate-intensity exercise per week, which is in excess of the minimum threshold of the American College Sports Medicine guidelines for cancer survivors, there is strong evidence that aerobic exercise can

lower arterial stiffness in healthy and a range of clinical populations [8].

An inherent limitation of case studies is the use of only a single participant. It is unknown whether findings of this case study are representative of the wider body of lung cancer patients undergoing SABR. Nonetheless, increases in AIx of the magnitude observed in this case study have been associated with increased cardiovascular and all-cause mortality. As a result, future studies should investigate whether this increase in AIx following SABR is demonstrated consistently amongst a larger number of lung cancer patients.

Consent

The patient provided written informed consent prior to participation. The University of South Australia Human Research Ethics Committee indicated that ethical approval was not appropriate for this study, as the subject is one of the authors.

Competing Interests

The authors declared no potential conflicts of interest with regard to research, authorship and publication of this article.

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