Correspondence

Can radiotherapy for breast cancer increase breast arterial calcification?

It has been proven by randomized trials and meta-analyses that radiotherapy (RT) improves local control and survival in breast cancer. However, when RT is used for breast cancer, it is inevitable for adjacent healthy tissues and organs to be affected resulting in early and late side-effects. Early side-effects develop within the first 12 weeks of the initiation of RT while late side-effects develop months and years after RT is completed and are difficult to manage. These side-effects are mostly irreversible and have a negative impact on the quality of life of the patient.[1,2]

RT can produce various effects in the vascular system of the breast tissue (endothelium of small and large vessels) in the acute and chronic phases. In the acute phase, they manifest as inflammation, vascular dilatation and local oedema. In the chronic phase, stenosis and occlusion of small vessels occurs together with fibrosis. In the large veins, muscle cells in the media layer disintegrate and lead to cystic medial necrosis. As a result, the vein wall weakens and ruptures. In the radiation-affected vascular endothelium, cytokines induce atherosclerosis by triggering an inflammatory process in which growth factors play a role.[1–5] In an experimental study, Fonkalsrud *et al*. found that radiation accelerated the atherosclerotic process as a result of a combination of some indirect causes such as obliteration in adventitial vasa vasora as well as direct damage such as intimal proliferation in the vascular wall structure, necrosis in the media layer and fibrosis in the adventitial layer.[3] A meta-analysis showed that RT reduces local recurrence in patients with early-stage breast cancer and a statistically significant increase in blood vessel-related mortality (p=0.0003) 10 years after RT. This analysis shows that RT causes vascular disease in the long term.[2] In the past 10 years, it has been shown that vascular damage and coronary artery injury have decreased due to advances in RT techniques. Chang *et al*. compared adjuvant RT in patients with breast cancer to the general population and found that the risk of acute coronary events was similar for both groups (hazard ratio 0.94; 95% CI 0.69–1). However, in a subgroup analysis of breast cancer survivors, this risk was increased in the non-exercising group (hazard ratio 2.74; CI 1.27–5.91). They emphasized that individual cardiac radiation dose and confirmatory studies were necessary.[6] While Darby *et al*. showed that the dose of breast RT is not above the threshold for occurrence for late heart failure,[7] Cuoma *et al*. reported increased side-effects on the heart depending on the dose.[8] A literature review suggests that developments in the treatment of breast cancer and the investigation of factors caused by coronary events—one of the long-term side-effects caused by these treatments—are becoming critical. Roos *et al*. found a direct correlation with the calcium value of the coronary artery before treatment with acute coronary events in patients receiving RT for breast cancer.[9] James *et al*. found no difference in the rate of cardiac side-effects seen in conventional and hypofraction RT schemes.[10] No study has examined the damage to vascular tissues; some studies have examined carotid arteries after RT.[11,12] In their retrospective study, Woodward *et al*. compared both carotid arteries in patients who received supraclavicular RT treatment for breast cancer ≥8 years ago. They did not find a clinically significant stenosis and increase in intima–media thickness in the ipsilateral carotid artery.[11]

The prevalence of breast arterial calcification (BAC) is between 3% and 17.5%. The frequency of BAC increases with age. While it is seen in 9.1% of women under 50 years of age, its incidence is between 9% and 17% in those >65 years of age.[4] It has been reported that patients with arterial calcification in mammary tissue radiologically, have more frequent diabetes and hypertension.[8] BAC is known to be a harbinger and surrogate for the coronary arterial events.[13,14] It is not known whether or not RT that is applied for breast cancer causes BAC or it causes an increase in BAC.

As a consequence, the vascular system of the breast is under the influence of RT directly and/or indirectly in patients who receive RT for breast cancer treatment. Although many studies reveal a relationship between arterial calcification detected by mammography and diabetes and hypertension, it is not known whether there is a relation between RT and these conditions. Therefore, it is necessary to clarify whether the increase of calcification in BAC-positive patients is related to RT.

Conflicts of interest. None declared

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