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# MRI in breast cancer radiotherapy in prone and supine positions

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## 1. ABSTRACT

Contemporary radiotherapy (RT) planning utilizes both a computed tomography (CT) scan either in prone or supine position with no breast compression or magnetic resonance imaging (MRI). The application of MRI is limited by image distortion and a lack of electron density information. The standard supine position not only exposes the tumor to RT non-homogenously, it can cause damage to the neighboring benign tissues. Here, we compare the effectiveness of both the prone and supine positions in breast cancer RT and various aspects of breast cancer treatment planning using MRI and CT.

## 2. INTRODUCTION

Radiotherapy (RT) is an important method in the treatment of breast cancer (1). To reduce tumor recurrence and mortality, whole breast irradiation (WBI) is routinely performed after breast-conserving surgery (1, 2). The development of intensity-modulated radiation therapy (IMRT) has allowed for the treatment of targeted tumors, regardless of shape. In order to delineate tumor volume during treatment planning, various imaging modalities are utilized. Although a computed tomography (CT) scan is used more often in breast cancer RT, magnetic resonance imaging (MRI) provides a better imaging resolution for cancer detection and has demonstrated increasing potential in treatment planning (3-5).

MRI has been used in both the diagnosis of breast cancer and treatment planning to provide potential guidance for surgical and radiation therapies (5-8). MRI has shown advantages over CT in terms of soft tissue definition and target identification. Disadvantages of MRI include potential image distortions and the lack of electron density information, which can affect heterogeneous radiation dosage calculations (9, 10). The effects of image distortion must be corrected prior to the application of MRI in RT planning (11). On the other hand, CT is able to clearly delineate tumor size and provide useful information for tissue inhomogeneity calculations (12). Due to the intrinsic disadvantages of MRI, CT remains the primary imaging method in RT breast treatment planning.

A supine position is the current standard in breast RT. However, supine positions expose neighboring critical organs to potential radiation-induced toxicity (13-15). Treatment-related complications may include pneumonitis and cardiovascular diseases, presenting a constant challenge for irradiation oncologists (16). Fortunately, irradiation performed in the prone position decreases cardiovascular risk for left breast RT (13, 14). Breast coils are also utilized during MRI in the prone position to compress the breast tissue and minimizes respiration-induced movement (5, 6). Therefore, there are noteworthy applications of MRI in prone RT treatment planning. We aim to provide a comprehensive comparison between the supine and prone positions in breast cancer RT as well as discuss more critical roles that MRI may play in treatment planning.

## 3. MRI IN CANCER DIAGNOSIS AND TREATMENT PLANNING

The American Cancer Society (ACS) recommends an MRI scan for high-risk breast cancer populations, particularly women with a familial history of breast cancer (17). Compared to conventional imaging tools, such as mammography or ultrasound, MRI is more sensitive and accurate in identifying occult contralateral breast tumors and invasive lobular cancer (17, 18). The sensitivity of MRI can reach 100% in breast cancer diagnosis (5). In addition, MRI has shown more accuracy in determining tumor size than ultrasound and mammography (19). The diagnostic value of MRI may also provide support in detecting multicentric or multifocal breast cancer, as well as recognizing invasive portions in the ductal carcinoma (20, 21). Furthermore, MRI is routinely employed to monitor tumor responses following neoadjuvant chemotherapy (NAC). In a clinical trial study consisting of 32 breast cancer patients, Bhattacharyya *et al*. concluded that an MRI scan is superior to the conventional examination methods for assessing the pathological responses and residual tumor sizes following NAC. MRI thus serves as an important pre-operative examination approach in planning subsequent breast-conservation surgery (7).

MRI is currently considered a potential supplement to CT in RT (8). The cooperative application of MRI and CT scans has been suggested to improve diagnosis for a variety of RT treatment planning processes (22). However, MRI and CT can introduce image errors when used together; therefore, many approaches have been investigated to develop MRI-based examination (23-26). Related studies focus on resolving the intrinsic limitations of MRI (9, 11). Potential geometric distortions are attributed to nonlinear gradients and inhomogeneity of a static magnetic field. Many protocols have been proposed to reduce such errors; current commercial scanners are equipped with first and second order patient-specific shimming to remarkably decrease inhomogeneities (22).

Nowadays, the most common solution for MRI-based dose calculations is the bulk density assignment approach. This method relies on the assignment of a homogeneous density to different tissues and is also applicable to both brain and prostate cancer imaging (8). The dose calculation accuracy generated from MRI data is comparable to calculations based on CT data (<2% variation) using the method of bulk density assignment (27). The primary difference between the MR bulk density plan and the CT plan may be the change in external contours of patients from pelvic coil and MR couch-top (28). An image with precise representation of body structures, i.e., an MR image, may be used for accurate dose calculation with a bulk density assignment (8). Many studies aim to achieve a more accurate dose calculation using MRI with the help of auxiliary data and approaches such as diagnostic CT data and pseudo-CT images (8, 29). Furthermore, the feasibility of the sole usage of MRI to provide RT treatment planning for prostate, intracranial, and pelvic targets has been validated by a series of recent studies (23-26). The incorporation of the Statistical Decomposition Algorithm (SDA) enables the generation of synthetic CT from a single MR image for dose calculation in prostate RT. This approach has demonstrated high accuracy compared to conventional CT simulation (24). However, the feasibility and calculation accuracy of MRI-based treatment planning for breast cancer needs to be further elucidated.

## 4. MRI BREAST CANCER RT

CT scans are routinely employed to contour the glandular breast tissue and critical organs in RT planning. However, CT scans fail to clearly identify fatty non-breast tissues from fatty breast tissues (30). The accuracy of MRI and CT in target delineation has been studied in the supine position (30, 31). In breast-conservation therapy, glandular breast tissues in MR images are extended further into the cranial-lateral and cranial-medial directions in the supine position when compared with CT images (30). However, MRI application is limited for lumpectomy cavity volume (LCV) delineation in the supine position (31). The applications of MRI breast scans in the prone position for gross target volume delineation in the breast and lumpectomy cavity have not yet been fully studied.

Because accelerated partial breast irradiation (APBI) delivers radiation only to the lumpectomy bed, it is more clinically favorable to WBI (32). MRI scanning before APBI can prevent multicentric and multifocal diseases distant from the lumpectomy site (33). Intracavitary brachytherapy and external beam radiation therapy are commonly used techniques for APBI (34-36). There are few clinical studies that focus on external beam PBI performed in prone positions. Since recent publications show the optimal target representation, adequate contrast, spatial fidelity, and resolution of MRI scans, imaging protocols have been designed to incorporate MRI guidance for APBI with patients in the prone position (34). Prone breast boards have become essential for target delineation and treatment planning using MRI with breast coils since this requires patients to be in the prone position (6). Further applications of MRI prior to and during RT treatments are being explored in order to delineate target volume and adapt the treatment plan when target size has changed during RT.

## 5. SUPINE *VS.* PRONE POSITION IN BREAST CANCER RT

Supine positions are regarded as standard during RT for most patients undergoing breast conservation therapy (BCT) (37-39). Advantages associated with treatments in the supine position include



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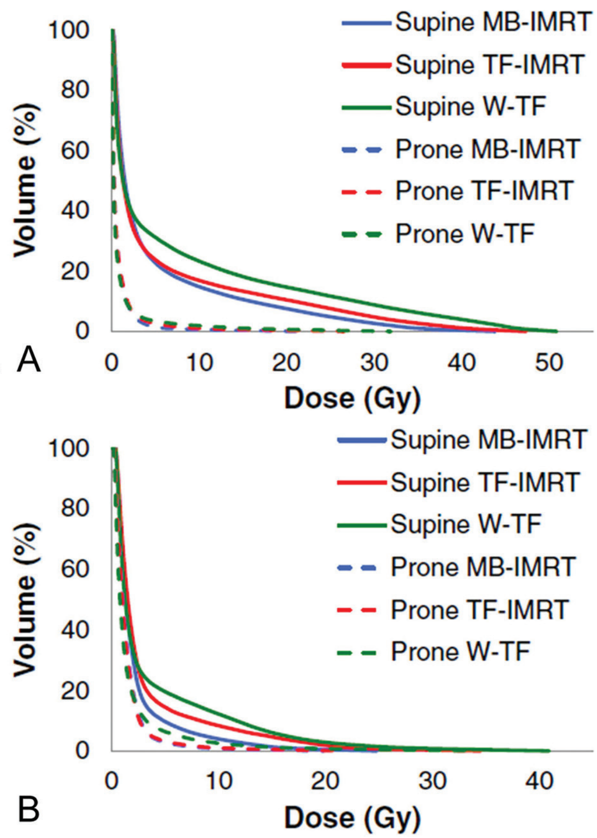


**Figure 1.** Histograms showing the dose distribution of the ipsilateral lung (a) among all the tested subjects and heart (b) among the left-sided breast cancer subjects with various irradiation techniques. Abbreviations: W-TF, wedged tangential fields; TF-IMRT, tangential field intensity-modulated radiotherapy; MB-IMRT, multi-beam intensity-modulated radiotherapy. Reproduced with permission from reference (51).

comfort, set-up reproducibility, and better immobilization during the measurement (40, 41). However, following RT in the supine position, patients with large breasts or large pendulous tissues may acquire acute skin reactions. Large breasts are also associated with increased dose inhomogeneity since tangential radiation fields are usually used as the standard choice for patients in supine positions. Increased dose inhomogeneity may increase the risk of latent edema and fibrosis in the high-dose areas and result in a poor cosmetic outcome. Exposure of irradiation toxicity in the supine position may also be detrimental to organs close to the breast (i.e., ribs, heart, and lungs) (40-43). In contrast to supine position, breast RT in the prone position can enhance dose distribution and improve the sparing of organ at risk (OAR) (40, 41). A recent study involving 100 subjects shows that prone setup is beneficial by reducing the irradiated dose of lung and heart tissue in most breast cancer patients, regardless of breast size (13). Prone position also decreases dose toxicity to critical organs by minimizing target motion caused by respiration (44, 45). However, benefits from the prone position vary with tumor location and breast size. For instance, the heart may move anteriorly towards the chest wall when the patient is treated in prone position. This movement shortens the distance between the heart and the irradiation target, potentially causing long-term cardiovascular morbidity (46). Unintended irradiation exposure of the heart is very much dependent on the patient's anatomy. Therefore, appropriate selection of treatment positioning should be based on both the patient's anatomic characteristics and personal preference (47). As shown by Kirby *et al.*, patients with larger breasts benefit from prone positioning for tangential-field partial and WBI as opposed to individuals with smaller breasts (15). Furthermore, in cases of APBI, in which radiation is delivered directly to the lumpectomy site, the prone position seems promising due to the adequate distance between the heart and irradiation site (34).

WBI is conventionally delivered to the patient in supine positions using tangential fields. Increased radio-dermatitis, chronic fibrosis, and poor cosmetic outcomes have all been observed following WBI in patients with large and pendulous breasts (43, 48, 49). Phase I/II trials for WBI in prone position have reported a drastic reduction in dose toxicity to the lungs and heart. In addition, a reduction in grade 1-2 acute skin toxicity was observed during 12-month follow-up of prone position WBI (50). Furthermore, the size of the high dose-exposed region at the base of the breast is ~15% smaller in those treated in a prone position rather than supine position (14). In another study of 245 patients during a 5-year follow-up, WBI delivered to patients in prone position showed comparable long-term disease control and a favourable toxicity profile when compared with WBI delivered to patients in supine position. Furthermore, treatment in prone position contributes to enhancement of the therapeutic ratio during post-lumpectomy radiation by improving dose homogeneity and minimizing doses to the heart and lungs (42). For instance, a key study by Kirby *et al.* evaluated the non-target tissue dose distribution for prone and supine treatment positions following WBI or PBI (15). Ipsilateral-lung mean doses were found to be lowered in the prone position for all WBI cases and 61/65 of PBI cases. Likely, the volume of the chest wall receiving 50 Gy was prominently reduced in all WBI cases using prone position. The study indicates a significant benefit of using prone position for patients with right-side or left-side cancer with large breast volume. However, for left-breast-affected patients, there was no difference in cardiac doses observed between prone and supine position under either WBI or PBI (15). Similar findings were proposed by Muliez *et al*. showing that optimal WBI techniques can minimize RT toxicity. Muliez *et al.* also examined the dose distribution of OAR for the prone and supine position using wedged tangential fields (W-TF), multi-beam IMRT (MB-IMRT), and tangential field intensity-modulated RT (TF-IMRT). As shown in Figure 1, ipsilateral lung and heart were subject to less dose toxicity in prone position for WBI with various irradiation techniques (51).

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Setup difficulty is a major reason as to why prone positioning is not broadly employed in breast RT (14, 52). Prone setup is associated with more equipment, an uncomfortably hard surface, and issues of plan summation in a treatment planning system (53). Previously, patients treated in prone position were required to lie on a platform, which is mounted on both an accelerator treatment table and a simulator couch (14). Different platforms have been developed in order to accommodate the various requirements of RT in prone position. For instance, Victoreen®, Model 37-018, is one of the early prone platforms designed according to the standard of Memorial Sloan-Kettering Cancer Center (MSKCC). Using this technique, a patient's ipsilateral arm is placed either above the head or at the side. Patients can perform an axial rotation toward the treated breast, which hangs away through an adjustable aperture on the platform. In recent years, other types of prone platforms have been designed to be compatible with both APBI and whole breast RT in prone position. The clinical application of these techniques has yielded ideal results (54). With the emergence of the "prone breast board" (e.g., Sagittilt® prone breast board and Varian Pivotal™ prone breast board), patients' comfort and treatment reproducibility in the prone position has significantly improved (44, 55, 56). The design of the prone breast board improves patient immobilization and target localization in the prone position. In fact, when using a delicate prone breast board, prone position drastically decreases the setup variability of interfraction and intrafraction as compared to supine position, thus demonstrating effective reproducibility (57). Because of the potential difficulties associated with fitting onto a prone breast board, additional care should be taken when recommending prone setup to patients with limited mobility (42). If the supine position is utilized, systematic errors during the localization process and prior to irradiation can be introduced due to breast deformation under the gravitational force. Therefore, the RT treatment position is required to be identical to the actual imaging position.

## 6. CONCLUSIONS AND FUTURE PERSPECTIVE

Pre-operative MRI is applied to specific groups of patients, mainly women with heterogeneously dense breasts or women at a high risk of breast cancer, for diagnosing unsuspected contralateral diseases and multicentric lesions (58). MRI is routinely performed in the prone position in order to minimize distortions induced by respiratory motion (6). Although it is the current standard position for breast cancer RT, supine position hinders the potential use of MRI during treatment planning (34). The advantages of prone position during imaging scans include a more homogeneous dose distribution, reduced respiratory movement, and reduced dose toxicity to nearby critical organs (7, 40, 52, 59-61). Therefore, utilizing prone position will likely increase MRI-use for breast cancer irradiation planning. However, the accuracy of planning an MRI scan in the prone treatment position has not been systematically investigated. The dosage calculation using MRI must be resolved with auxiliary approaches before it can be used alone in treatment planning. This remains an area of interest for further study in breast cancer treatment (9, 11). The future development of breast treatment includes incorporating both supine and prone positions into MRI treatment planning for external beam PBI or breast boost RT.

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