E17. Modern radiotherapy planning in the treatment of breast cancer

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Radiotherapy (RT) is an integral part of the management of early stage breast cancer following breast-conserving surgery and after mastectomy in patients at moderate to high risk for loco-regional recurrence. Absolute improvements in breast cancer-specific and overall survival have been demonstrated by the Early Breast Cancer Trialists' Collaborative Group due to improvements in loco-regional control with RT and are approximately 4–5% at 15 years.[1] The gains in survival would likely be greater were it not for excess mortality observed from causes other than breast cancer, which have been shown to be primarily cardiac in nature. Therefore, treatment planning approaches which minimise treatment of uninvolved tissues are critical to the ultimate success achieved with RT.

Radiation treatment planning for breast cancer has changed dramatically through the years with modifications in clinical target volumes, treatment delivery systems, and techniques. Early target volumes reflected a Halstedian philosophy in which extensive loco-regional fields were felt to be necessary for cure but through successive studies, volumes have been refined that maintain high rates of loco-regional control while minimising toxicity. Treatment delivery systems have evolved from orthovoltage units where skin dose and shallow depth dose distributions limited dose delivery to deep seated lesions to sophisticated computer-controlled treatment delivery systems which allow highly conformal therapy by the creation of dose distributions that closely conform to the shape of the target in three dimensions. While improvements in target definition, treatment delivery systems and changes in techniques are all critical in radiation delivery, the remainder of the discussion will be devoted to modern treatment planning techniques.

Two-dimensional (2D) planning systems utilising tangential fields to the breast have resulted in high rates of tumour control. However, dose homogeneity across the entire breast is difficult to achieve with 2D planning due to variations in breast contour and tissue density. Use of wedges with lung density correction significantly reduced dosimetric hot spots along the central axis[2]; however, lack of homogeneity within the entire field was still problematic particularly in large-breasted women, with consequential increased rates of acute skin changes and long-term skin and breast fibrosis. Three-dimensional (3D) planning systems evolved which generally mark the beginning of the modern treatment planning era. These systems have allowed quantitative dosimetric studies of dose distributions and normal tissue complication probabilities utilising the entire treatment volume such that planning can be individualised by patient body habitus to limit exposure of normal tissues such as the heart and lungs.[3,4] Studies using 3D planning have shown that no one technique provides the best target coverage with the lowest normal tissue complication probabilities for all patients. They also demonstrate the planning flexibility that CT-based 3D planning systems can offer.

3D computed tomography (CT)-based planning systems have also been shown to aid in the definition of the anatomic regions containing the supraclavicular and infraclavicular nodal groups and to estimate the difference in dose received using either traditional dosing or optimised dosimetric techniques to nodal targets. Madu and colleagues identified target supraclavicular and infraclavicular nodal regions which themselves are radiographically occult on CT scan by first correlating the location of these nodes from cadaveric dissection with readily identifiable radiographic structures on CT scans.[5] Coverage of these volumes with the 90% isodose surface was significantly less with traditional planning versus conformal 3D planning.

In recent years, there has been considerable interest in the development and application of optimisation or inverse planning techniques along with the use of a type of 3D planning known as intensity modulated radiation therapy (IMRT). IMRT removes the usual reliance upon flat (uniform intensity) radiation fields and instead uses a variable intensity pattern usually determined with a computerised optimisation algorithm. The main goal of much of the IMRT and optimisation work is the delivery of more conformal plans to the patient, i.e., delivery of a high dose volume which conforms in three dimensions to the shape of the defined target while at the same time minimising normal tissue dose. The combination of IMRT delivery with inverse planning tools is expected to achieve better dosimetric results than normal plans with the goal of either 1) the improvement in local control due to improved coverage of the target or 2) reduced normal tissue dose while achieving the same tumour coverage.

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Most applications of IMRT treatment delivery technology for breast cancer have focused upon use of IMRT to improve dose uniformity within the breast target volume. Fraass described the clinical use of multi-segment IMRT for a series of clinical sites with the goal mainly of improving target uniformity,[6] and Kestin and colleagues at the William Beaumont Hospital have described a similar technique specifically for tangential breast plans.[7] Using IMRT fields similar to those proposed by the Beaumont group, randomised trials have been conducted comparing tangential irradiation planned using 2D treatment versus IMRT.[8,9] In a study by Pignol and colleagues, 358 women were randomly assigned between breast IMRT versus standard radiotherapy using wedges.[8] Study endpoints were acute skin reactions, breast discomfort, and quality of life. As expected, breast IMRT plans utilising the entire breast volume resulted in improved dose distributions of the breast compared to 2D plans optimised only along the central axis. This translated to a lower percentage of women experiencing moist desquamation with IMRT compared to the 2D RT. A multivariate analysis indicated that use of breast IMRT was an independent predictor of decreased risk of moist desquamation. A trial by Donovan and colleagues from the Royal Marsden compared late adverse effects after whole breast RT using breast IMRT versus 2D planned RT.[9] In this study, 306 women were randomly assigned between the two treatment arms and the primary endpoint was change in breast appearance in serial photographs taken at 1, 2, and 5 years after treatment. For patients available for analysis at 5 years, more women treated with 2D RT had a change in the appearance of the breast compared with women treated with IMRT (58% versus 40%), with a 1.7-fold increase in changes following standard 2D treatment ($p=0.0008$). Significantly less induration was noted after IMRT; no significant difference was identified between the groups in quality of life.

Thus both studies suggest benefit with segmental IMRT compared to 2D RT secondary to improved dose homogeneity but neither address use of IMRT techniques to spare normal tissues such as heart and lung. In an effort to reduce normal tissue exposures, Remouchamps and colleagues reported significant reductions in heart and lung doses using deep inspiration breath hold with active breathing control (ABC) and forward planned IMRT in patients with left-sided breast cancer.[10] Other investigators have used inversely planned IMRT and optimisation parameters (i.e. cost functions that specify normal tissue constraints) with or without ABC.[11–14] We recently presented a dosimetric comparison of four IMRT plans, with two forward-planned multi-segment techniques with and without a heart block and two plans using inverse-planned beamlets where the beams were divided into 1×1 cm segments (one beamlet plan of historical interest with nine equi-spaced axial beams and a second beamlet plan (the 'clinical' beamlet plan) where beamlets were angled using fields similar to 3D configured tangential fields).[14] All plans were generated using deep inspiration breath hold with ABC. Mean heart and left anterior descending artery doses were similar between the clinical beamlet and heart blocked forward planned arrangement but were lower than doses received using the segmental and nine-field plans. In addition, the clinical beamlet plan resulted in better coverage of the internal mammary nodes compared to the forward planned blocked segmental technique. A pilot prospective study is in progress evaluating the clinical benefits of the clinical beamlet plan compared to 3D planned loco-regional fields. This trial will be discussed.

Conflict of interest statement

None declared.

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