Case Report

Helical tomotherapy based intensity modulated radiotherapy for the management of difficult clinical situations in breast cancer

Animesh Saha, Anurupa Mahata, Rajkumar Shrimali, Rimpa Achari, Indranil Mallick, Sanjoy Chatterjee

Department of Radiotherapy, Tata Medical Center, Kolkata, West Bengal, India

ABSTRACT

Helical tomotherapy (HT) can achieve a homogenous dose distribution in the planning target volume while minimizing the dose to the organ at risk. Tomotherapy has been used for complex breast cancer radiotherapy including bilateral breast irradiation, pectus excavatum, and internal mammary chain (IMC) nodal irradiation. This report details our experience of using HT in breast cancers in newer clinical indications. Three patients with SCF nodal involvement (case 1), high level III axillary node recurrence (case 2), and composite irradiation of SCF, IMC, and whole breast (case 3) were treated using brachial plexus sparing HT. It was possible to boost the SCF, reirradiate the high level III axillary nodal recurrence and treat complex volume of breast, SCF, and IMC with acceptable and safe dose volume histogram constraints and with good homogeneity and conformity indices. The treatment was successful in controlling disease locoregionally at a 15 months follow-up. No patients reported symptoms suggestive of brachial plexopathy.

Key words: Brachial plexopathy, breast cancer, helical tomotherapy, supraclavicular fossa

INTRODUCTION

Helical tomotherapy (HT) is an advanced form of image-guided intensity modulated radiotherapy (IMRT) and can achieve homogenous dose distribution in planning target volume (PTV) while minimizing dose to organs at risk (OAR).[1] HT is being used in various complex situations in breast cancer radiotherapy such as bilateral breast irradiation, pectus excavatum.[2] Brachial plexopathy is considered to be a highly morbid late radiotherapy toxicity, especially after treatment of the Supraclavicular fossa (SCF) to a high doses.[3] The ability to include the internal mammary chain (IMC) in adjuvant breast radiotherapy without overdosing the underlying structures (like the heart) is often a challenge. We report our experience of using HT in three difficult situations with special attention to reducing brachial plexus dose while covering the target volumes.

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CASE REPORTS

Case 1

A 67-year-old female presented with a right-sided 5 cm breast lump with mobile 3 cm axillary node and a right SCF node. A biopsy confirmed a grade III, estrogen receptor (ER) +ve, progesterone receptor (PR) −ve, Her2-neu +ve invasive ductal carcinoma (IDC). Computed tomography (CT) thorax and fine-needle aspiration cytology (FNAC) confirmed a 1.1 cm metastatic right SCF node. CT abdomen and bone scan were normal. Six cycles of neoadjuvant chemotherapy (NACT) with 5-flurouracil, epirubicin, cyclophosphamide for 3 cycles, and docetaxel for 3 cycles (FEC-T) resulted in a good clinical response. Simple mastectomy with axillary dissection (AD) showed a residual 2.2 cm primary tumor with 2 involved axillary nodes. Postoperatively 40 Gy in 15 fractions was prescribed to the right chest wall and SCF (phase 1) followed by a sequential boost of 10 Gy in 5 fractions to the SCF with brachial plexus sparing, delivered as phase 2 using HT.

Address for correspondence: Dr. Animesh Saha, Department of Radiotherapy, 121/B, Pramanick Ghat Road, Kolkata - 700 036, West Bengal, India. E-mail: mesh.vicky@gmail.com

Case 2

A 41-year-old female received NACT with 4 cycles of AC (doxorubicin, cyclophosphamide) followed by a right-sided modified radical mastectomy for a "triple negative" IDC in 2011. Chest X-ray and ultrasound abdomen were normal. Postoperative histopathology revealed a 5 cm residual tumor with 1 axillary lymph node positive. The patient then received 4 cycles of adjuvant chemotherapy with paclitaxel and completed her adjuvant radiotherapy to the right chest wall and SCF to a dose of 50 Gy in 25 fractions in February, 2012. She developed a 4 cm × 3.4 cm high-level III ipsilateral axillary nodal recurrence, confirmed by CT scan and FNAC in August, 2013. CT abdomen and bone scan were normal. Patient had a good response to 4 cycles of chemotherapy with gemcitabine and carboplatin. She was then planned for salvage radiotherapy after explaining the risk of brachial plexopathy with reirradiation. 60 Gy in 30 fractions was prescribed using brachial plexus sparing HT technique.

Case 3

A 35-year-old female presented with a right-sided 6 cm × 4 cm breast lump with mobile ipsilateral axillary lymph nodes. A biopsy confirmed a grade II, "triple negative" IDC. CT thorax showed a 1.37 cm right IMC node. CT abdomen and bone scan were normal. Positron emission tomography CT (PET-CT) scan showed a metabolically active right breast, right axilla, and right IMC node. Totally, 6 cycle of chemotherapy with FEC regimen resulted in near complete metabolic response on repeat PET-CT scan. Right breast conservation surgery with AD confirmed residual multiple foci of tumor (up to 0.6 cm) with uninvolved axillary nodes. The patient was planned for adjuvant radiotherapy using HT in view of IMC nodal involvement. 40 Gy in 15 fractions was prescribed to whole right breast, SCF and IMC; followed by electron boost of 16 Gy in 8 fractions to the primary tumor bed.

All 3 patients were treated supine with headrest lying on a "breast board." The patient's arms were abducted on the armrest with hand grip pole to clasp their hands. Contrast-enhanced CT of 2.5 mm thickness was done in the treatment position. Volume definition was carried out on ECLIPSE contouring station before exporting the contours to the tomotherapy planning station.

Case 1 was treated initially using a conventional technique for phase 1. Treatment fields were set up on the treatment planning system using CT data and standard geometry. The SCF clinical target volume (CTV) was delineated as described in the published guidelines. OARs such as heart, lung, and brachial plexus were contoured. The brachial plexus was outlined [Figure 1] as described by Hall *et al*.[4] The SCF CTV was grown by 1 cm to provide the PTV, but was retracted by 3 mm from the skin. 40 Gy in 15 fractions to the isocenter of the tangential chest wall fields and Dmax of the matched SCF field was prescribed for phase 1. Three-dimensional (3D) planning was done to achieve dose homogeneity as nearly as possible conforming to ICRU 50/62. A further dose of 10 Gy in 5 fractions was prescribed as a sequential boost to the SCF in phase 2 using HT. In case 2, prechemotherapy gross tumor volume was contoured and expanded with 1 cm margin and edited by 3 mm from the skin to get a PTV. 60 Gy in 30 fractions was prescribed to the PTV. In case 3, IMC and whole breast CTV were contoured following the Radiation Therapy Oncology Group (RTOG) guidelines.

In radiotherapy planning "dummy volumes," ring structures, overlapping structures, and nonoverlapping structures were created by the physicist to prevent "dose dumping" in unusual sites and to assist in the optimization process. Dose volume histogram points and penalties were adjusted throughout the optimization process to achieve adequate PTV coverage with set dose constraints to OARs. We used a pitch of 0.3, modulation factor of 2.1, with a field width of 1 cm for planning all three cases. During HT treatment daily online megavoltage CT image guidance was done by trained Radiographers, while during phase 1 treatment of case 1, clinical coverage using tattoos and light fields were used to ensure target coverage. Homogeneity index (HI) was calculated by dividing the maximal PTV dose by the prescription dose; the conformity index (CI) was calculated by dividing the minimum PTV dose by the prescription dose.[5]

During phase 1 treatment of case 1, the median dose achieved to right chest wall was 38.57 Gy, and right SCF was 34.47 Gy [Figure 2]. In phase 2 (HT treatment) the median achieved at SCF PTV was 10.37 Gy with HI of 1.115 and CI 0.92 [Table 1]. Dose constraints for OARs were met [Table 2]. In case 2 [Figure 3], a median dose achieved to PTV was 59.68 Gy with HI of 1.08 and CI of 0.72 [Table 1].

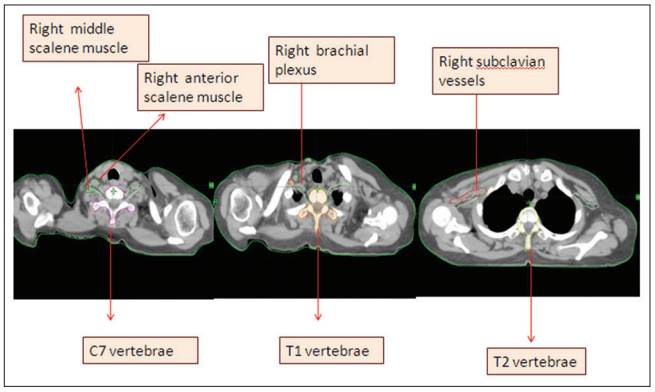

Figure 1: Brachial plexus contouring

A maximum dose of 59.9 Gy and mean dose of 21.8 Gy was received by ipsilateral brachial plexus [Table 3]. In case 3, adequate dose coverage of the three PTVs was achieved (breast, SCF, and IMC) as is evident from Figure 4. The HI of the three PTVs were 1.119 (breast), 1.06 (SCF), and 1.116 (IMC) with CI ranging between 0.37 and 0.54 [Table 1]. Dose constraints for OARs were met [Table 4].

All three patients had RTOG grade I acute skin toxicity. At a median follow-up of 15 months, all three patients are locoregionally controlled. None of them complained of early brachial plexus-related symptoms.

DISCUSSION

Fibrosis of perineural connective tissues, damage to capillaries resulting in ischemia and changes in axons have been described as the etiopathogenesis of radiation-induced brachial-plexopathy. Symptoms include pain, paraesthesia and motor deficits of the ipsilateral upper extremity. The incidence of brachial plexopathy in patients irradiated for breast cancer was shown to increase with total radiation dose and dose per fraction. The median interval between completion of radiotherapy and occurrence of symptoms was reported to be 1–4 years.[3] Breast IMRT is now being explored in a number of centers either for the treatment of isolated complex anatomy or within a controlled clinical trial (IMPORT high) setting.[9] HT techniques have been refined in recent years to provide a homogenous dose distribution to the chest wall and breast with acceptable doses to the heart, lungs and contralateral breast.[10] Dosimetric studies have pointed toward the feasibility of treating the IMC in conjunction with the SCF and chest wall/breast, achieving low dose to the OARs with inverse planned IMRT techniques. Our study confirmed the clinical implementation of more complex plans with HT respecting most dose constraints, giving quite acceptable HI and CI.

In case 1, we describe a simply phased approach of salvaging isolated SCF nodal disease combining the standard forward planned tangential 3D conformal techniques and sequential inversed planned HT technique. This resulted in less doses to the contralateral lung if HT would have been used as a single-phase technique in this case. The 2nd case posed challenges to the planning team as it required reirradiation to high-level III axillary node, which was in close proximity to the brachial plexus. This is the first report in breast cancer where nonsurgical salvage to the high axillary nodal recurrence was successfully and safely achieved using HT. In case 3, we use a hypofractionated regime to treat the IMC nodal volume along with breast and SCF. The contours provide a complex treatment target in close proximity to OAR such as the lungs, heart, and contralateral breast.

Although our patients remained asymptomatic following HT treatment, the risk of brachial-plexopathy with

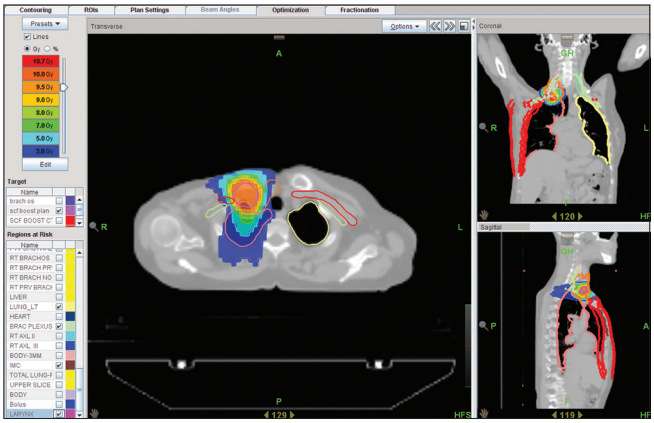

Figure 2: dose distribution to supraclavicular fossa boost volume with sparing of brachial plexus for case 1

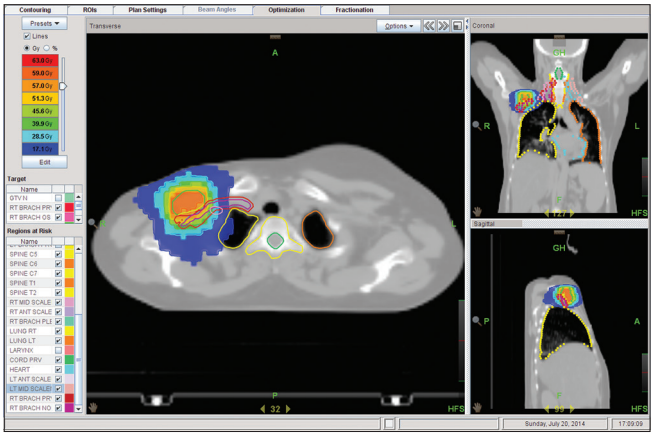

Figure 3: Dose distribution to high-level III axillary nodal planning target volume with sparing of brachial plexus for case 2

Table 1: Median dose, HI and CI of chest wall, IMC, SCF PTVs in all three cases with their beam on time

Number	Structures	Side	Prescribed dose	Median dose	HI	CI	Beam on time (min)
Case 1	Phase 1	Right					
	Chest wall PTV		40 Gy	38.57 Gy			
	SCF PTV		40 Gy	34.47 Gy			
	Phase 2	Right	10 Gy	10.37 Gy	1.115	0.92	6.06
Case 2	PTV	Right	60 Gy	59.68 Gy	1.08	0.72	5.2
Case 3	PTV breast	Right	40 Gy	40.36 Gy	1.119	0.534	24.1
	PTV SCF		40 Gy	39.8 Gy	1.09	0.36	
	PTV IMC		40 Gy	37.96 Gy	1.116	0.37	

HI: Homogeneity index, CI: Conformity index, PTV: Planning target volume, SCF: Supraclavicular fossa, IMC: Internal mammary chain

Table 2: Dose/constraints prescribed and dose/constraints achieved for case 1

Structure name	Dose/constraints prescribed	Dose/constraints achieved
Right brachial plexus	EQD2=60 Gy (conservative estimate based on with α/β=2 for brachial plexus, acceptable BED=120 Gy)[6]	Phase 1: Median=35.41 Gy Phase 2: Maximum=10.46 Gy Median=1.35 Gy Mean=2.96 Gy
Heart	Mean 12 Gy[7] D10 <20 Gy D25 <10 Gy[7]	Phase 1: Mean=0.53 Gy D10=0 Gy D25=0 Gy Phase 2: Mean=0.01 Gy D10=0 D25=0
Ipsilateral lung	D15 <35 Gy D20 <30 Gy D35 <20 Gy[8] Mean dose <20 Gy[7]	Phase 1: D15=34.93 Gy D20=30 Gy D35=6.63 Gy Mean=11.39 Gy Phase 2: Mean=0.25 Gy D15=0.1 Gy D20=0.07 Gy D35=0.04 Gy
Spinal cord PRV	Maximum <48 Gy	Phase 1: 17.21 Gy Phase 2: 3.42 Gy
Esophagus	Mean dose <34 Gy V35 <50% V50 <40% V70 <20%	Phase 1: Mean dose=0.26 Gy V35=5.4% V50=0% V70=0% Phase 2: Mean dose=0.48 Gy V35=0% V50=0% V70=0%
Thyroid		Phase 1: Mean=0.27 Gy Maximum dose=1.03 Gy Phase 2: Mean=0.44 Gy Maximum dose=5.27 Gy
Bronchus	Maximum dose <80 Gy	Phase 1: Maximum dose=2.43 Gy D1cc=1 Gy Phase 2: Maximum dose=0.2 Gy D1cc=0.14 Gy

PRV: Planning organ at risk volume, EQD2: Equivalent dose in 2-Gy fractions, BED: Biologically equivalent dose

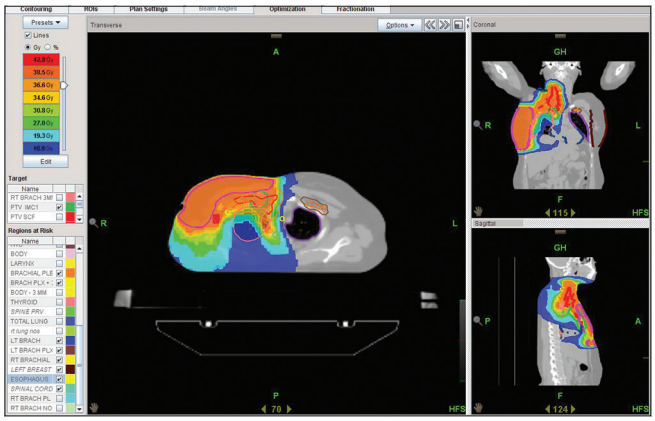

Figure 4: Dose distribution to whole right breast, right supraclavicular fossa, and right internal mammary nodal chain without any hotspot for case 3

Table 3: Dose/constraints prescribed and dose/constraints achieved for case 2

Structure name	Dose/constraints prescribed	Dose/constraints achieved
Right brachial plexus	EQD2=60 Gy (conservative estimate based on with α/β=2 for brachial plexus, acceptable BED=120 Gy)[6]	Maximum dose: 59.9 Gy, median: 14.67 Gy, mean dose: 21.8 Gy
Heart	Mean=12 Gy[7] D10 <20 Gy D25 <10 Gy[7]	Mean=0.14 Gy D10=0 Gy D25=0 Gy
Ipsilateral lung	D15 <35 Gy D20 <30 Gy D35 <20 Gy[8] Mean dose <20 Gy[7]	D15=1.07 Gy D20=0.8 Gy D35=0.475 Gy Mean=1.21 Gy
Contralateral lung	D20 <15 Gy D35 <12 Gy[8]	D20=0.36 Gy D35=0.23 Gy
Spinal cord PRV	Maximum <48 Gy	8.68 Gy
Esophagus	Mean dose <34 Gy V35<50% V50<40% V70<20% Maximum dose <72 Gy Mean dose <34 Gy	Mean dose=1.31 Gy V35=1.31% V50=0% V70=0%
Thyroid		Mean=1.79 Gy Maximum dose=6.16 Gy
Bronchus	Maximum dose <80 Gy D1cc <72 Gy	Maximum dose=1.33 Gy D1cc=1 Gy

PRV: Planning organ at risk volume, EQD2: Equivalent dose in 2-Gy fractions, BED: Biologically equivalent dose

Table 4: Dose/constraints prescribed and dose/constraints achieved for case 3

Structure name	Dose/constraints prescribed	Dose/constraints achieved
Right lung	D15 <35 Gy D20 <30 Gy D35 <20 Gy[8] Mean dose <20 Gy[7]	D15=32.89 Gy D20=29.6 Gy D35=19 Gy Mean dose=14.72 Gy
Left lung	D20 <15 Gy D35 <12 Gy[8]	D20=1.85 Gy D35=1.5 Gy
Right brachial plexus	EQD2=60 Gy (conservative estimate based on with α/β=2 for brachial plexus, acceptable BED=120 Gy)[6]	Median=39.63 Mean=38.93 Maximum=41.59 Gy
Left brachial plexus	Same as above	Median=2.63 Gy Mean=1.58 Gy Maximum=23.27 Gy
Heart	Mean=12 Gy[7] D10 <20 Gy D25 <10 Gy[7]	5.13 Gy 12.66 0.531
Spinal cord PRV	Maximum <48 Gy	37.57 Gy
Esophagus	Mean dose <34 Gy V35<50% V50<40% V70<20% Maximum dose <72 Gy Mean dose <34 Gy	Mean dose=23.22 Gy V35=38.9% V50=0% V70=0%
Thyroid		Mean dose=27.55 Gy Maximum dose=41.55 Gy
Bronchus	Maximum dose <80 Gy D1cc <72 Gy	Maximum dose=35.9 Gy D1cc=31.7 Gy

PRV: Planning organ at risk volume, BED: Biologically equivalent dose

high-dose radiation needs to be discussed in details before radiation.

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