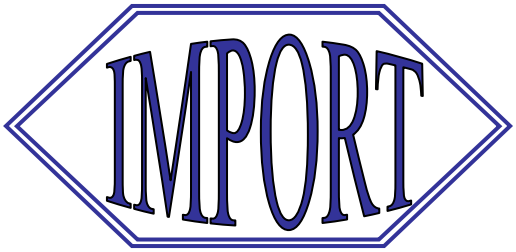


(Intensity Modulated and Partial Organ Radiotherapy)

Planning Pack for the IMPORT HIGH Trial

A guide to outlining, planning & verifying IMPORT HIGH patients

Version 4.0 23/05/2013

IMPORT Trial Management Group

1. Introduction

This document should be used as an accompaniment to the IMPORT HIGH trial protocol by all clinicians, physicists, radiographers and dosimetrists involved in the planning and treating of IMPORT HIGH patients. It provides detailed guidance on localisation, outlining, planning and treatment verification. However it should be noted that the planning methods are not intended to be totally prescriptive – it is hoped that they will provide a good starting point from which each centre may decide to develop its own technique to meet the planning aims. Please feel free to discuss any aspect of this planning pack with the IMPORT QA team.

2. Localisation

Since daily verification imaging is a requirement for IMPORT HIGH, it is mandatory that some form of implanted marker is used for tumour bed localisation. If kV planar imaging, cone-beam CT or MVCT is available on the treatment machine, titanium clips will suffice. However if MV electronic portal imaging is the only verification option, gold seeds must be sutured into the tumour bed as it is unlikely that titanium clips will be visible. The markers will also be used to guide tumour bed outlining as in IMPORT LOW. It is recommended that pairs of clips/seeds are positioned at the medial, lateral, superior, inferior, anterior and posterior margins of surgical resection. Placing the clips in pairs as shown in Figure 1. limits the potential problem of clips migrating from the tumour site:

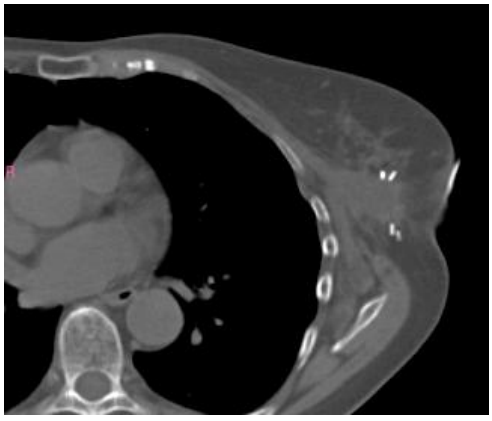


Figure 1. CT slice showing 2 pairs of titanium clips implanted around the tumour bed

For more detailed guidance, please refer to the IMPORT surgical clips protocol. The same method of localisation, outlining and planning must be adopted for each of the three test arms.

3. Outlining

3.1 Target Volumes

	CTV	**PTV**
Boost (TB)	CTV_{TB} = tumour bed	PTV_{TB}= CTV_{TB} + 5 mm margin
Partial breast (PB)	CTV_{PB} =CTV_{TB} + 15 mm margin	PTV_{PB} = CTV_{PB} + 10 mm margin
Whole Breast (WB)	CTV_{WB} = Soft tissues of whole breast	PTV_{WB} = CTV_{WB} + 10 mm margin

Table 1. Summary of radiotherapy planning volumes and margins

It is recommended that the tumour bed CTV (CTV_{TB}) is less than or equal to 5% of the whole breast PTV before treatment. It can be challenging to generate an acceptable treatment plan for patients with very large seromas. These can be drained to enable trial recruitment.

CTV_{TB} is outlined by drawing around the implanted markers and any changes in the surrounding tissue architecture (Figure 2).

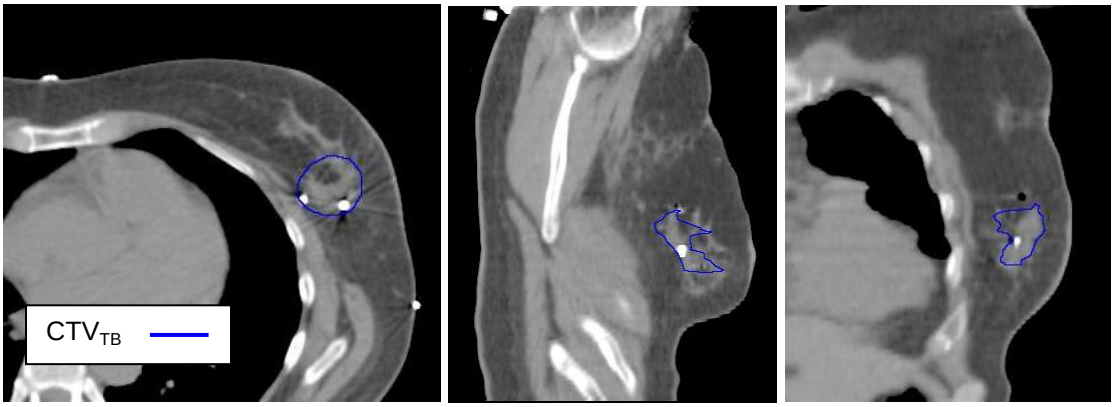


Figure 2. Tumour bed CTV shown in axial, sagittal, and coronal planes

This is grown by 5mm to give the tumour bed PTV or PTV_{TB} (Figure 3).

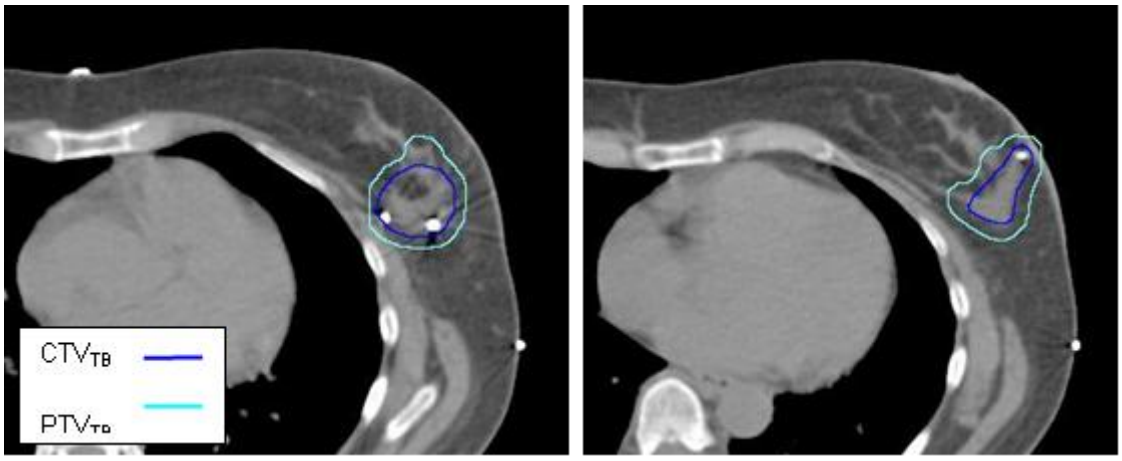


Figure 3. Axial slices showing tumour bed PTV on central axis and 3cm inferior to central axis

For reporting purposes the PTV is then modified to be 5mm inside the skin surface (Figure 4). This structure is denoted PTV_{TB} DVH and will generally be used in place of PTV_{TB} throughout the rest of this planning pack.

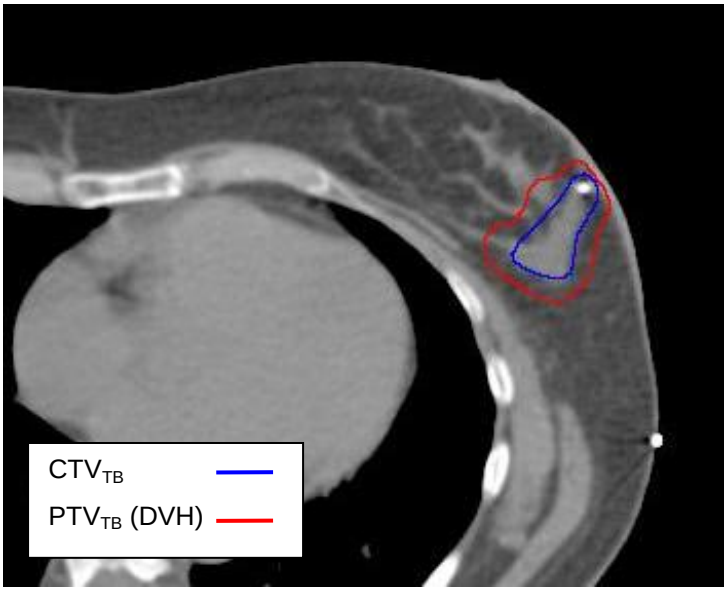


Figure 4. Axial slice showing modified tumour bed PTV

CTV_{TB} is then grown by a minimum of 15mm to give the partial breast CTV (CTV_{PB}), which approximates to a quadrant of the breast. The CTV_{PB} is modified according to the individual breast anatomy. The posterior margin should not extend beyond the deep fascia (unless clearly breached by the tumour). If the anatomy of this region cannot be easily visualised, the posterior margin should be limited to 5 mm anterior to the lung/chest wall interface. CTV_{PB} should also be bound by 5mm from the skin surface, and should not extend medially or laterally beyond the edges of the visible/palpable breast (Figure 5).

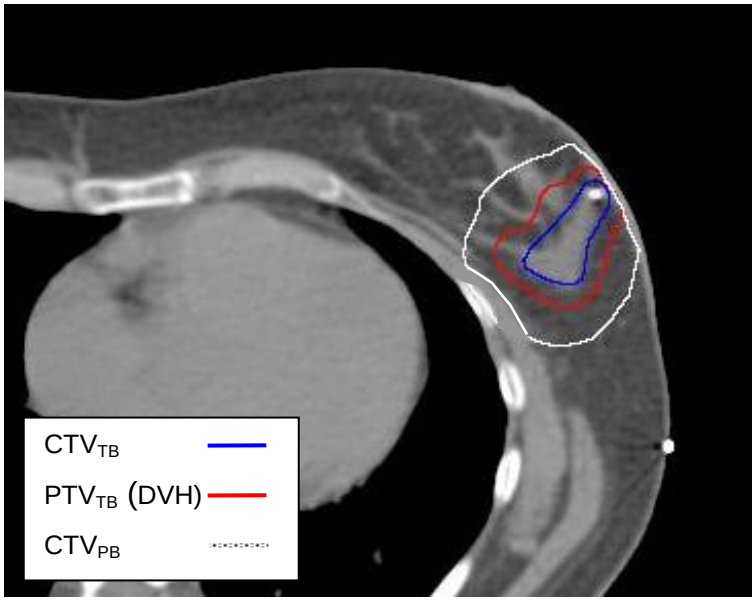


Figure 5. Axial slice showing partial breast CTV

CTV_{PB} is expanded by 10mm to generate the partial breast PTV or PTV_{PB} (Figure 6).

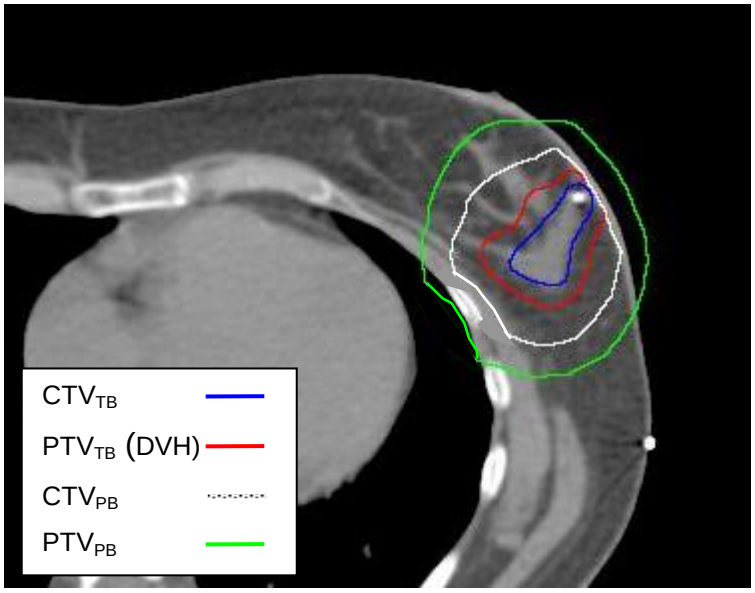


Figure 6. Axial slice showing partial breast PTV

For reporting purposes the PTV is then modified to be 5mm inside the skin surface. This structure is denoted PTV_{PB} DVH and will generally be used in place of PTV_{PB} throughout the rest of this planning pack (Figure 7).

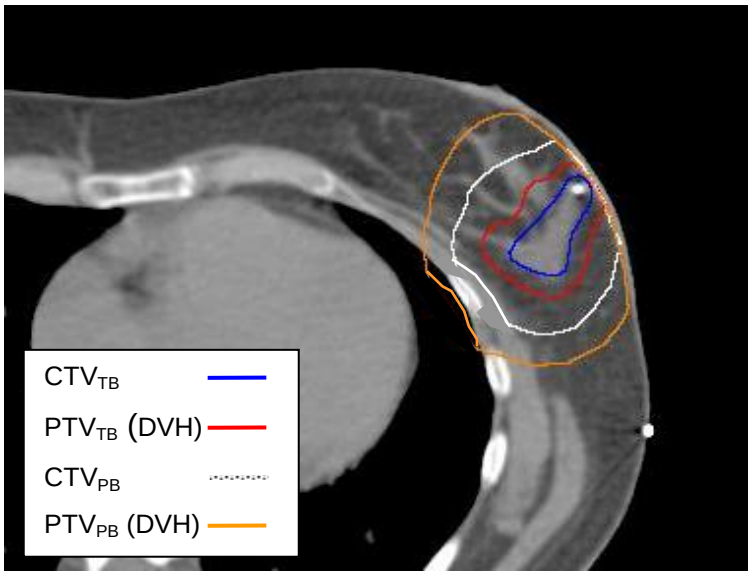


Figure 7. Axial slice showing modified partial breast PTV

Whole breast outlining on CT requires outlining a CTV volume on each axial slice, adding an appropriate PTV margin, and then a margin for field penumbra. This is the principle IMPORT is working towards, however it can be very difficult to accurately delineate breast tissue on x-ray CT images, and this can result in an overestimate of the whole breast volume, especially in obese patients. An alternative strategy is to generate a field-based structure which is not a true PTV, but is helpful for reporting purposes. The planner/clinician selects a provisional tangential field pair, to cover the breast tissue and minimise dose to the normal tissues, by scrolling up and down the CT dataset. The field based PTV structure is then generated 5 mm from the skin surface, 5 mm from the posterior field edge and lung/chest wall interface, and 10 mm from the superior and inferior field edges (Figure 8).

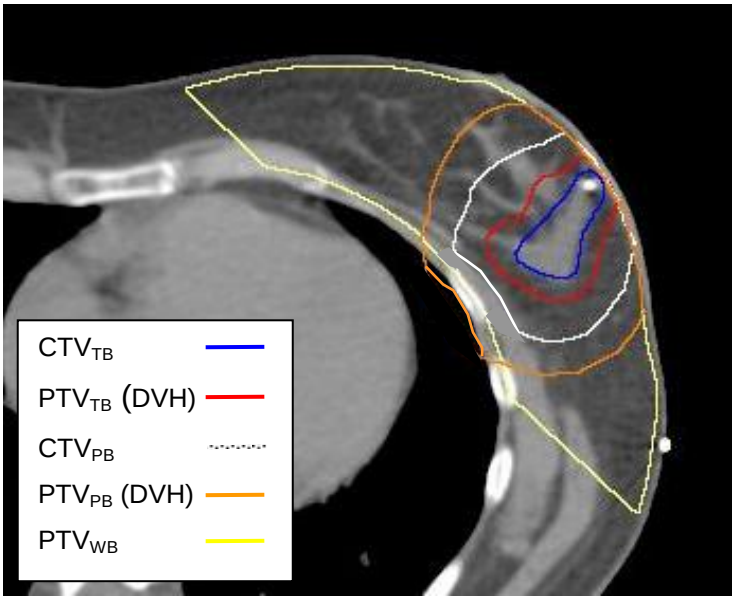


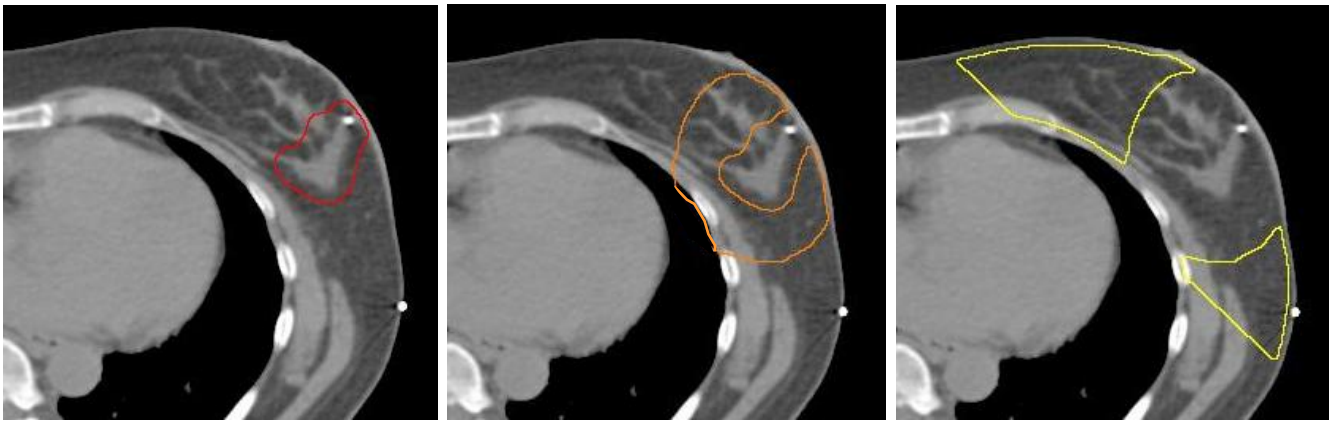
Figure 8. Axial slice showing field-based whole breast PTV

The clinician can then assess whether the field borders need to be modified to provide good coverage to the partial breast PTV based on the available clinical information. The

histology report will give the tumour-free margin, which may assist the modification of fields. Care should be taken when modifying the field borders that the dose to normal tissues and organs at risk is not significantly increased. The heart should be excluded from the fields if the tumour location allows this, and the maximum lung depth should not exceed 2 cm. This will help to achieve the volumetric dose constraints to organs at risk described in the protocol.

There should be an implanted clip or seed marker at the deep fascia, depending on the operation performed, and in some cases this will cause the partial breast PTV to extend outside of the previously defined whole breast volume at the posterior edge. However this is not problematic, as all whole breast DVH analysis and reporting will be carried out on a subtracted structure ($PTV_{WB} – PTV_{PB}$) shown below.

Target volume DVH analysis and reporting is carried out on the structures shown in Figure 9.



PTV_{TB} DVH *PTV_{PB} - PTV_{TB}* *PTV_{WB} - PTV_{PB}*

Figure 9. Axial slices showing subtracted structures for DVH analysis.

3.2 Organs at Risk

Both lungs, the heart and contralateral breast are contoured for dose volume histogram assessment (Figure 10).

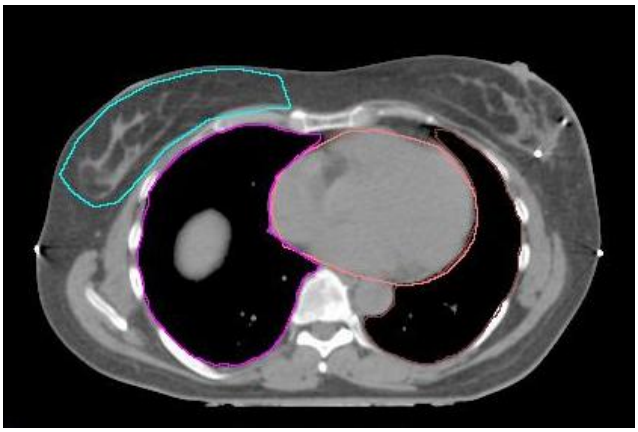


Figure 10. Axial slice showing delineation of organs at risk: lungs, heart & contralateral breast

The following guidelines for heart delineation have been adapted from the Wales Cancer Trials Unit SCOPE1 Radiotherapy Treatment Planning and Delivery Document, leads: T Crosby, J Staffurth and L Wills.

'The whole heart should be outlined to the extent of the pericardial sac (if visible). The major blood vessels (superior to the organ) and the inferior vena cava (towards the inferior extent of the heart) are excluded. The superior extent is often difficult to define and may be simplified by identification of the vessels superior to the heart. Use the point where the pulmonary trunk and the right pulmonary artery are seen as separate structures as indication of the superior extent of the heart. Shown below in Figure 11 are alternate CT images for a scan taken at 0.3cm intervals.

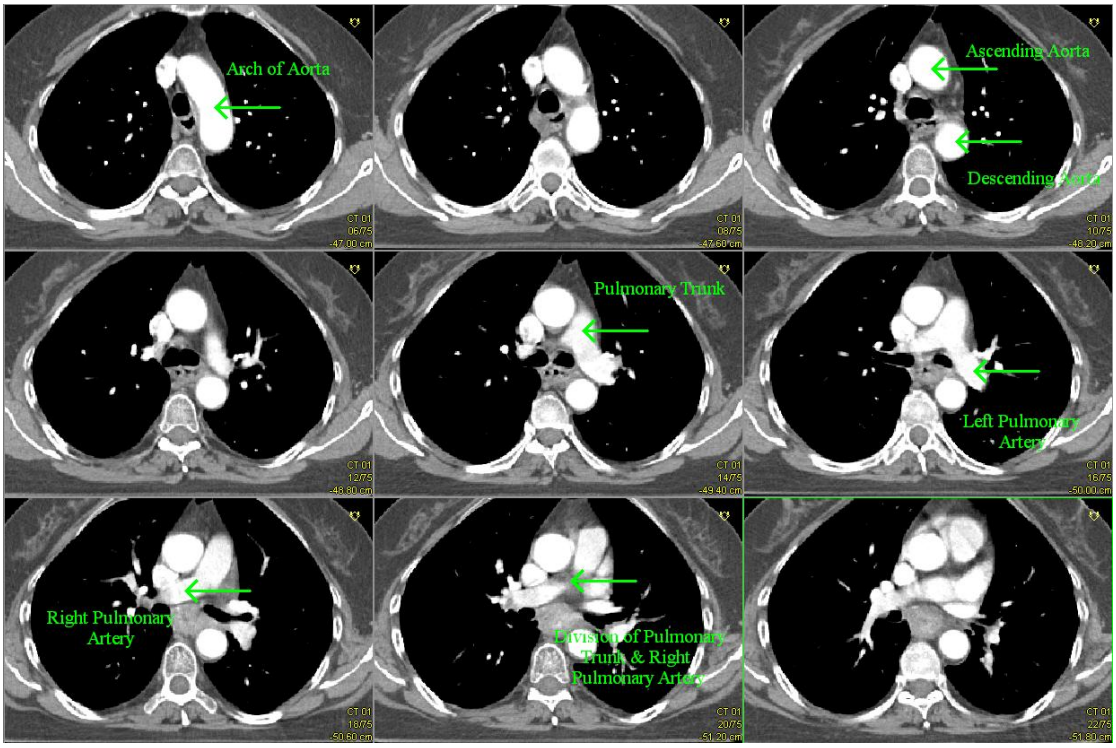


Figure 11. Alternate 0.3cm CT slices indicating cardiac anatomy

The definition of the heart is shown in Figure 12 on the same data set. The superior extent of the heart has been interpreted as the 1st section on which the right and left pulmonary arteries have separated. Throughout the heart is outlined to the extent of the pericardial sac. The inferior extent is less problematic to delineate as the organ appears well defined compared to the surrounding tissues in the abdomen however if possible the inferior vena cava should be excluded.'

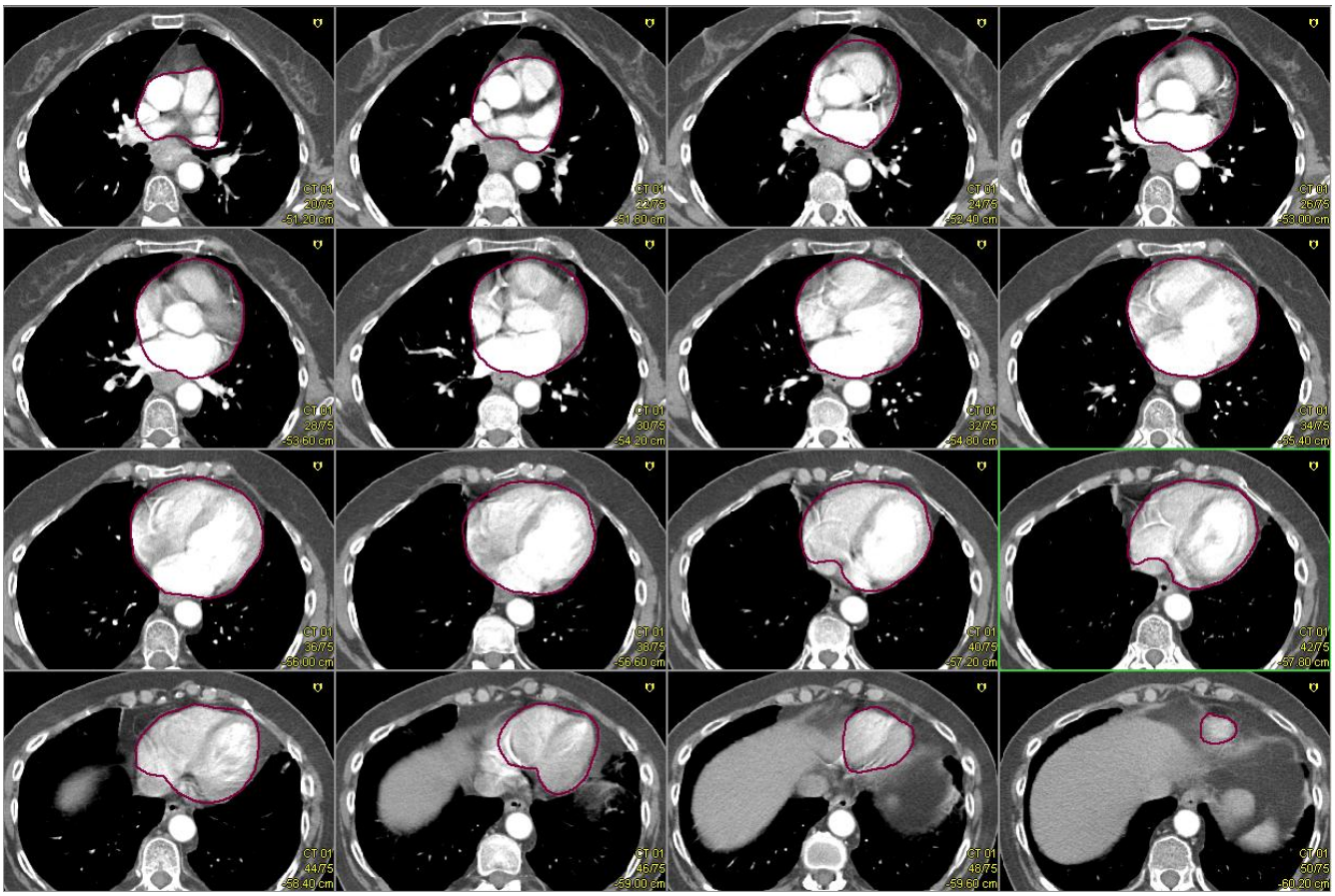
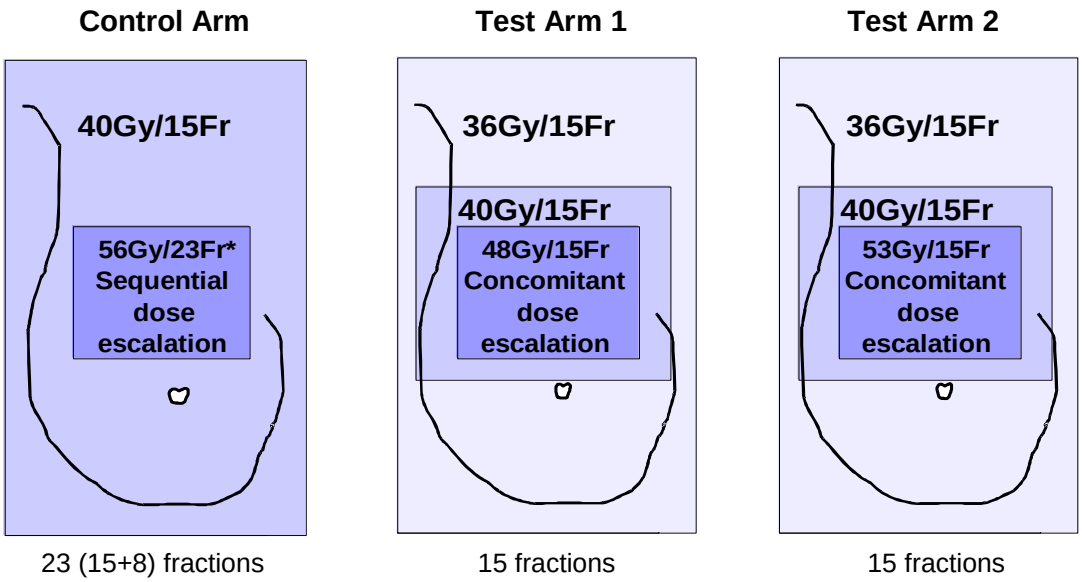


Figure 12. Alternate 0.3cm CT slices indicating heart delineation

4. Treatment Planning

4.1 Dose Prescription

IMPORT HIGH requires a concomitant 3 level dose distribution to the whole breast (Figure 13), using a linear accelerator with either forward or inverse-planned IMRT, or tomotherapy.



*56 Gy/23F represents 40 Gy/15 F to whole breast plus 16 Gy/8 F sequential photon boost.

Figure 13. IMPORT HIGH trial schema

The control arm delivers 23 fractions: 40 Gy in 15 fractions to the whole breast plus 16 Gy in 8 fractions sequential photon boost to the tumour bed. The test arms deliver 15 fractions: 36 Gy in 15 fractions to the whole breast; 40 Gy to the partial breast plus 48 Gy (Test Arm 1) or 53 Gy (Test Arm 2) in 15 fractions simultaneous photon boost to the tumour bed.

Trial Arm	Target volume	Fractions	Dose per fraction (Gy)
Control	Whole breast	15	2.67
	Tumour bed	15 + 8	2.67 → 2.0
Test Arm 1	Low dose (whole breast) volume	15	2.40
	Standard dose (partial breast) volume	15	2.67
	Tumour bed	15	3.2
Test Arm 2	Low dose (whole breast) volume	15	2.40
	Standard dose (partial breast) volume	15	2.67
	Tumour bed	15	3.5

Table 2. Summary of dose prescriptions

4.2 Dose Targets & Constraints

The constraints highlighted in grey in table 3 and 4 must be adhered to. The rest are not strict tolerances but should be achievable in most cases if planning appropriately.

4.2.1 Target Volumes

Control Arm

Volume	Lower dose limit	Reference Dose	Upper dose limit
PTV_{WB} - PTV_{TB}	> 90% of the volume should receive 36 Gy	median dose = 40 Gy (allow 40 - 44 Gy)	< 5% of the volume should receive > 56Gy
PTV_{TB}	> 95% of the volume should receive 53.2 Gy	median dose = 56 Gy (allow 55.5 - 56.5 Gy)	< 5% of the volume should receive > 60 Gy with a global max < 61.6 Gy

Test Arm 1

Volume	Lower dose limit	Reference Dose	Upper dose limit
PTV_{WB} – PTV_{PB}	> 90% of the volume should receive 32.4 Gy	median dose = 36 Gy (allow 34 - 37 Gy)	< 5% of the volume should receive > 40 Gy
PTV_{PB} – PTV_{TB}	> 90% of the volume should receive 36 Gy	median dose = 40 Gy (allow 40 - 44 Gy)	N/A
PTV_{TB}	> 95% of the volume should receive 45.6 Gy	median dose = 48 Gy (allow 47.5 - 48.5 Gy)	< 3% of the volume should receive > 51.4 Gy with global max < 52.8 Gy

Test Arm 2

Volume	Lower dose limit	Reference Dose	Upper dose limit
PTV_{WB} – PTV_{PB}	> 90% of the volume should receive 32.4 Gy	median dose = 36 Gy (allow 34 - 37 Gy)	< 5% of the volume should receive > 40 Gy
PTV_{PB} – PTV_{TB}	> 90% of the volume should receive 36 Gy	median dose = 40 Gy (allow 40 - 44 Gy)	N/A
PTV_{TB}	> 95% of the volume should receive 50.4 Gy	median dose = 53 Gy (allow 52.5 - 53.5 Gy)	< 3% of the volume should receive > 56.7 Gy with global max < 58.3 Gy

Table 3. Summary of dose targets for each trial arm

4.2.2 Dose constraints for organs at risk

Organ at risk	Mandatory Constraint	Optimal Constraint
Ipsilateral Lung	V18Gy <15%	V18Gy <10%
		Mean Dose <6Gy
Contralateral Lung	V2.5Gy < 15%	V2.5Gy < 3%
		Mean Dose <1Gy
Heart (Left sided tumour)	V13Gy < 10%	V13Gy < 2%
		Mean Dose < 3Gy
Heart (Right sided tumour)	N/A	V5Gy < 6%
		Mean Dose < 1.7Gy
Contralateral Breast	Mean Dose < 1.5Gy	Mean Dose < 0.5Gy

Table 4. Summary of organs at risk dose constraint

No bolus should be applied to the skin, including the excision scar. Beam energies for treatment as for local practice, usually 4 - 6 MV, but 10 MV or a mixture of energies e.g. 6 MV and 15 MV can be used to improve dosimetry. All plans should be evaluated with the help of the IMPORT HIGH plan assessment form which should be filled in and submitted for every patient.

4.3 Inverse planning technique

A combination of forward and inverse planned IMRT can be used to satisfy the treatment planning requirements for the trial test arms. This solution comprises two co-planar plans with a common isocentre at the centre of PTV_{WB} treated synchronously for a total of 15 fractions. In order to minimise the dose to the organs at risk the majority of the dose is delivered by forward planned standard whole breast tangent fields (base dose plan). Inverse planned IMRT is then used to provide the concomitant boost doses to PTV_{PB} and PTV_{TB} (boost dose plan). The example below was calculated with the Analytical Anisotropic Algorithm (AAA) from Varian Eclipse planning system.

4.3.1 Plan 1: Base Dose Plan

The base dose plan consists of two standard tangential fields with non-divergent posterior field edges and the isocentre at the centre of PTV_{WB} (Figure 14). The field sizes are selected to cover PTV_{WB} and PTV_{PB} with collimator rotation to minimise the

irradiated lung volume. MLC can be used to shield the ipsi-lateral lung and heart where possible without compromising PTV coverage.

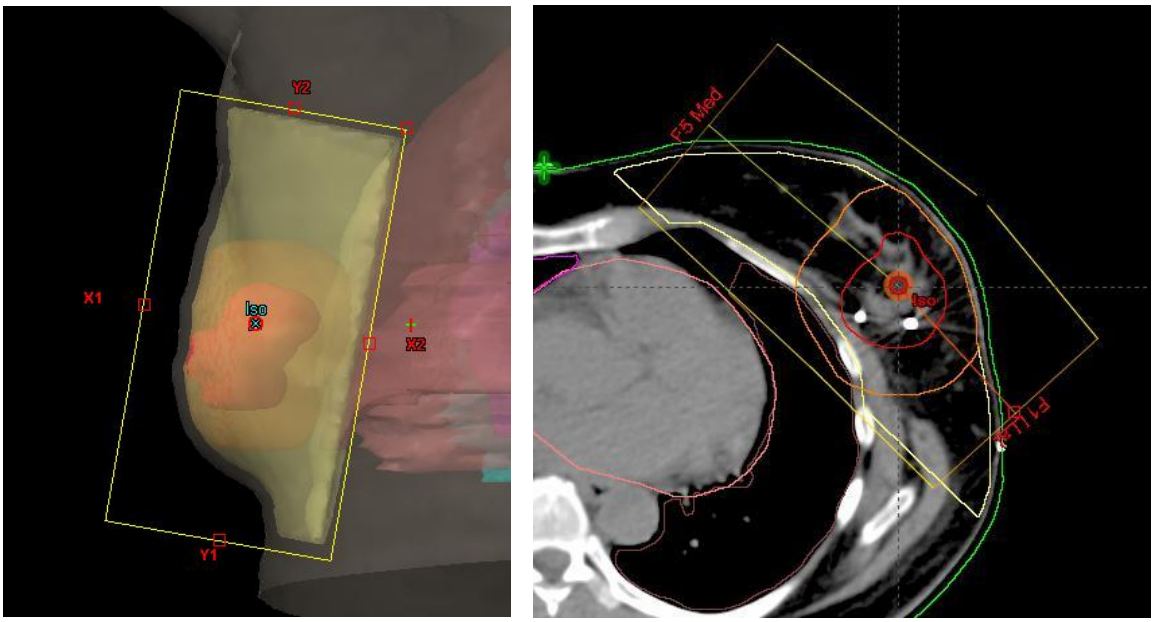


Figure 14. Beams eye view of whole breast tangent & beam orientation for base dose plan

A combination of wedges, simple field-in-field modulation, mixed energies or electronic compensation with step-and-shoot MLC can be used to create a homogeneous dose distribution to PTV_{WB}. Planners should aim to achieve coverage of between 95% and 107% of the normalised dose. The dose is prescribed as 34Gy in 15 fractions and plans can be normalised to either the isocentre or to the mean dose to PTV_{WB}, dependent on which method results in the most homogeneous dose distribution. The example shown below in Figure 15 has been planned at 6MV for step-and-shoot MLC with 10 intensity levels and the dose is normalised to the mean dose to PTV_{WB}.

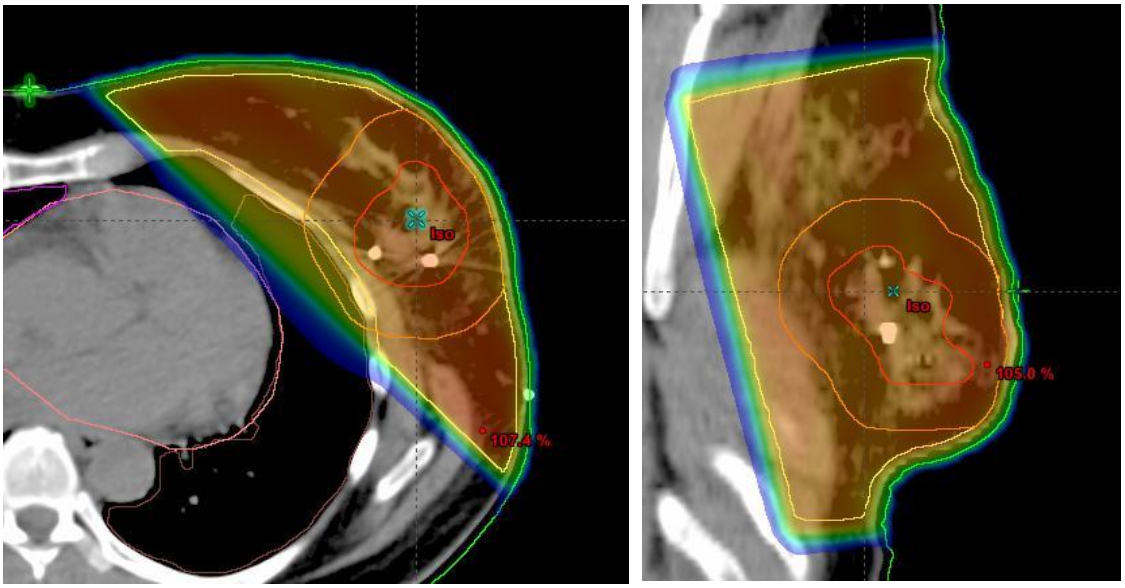


Figure 15. Transverse and sagittal slices with colour wash showing dose distribution from 34Gy base dose plan

4.3.2 Plan 2: Boost Dose Plan

The second plan is a 5 co-planar field concomitant boost prescribed to 14Gy in 15 fractions (test arm 1) or 19Gy in 15 fractions (test arm 2). The aim of the plan is to deliver 3 clearly defined dose levels to the PTV_{TB} (14 or 19Gy), PTV_{PB} (6Gy) and PTV_{WB} (2Gy) using inverse planned IMRT, in addition to the 34Gy being delivered by the base dose plan.

Beam orientation

The gantry angles, collimator angles and field sizes of the tangent fields from the base dose plan are incorporated with three additional fields at gantry angles around 0°, 45° and 90° for left breast treatments and 0°, 315° and 270° for right breast treatments (Figure 16). These additional fields should be fitted to PTV_{PB} with a 1cm margin and their collimator angle should be set to 0°. The plan isocentre is the same as that for the base dose plan.

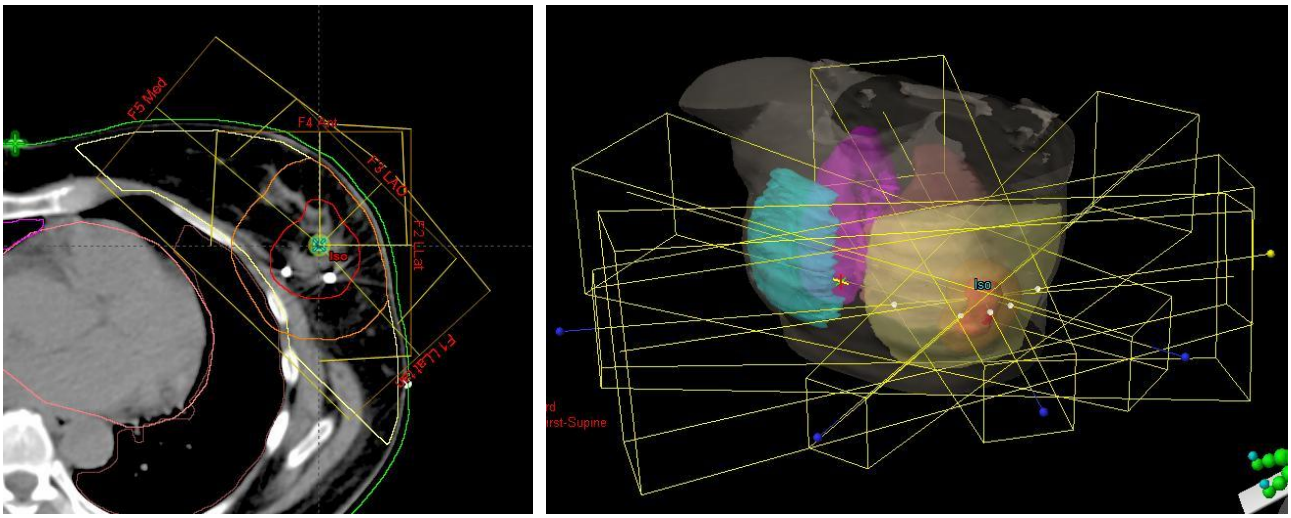


Figure 16. Five co-planar field beam orientation for boost dose plan shown in 3D and on transverse slice

4.3.3 Plan optimisation

Inverse planning can be used to optimise the beam fluences. Target doses and priorities should be applied to PTV_{TB} and subtracted volumes PTV_{PB}-PTV_{TB} and PTV_{WB}-PTV_{PB} along with dose constraints / dose-volume constraints to the organs at risk (ipsi-lateral lung, contra-lateral lung, heart and contra-lateral breast). If possible the dose distribution from the base dose plan should be incorporated in the optimisation. The resulting beam fluences should be checked to ensure there are no hotspots outside of PTV_{PB}. It may be necessary to delete localised hotspots along the posterior border of the tangent fields as their presence may unnecessarily increase the plan monitor units.

When editing any fluence, the resulting dose distribution should always be carefully assessed.

4.3.4 Plan normalisation

Optimal fluences should be converted to deliverable fluences and a full 3D dose calculation carried out. Step-and-shoot deliveries with a relatively small number of intensity levels should be considered in order to try and minimise the total plan monitor units. As is the case with IMRT treatments in general, the boost dose plan should not be normalised to a point. The most appropriate method is to combine the boost dose plan with the base dose plan and normalise the boost dose plan to the isodose that ensures the median dose to PTV_{TB} is 48Gy or 53Gy, depending on randomised treatment arm, in the composite plan.

4.3.6 Evaluation

Table 5 is taken from the IMPORT HIGH Trial Plan Assessment Form showing dose target coverage and normal tissue dose constraints. It has been filled in for the worked example described above for test arm 2, generated with inverse-planned IMRT. The dose distribution is illustrated below in Figures 17 and 18.

Volume	Lower dose limit		Reference Dose		Upper dose limit	
	Target	Achieved (%)	Target	Achieved (Gy)	Target	Achieved (%)
$PTV_{WB} - PTV_{PB}$	> 90% of the volume should receive 32.4 Gy	97.6	median dose = 36 Gy (allow 34 - 37 Gy)	36.3	< 5% of the volume should receive > 40 Gy	1.8
$PTV_{PB} - PTV_{TB}$	> 90% of the volume should receive 36 Gy	99.9	median dose = 40 Gy (allow 40 - 44 Gy)	41	n/a	
PTV_{TB}	> 95% of the volume should receive 50.4Gy	95.1	median dose = 53 Gy (allow 52.5 - 53.5 Gy)	53	< 3% of the volume should receive > 56.7 Gy	0
					Global max < 58.3 Gy	55.9

NORMAL TISSUE DOSE CONSTRAINTS

Organ at risk	Mandatory Constraint	Optimal Constraint	Achieved
Ipsilateral Lung	V18Gy <15%	V18Gy <10%	**10.8%**
		Mean Dose <6Gy	**5.9 Gy**
Contralateral Lung	V2.5Gy < 15%	V2.5Gy < 3%	**0.3 %**
		Mean Dose <1Gy	**0.7 Gy**
Heart (Left sided tumour)	V13Gy < 10%	V13Gy < 2%	**0.6%**
		Mean Dose < 3Gy	**2.9 Gy**
Heart (Right sided tumour)	N/A	V5Gy < 6%	**N/A**
		Mean Dose < 1.7Gy	**N/A**
Contralateral Breast	Mean Dose < 1.5Gy	Mean Dose < 0.5Gy	**0.6Gy**

Table 5. Extract from plan assessment form for inverse-planned IMRT worked example

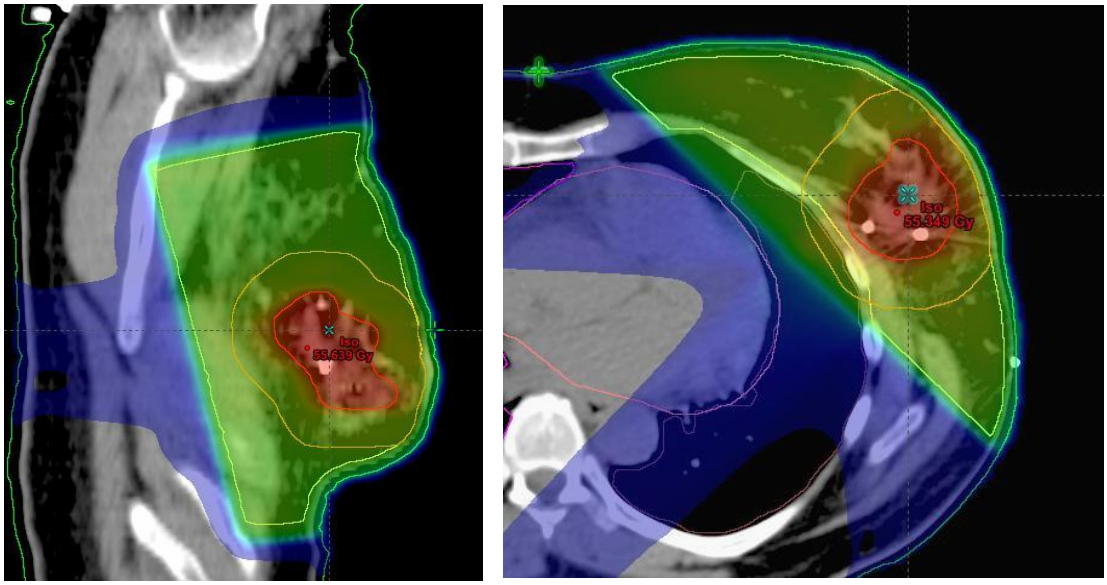


Figure 17. Transverse and sagittal slices showing the combined dose from a base dose plan and boost dose plan for test arm 2 (53Gy total dose)

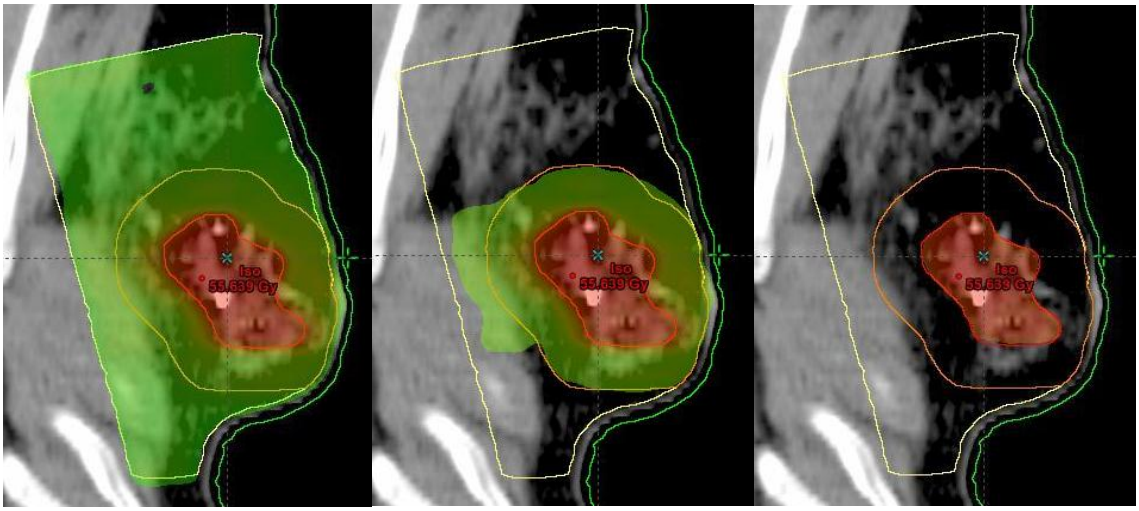


Figure 18. Sagittal slices showing 95% dose coverage for each of the three dose levels in test arm 2 (36Gy, 40Gy and 53Gy).

NOTE

A similar technique can be used for planning the control arm of the trial. The base dose plan can be prescribed to 40Gy in 15 fractions. For the boost dose plan the same 5 co-planar field beam arrangement can be used as above with the fields fitted to PTV_{TB}. The plan can be optimised with a prescribed dose of 16Gy in 8 fractions and the two plans can be treated sequentially for a total of 23 fractions.

4.4 Forward planning technique

Treatment planning requirements for each of the 3 arms of the trial may be satisfied with a variety of beam arrangements, however for ease of patient set-up and treatment delivery the following coplanar forward-planning technique is recommended. Like the inverse planning method, this solution also comprises two co-planar plans with a common isocentre treated synchronously for a total of 15 fractions. The following details a suggested method for the test arms, but the general processes can also be applied to the control arm. The example below was calculated with the Pencil Beam Convolution Algorithm from Varian Eclipse planning system.

4.4.1 Whole Breast

This is very similar to the base dose plan method described above. The PTV_{WB} is planned using a pair of wedged tangential fields with a non-divergent back edge (Figure 19). The isocentre can be placed on the slice which falls in the centre of the tumour bed, either on the posterior border or in the centre of the tumour bed volume. The fields are positioned to cover the PTV_{WB} and PTV_{PB}, so that the maximum lung distance and maximum heart distance do not exceed 2cm and 1cm respectively.

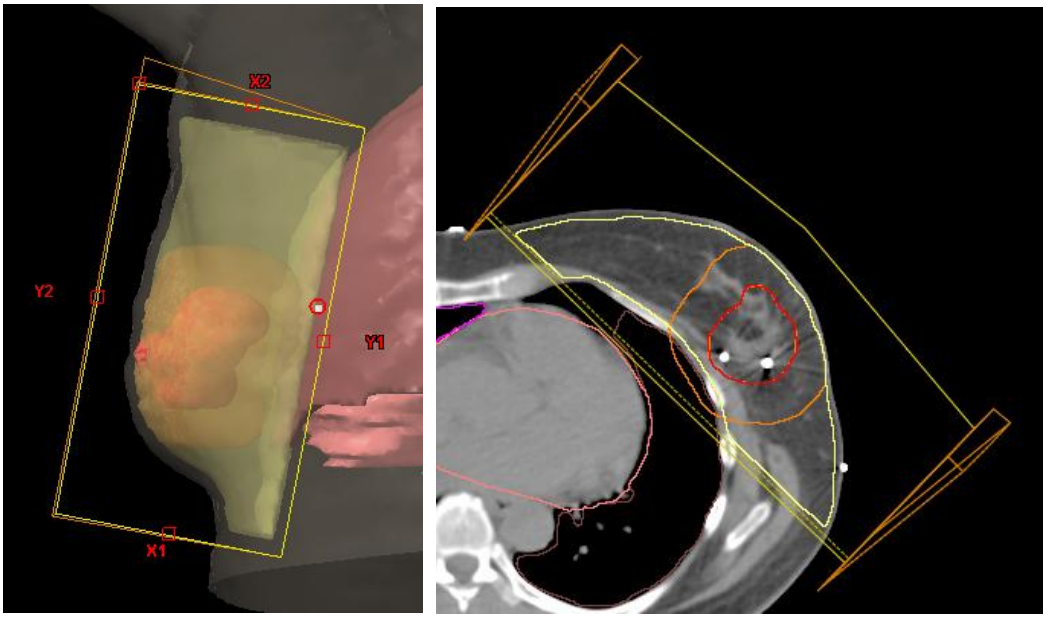


Figure 19. Beams eye view of whole breast tangent & beam orientation for whole breast plan

In most cases some form of dose compensation such as 'field-in-field' MLC segments are required in order to generate an acceptable whole breast plan fulfilling the dose constraints. In some cases a longitudinal wedge may also be required. For the test arms this plan aims to deliver 36 Gy to PTV_{WB} and can be normalised to either the centre of PTV_{TB} or to the mean dose to PTV_{WB}, dependent on which method results in the most homogeneous dose distribution. The example shown in Figure 20. has been planned at 6MV with a single MLC segment on the lateral field and a longitudinal wedge on the medial field to optimise dose homogeneity. The dose is normalised to the centre of PTV_{TB}:

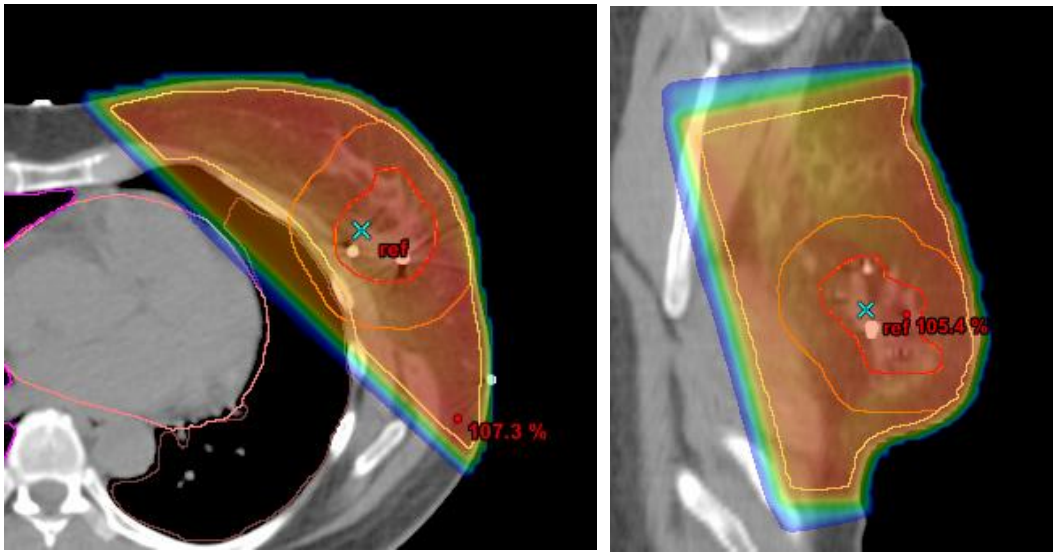
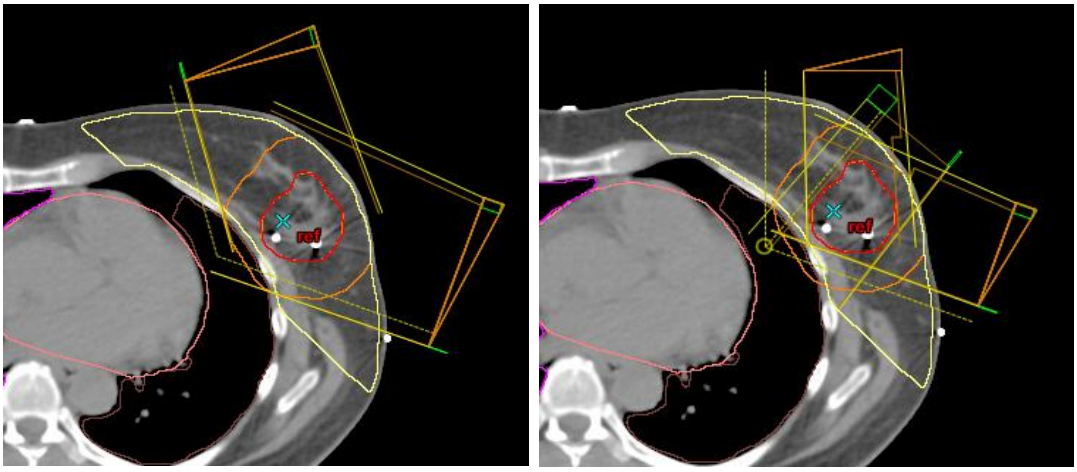


Figure 20. Axial and sagittal slices showing dose distribution from 36 Gy whole breast plan

4.4.2 Partial breast and tumour bed

The second stage is the addition of 5 to 6 beams at gantry angles between the whole breast tangents positioned to avoid the heart and contralateral breast (Figures 21 & 22). These aim to deliver 40Gy to the partial breast and 48 or 53Gy to the tumour bed for test arm 1 and test arm 2, respectively, so that when combined with the whole breast plan, 3 distinct dose levels can be delivered simultaneously. Two beams are set to cover PTV_{PB} and three further beams cover PTV_{TB} with no margin for penumbra (except at the skin surface). Wedges & MLC shaping on these fields may improve the dose distribution:



2 beams set to cover the partial breast *3 beams set to cover the tumour bed*

Figure 21. Axial slices showing beam arrangement to cover partial breast and tumour bed

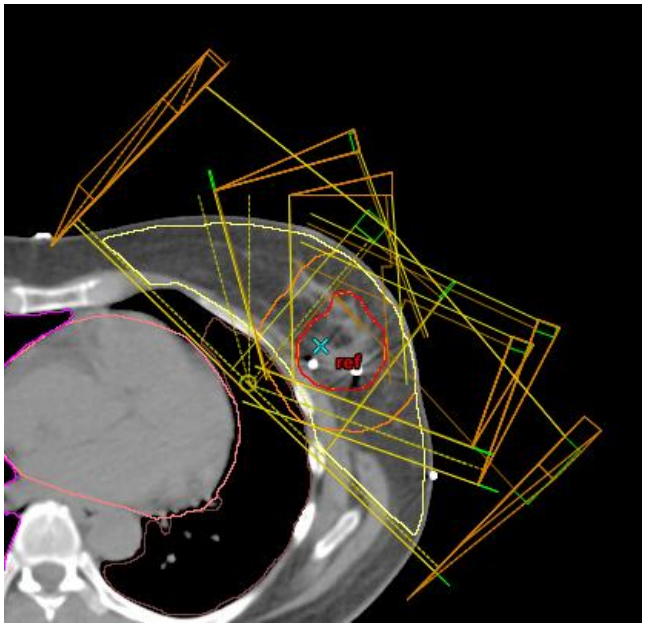


Figure 22. Combined beam arrangement showing 7 coplanar fields

4.4.3 Plan normalisation

The combined plan should be normalised to the isodose that ensures the median dose to PTV_{TB} is 48Gy or 53Gy according to test arm, and the beam weights adjusted to give the 3 desired dose levels (Figure 23). Modification of the relative weightings, gantry angles, wedges and MLC shaping of the boost plan may be necessary in order to achieve the dose constraints.

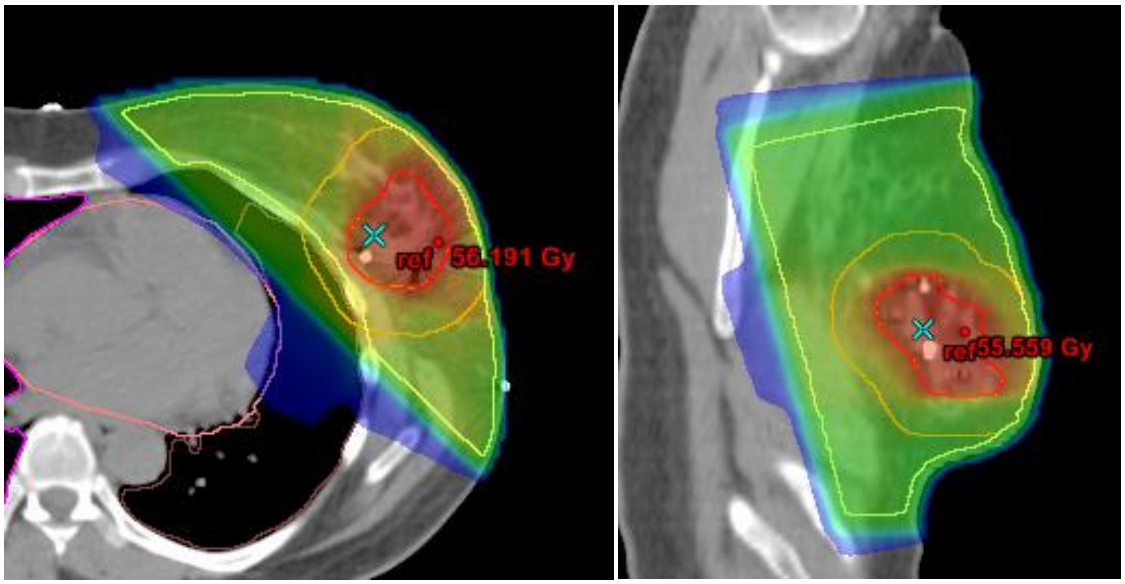
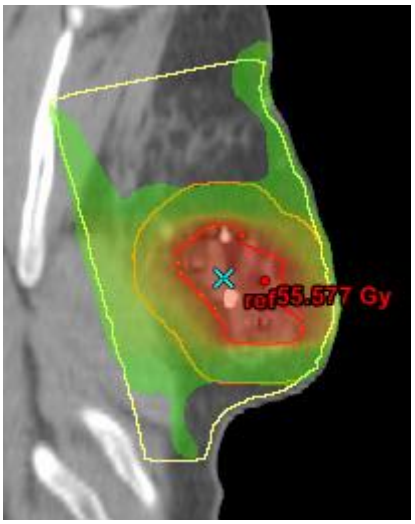


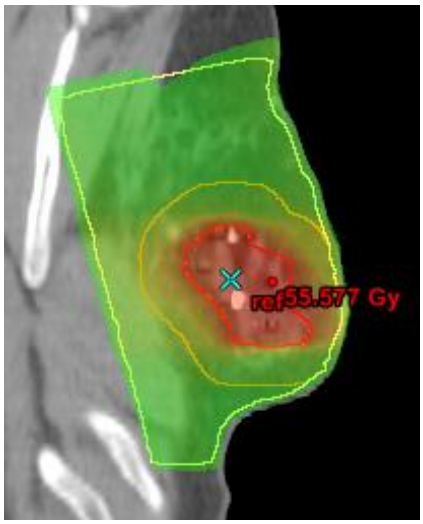
Figure 23. Axial and sagittal slices showing the combined dose from all 7 fields for test arm 2 (53Gy total dose). Reference point and slice max dose is shown.

4.4.4 Evaluation

A note on whole breast coverage (36 Gy dose level): in contrast with the inverse planning method, it can be difficult to achieve 95% coverage (34.2 Gy) for the whole breast PTV using forward planning whilst keeping the median dose within acceptable limits (Figure 24 left). However the dose target in the protocol for this volume states that 90% of the volume should be covered by 90% of the dose (32.4 Gy). It is usually possible to achieve this whilst maintaining an acceptable median dose (Fig. 24 right):



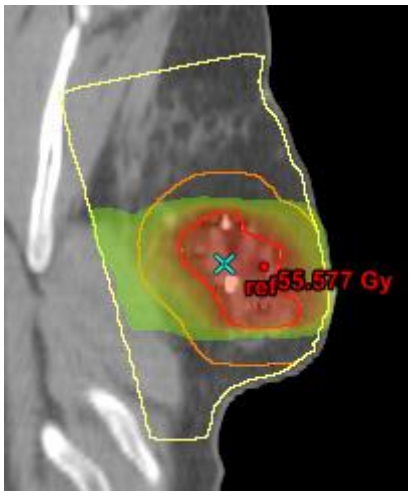
Sagittal slice showing 95% coverage the whole breast PTV



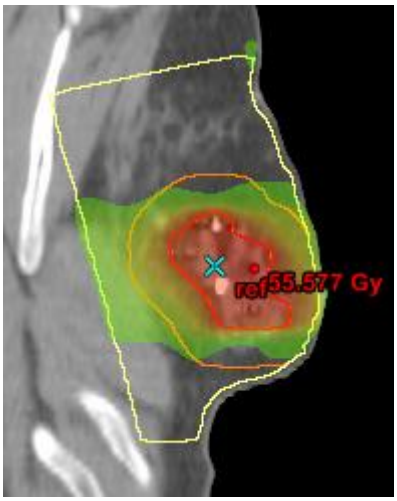
Sagittal slice showing 90% coverage for for the whole breast PTV

Figure 24. Whole breast coverage

Similarly for partial breast coverage (40 Gy dose level) it is difficult to achieve 95% coverage (38 Gy) with an acceptable median dose with forward planning (see Fig. 25 left). The protocol dose target in this case states that 90% of the volume should be covered by 90% of the dose (36 Gy) which is usually achievable (see Fig. 25 right):



Sagittal slice showing 95% coverage for the partial breast PTV



Sagittal slice showing 90% coverage for the partial breast PTV

Figure 25. Partial breast coverage

Bear in mind that it may be more difficult to achieve the desired median doses required for the whole breast and partial breast volumes when using forward rather than inverse planning. On the plus side, forward planning may result in reduced dose to contralateral breast, reduced total MU and reduced whole body effective dose compared with inverse planning.

95% coverage of the tumour bed PTV (53 Gy dose level in test arm 2) should not present a problem with forward planning (Figure 26).

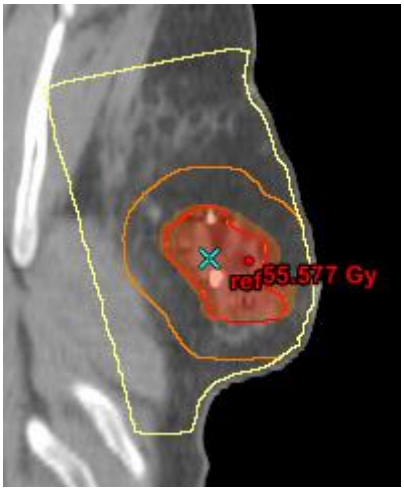


Figure 26. Sagittal slice showing 95% dose coverage for the tumour bed PTV

Table 6 below is taken from the IMPORT HIGH Trial Plan Assessment Form showing dose target coverage and normal tissue dose constraints. It has been filled in for the worked example described above for test arm 2, generated with forward-planned IMRT.

Volume	Lower dose limit		Reference Dose		Upper dose limit	
	Target	**Achieved (%)**	**Target**	**Achieved (Gy)**	**Target**	**Achieved (%)**
PTV_{WB} – PTV_{PB}	> 90% of the volume should receive 32.4 Gy	91.2	median dose = 36 Gy (allow 34 - 37 Gy)	34.4	< 5% of the volume should receive > 40 Gy	4.3
PTV_{PB} – PTV_{TB}	> 90% of the volume should receive 36 Gy	90.0	median dose = 40 Gy (allow 40 - 44 Gy)	42.9	n/a	
PTV_{TB}	> 95% of the volume should receive 50.4Gy	99.4	median dose = 53 Gy (allow 52.5 - 53.5 Gy)	53.4	< 3% of the volume should receive > 56.7 Gy	0
					Global max < 58.3 Gy	56.5

NORMAL TISSUE DOSE CONSTRAINTS

Organ at risk	Mandatory Constraint	Optimal Constraint	Achieved
Ipsilateral Lung	V18Gy <15%	V18Gy <10%	**14.0%**
		Mean Dose <6Gy	**6.8 Gy**
Contralateral Lung	V2.5Gy < 15%	V2.5Gy < 3%	**0 %**
		Mean Dose <1Gy	**0.6 Gy**
Heart (Left sided tumour)	V13Gy < 10%	V13Gy < 2%	**1.1 %**
		Mean Dose < 3Gy	**1.9 Gy**
Heart (Right sided tumour)	N/A	V5Gy < 6%	**N/A**
		Mean Dose < 1.7Gy	**N/A**
Contralateral Breast	Mean Dose < 1.5Gy	Mean Dose < 0.5Gy	**0.5 Gy**

Table 6. Extract from plan assessment form for forward-planned IMRT worked example

NOTE: a similar technique can be used for planning the control arm of the trial. The whole breast plan is prescribed to 40Gy in 15 fractions. For the boost 3 to 5 co-planar field beam arrangement can be used as above with each of them fitted to the tumour bed. It may be necessary to shape the MLCs to CTV_{TB} rather than PTV_{TB} in order to prevent blurring of the dose levels in the composite plan. The boost plan is prescribed a dose of 16Gy in 8 fractions and the two plans can be treated sequentially for a total of 23 fractions.

5. Lymph nodes

A single anterior field encompassing the planning target volume is recommended. Posterior fields may only be used if the nodal region is CT planned, and if the nodal fields and breast fields are matched or there is a gap between the nodal fields and breast fields. Fields may be angled as required to avoid treating the spinal cord and to avoid any overlap with the tangential fields. If there is no gap then a match should be obtained between the inferior border of the supraclavicular field and the superior border of the tangential fields. The method of matching will be checked by the QA team. ICRU recommendations on dose homogeneity should be adhered to if possible and in no case should the maximum dose (either inside or outside the PTV) exceed 110% of the prescribed dose. Segment fields and/or mixed energy beams may be necessary to

achieve this. The plan should be assessed as a composite of all beams, including all breast fields and nodal fields. The normal tissue constraints in the planning pack are used to assess the breast plan only without any nodal field dose contributions. It is recommended the volume of ipsilateral lung receiving 18Gy should be less than 30 % with the composite plan. Please contact the QA team if there are any enquires regarding to the nodal field treatments.

6. Verification imaging

6.1 General

Tumour bed markers are mandatory unless the position of a clearly defined seroma can be verified daily with volumetric imaging. In all cases a range of technology may be used as long as each allows the implanted markers to be matched and appropriate couch movements generated to allow corrections to be made.

Note that not all commercial systems have good functionality for both 2D and 3D kV imaging so that the limitations of the system may not allow a choice between the two. Careful considerations should be made to the isocentre placement to avoid collision risk. For Elekta system, an isocentre position which is a maximum of 8cm lateral to midline tattoo and a couch height of 30cm or less has enabled cone beam CT scanning without collision for 190 degree scans. This is for a maximum breast board tilt of 5 degrees. The breast board tilt should be ideally less than 15 degrees for Varian 2D KV imaging to reduce the collision risk. Each centre must check their own possible collision risk.

If 3D kV cone beam CT is to be used, a measurement of the dose for the imaging protocol is useful and the imaging protocol should be optimised as much as possible to reduce this e.g. by using a 190° scan, and adjusting scan parameters. Where a tomotherapy system is the treatment delivery technology of choice, then an appropriate scan protocol which allows the implanted markers to be seen, but does not deliver a higher than necessary dose is recommended. For the test arms, if all treatment fields are to be delivered in a sequence forming an arc around the patient then the verification can take place before the delivery of all fields. If the whole breast fields are delivered first, then verification of the tumour bed position can occur after the delivery of the large whole breast fields and prior to the delivery of the boost dose plan.

6.2 Type of Implanted Marker

If gold seeds have been used to identify the tumour bed then these will be visible on both MV portal images and 2D kV images and either may be used. The artifacts generated in a cone beam CT scan from gold makers may make this a poor option. If titanium clips have been used to locate the tumour bed these are visible easily only on kV quality images; either 2D planar images or 3D cone beam CT maybe used to generate the centre of mass positions.

6.3 Verification - Control Arm: Whole Breast Fields

Treatment verification is required for at least three fractions in the first week of treatment to determine and correct for any systematic error. Verification is then carried out once weekly throughout the remaining whole breast treatment. The alignment of the main tangential fields in relation to the planned values should be verified in terms of light field coverage from the medial and lateral tattoos, the anterior focus-to-skin distances (FSDs) of isocentre and tangential beam entry points' FSDs etc. Verification of the central lung depth (CLD) or maximum lung distance (MLD) can be carried out with electronic portal imaging. If there is gross discrepancy (>0.5cm), check the set-up of the patient. A tolerance of 5 mm is recommended for the weekly imaging following correction of the systematic error. The whole breast treatment fields are appropriate for this verification.

6.4 Verification - Control Arm Sequential Photon Boost and Test Arms

Either an on-line, or off-line correction protocol may be used. Apart from bony anatomy and lung inclusion matching, marker information should be used to determine the setup errors. Prior to the first treatment a dummy run is strongly recommended to ensure the imaging parameters are achievable. Centres are encouraged to measure their own treatment set-up errors in order to evaluate the population systematic and random errors.

6.4.1 On-line verification protocol

This method corrects for both systematic and random errors in patient set-up but has a time and dose penalty as it requires daily imaging and correction.

6.4.2 Off-line verification protocol

The 'No Action Level' NAL or eNAL protocol of de Boer is recommended. These methods correct for the systematic error of the set up variation but have the advantage of a reduced imaging burden as daily imaging is not required. The application of both methods to breast radiotherapy patients showed that the use of these protocols enables the requirement for the tumour bed CTV to PTV margin to be 5 mm to be fulfilled but only if ALL the systematic error is corrected i.e. the tolerance = 0mm.

An example of the use of the NAL protocol

Image every day for fractions 1 to 5.
Determine the systematic error.
Apply all the correction to all subsequent fractions : 6 to 15.
No further imaging.

An example of the use of the eNAL protocol (recommended)

Image every day on fractions 1 to 3.
Determine the systematic error.
Apply all the correction to fractions 4 to 7.
Image on fraction 7.
Determine the systematic error using data from fraction 1 to 3 and 7 (i.e. four data sets).
Apply all the correction to fractions 8 to 11.
Image on fraction 11.
Determine the systematic error using data from fractions 1 to 3, 7, and 11 (i.e. five data sets).
Apply all the correction to fractions 12 to 15.

6.5 Imaging Technologies: Use in Correction Protocols

6.5.1 MV portal imaging (Gold seeds only)

If possible, use at least one treatment beam which would be selected from the smaller tumour bed boost fields; ideally, two of these fields would be used. If an additional field is required for imaging then this field size should be no larger than is necessary to encompass the implanted markers and would deliver the lowest MU possible to see the markers clearly. Please note that for centres in the EME IMPORT_IGRT study, all fields must contain sufficient anatomy to allow a bony anatomy match.

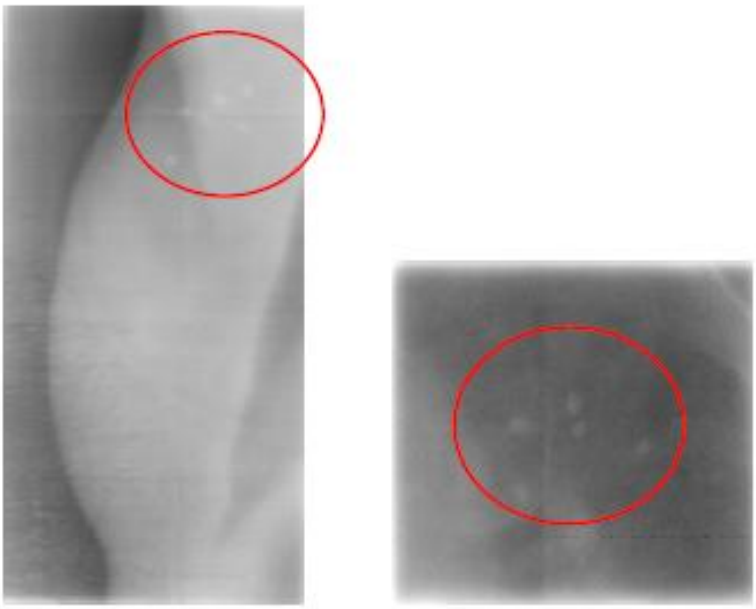


Figure 27. Example of MV imaging with gold seeds. LPO treatment field (left) and orthogonal LAO field imaged with 1MU(Right). Red circle indicates area of markers.

6.5.2 kV planar imaging (Gold seeds or titanium clips)

Two planar kV exposures are used for the verification. It is recommended that kV source angles should be determined by planning staff and treatment radiographer together before treatment starts. This should be based on what is achievable without gantry/couch/patient collision and where the clips are in relation to the underlying bony anatomy (i.e. the clip visualisation without ribs/spines' obstructions) as viewed on the DRR.

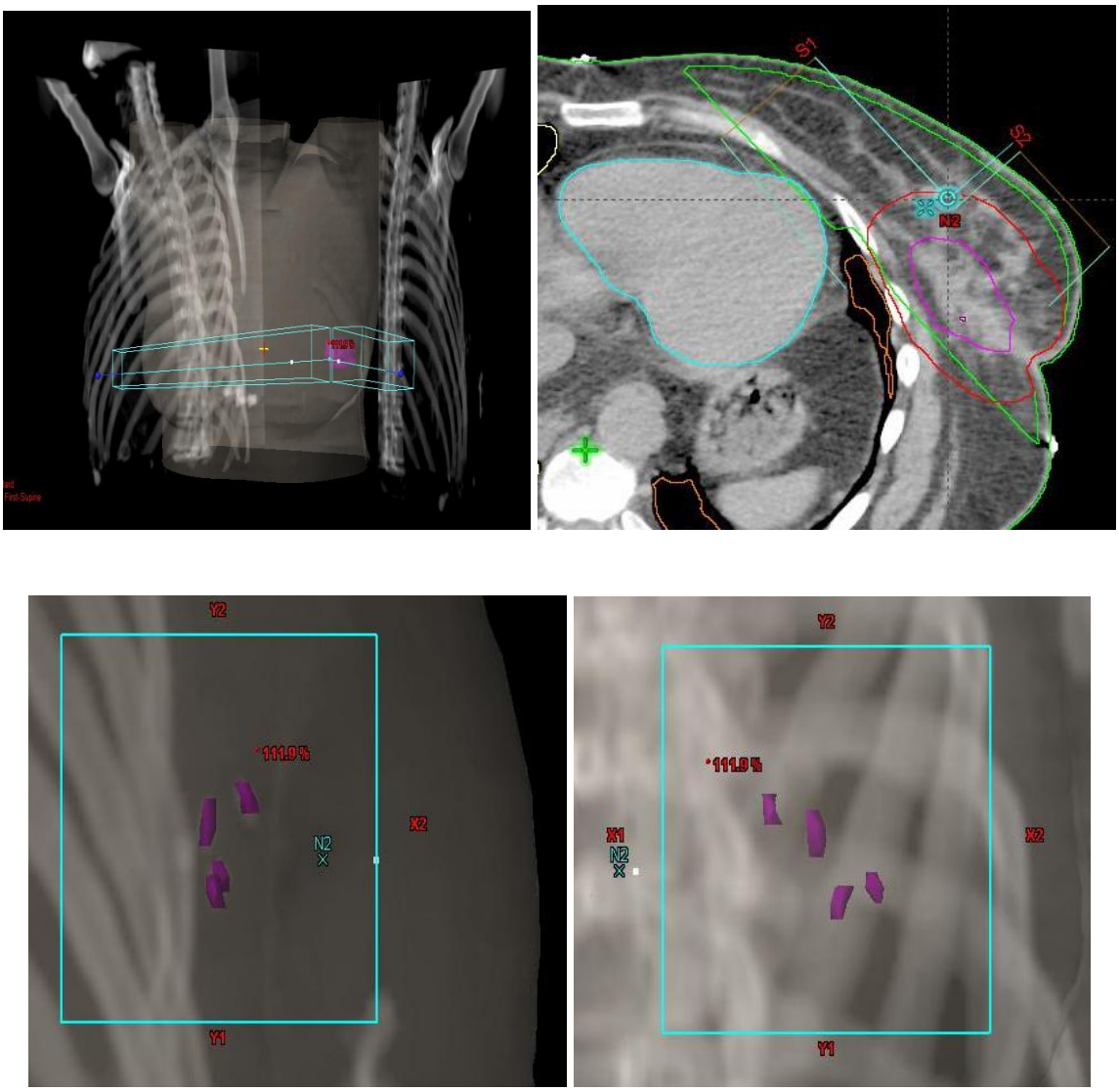


Figure 28 Example of how KV imaging fields could be determined on Varian linac using titanium clips *implanted markers.*

Please note that for centres in the EME IMPORT_IGRT study, all fields must contain sufficient anatomy to allow a bony anatomy match.

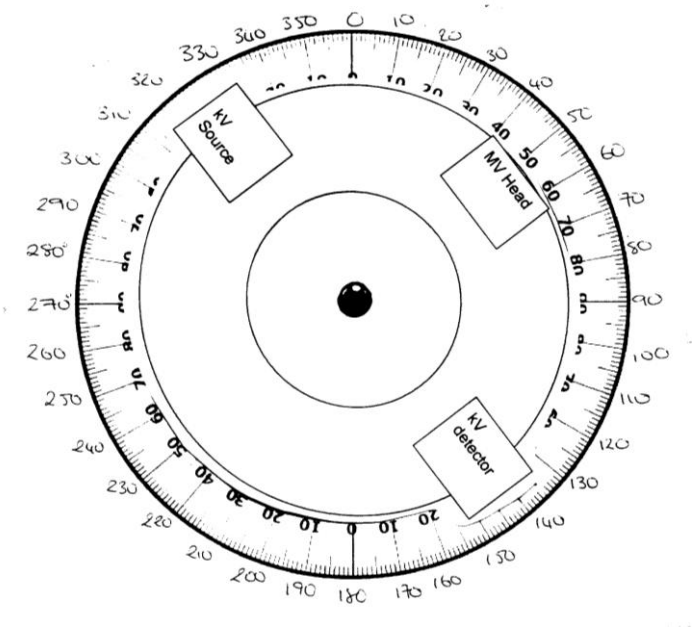


Figure 29 Determined limits for kV source angles. The chart above is developed by Ipswich Hospital for Varian Linac

Suggested imaging angle:

Left Breast 180° → 50° Ideal 315° and 45°

Right breast 120° → 0° Ideal 225° and 315°

6.5.3 Cone Beam kV (Titanium clips)

An imaging protocol which minimizes the imaging dose is used. A scan protocol of 190° may assist in reducing imaging dose and avoiding collisions of the equipment. It is recommended that the tumour bed PTV (PTV_{TB}) is exported as a structure to aid the treatment verification. A suggested method is to use automatic bony anatomy matching at the beginning of the verification process and then a manual match using the clip markers with a "best-fit" approach. It is important to check that clips are contained within PTV_{TB} and that the breast/chest wall position is acceptable (within 5mm). Care must be taken if applying a shift to consider how this will affect the OAR doses. If a superior/inferior shift is applied, the same shift will probably need to be applied to any SCF field.

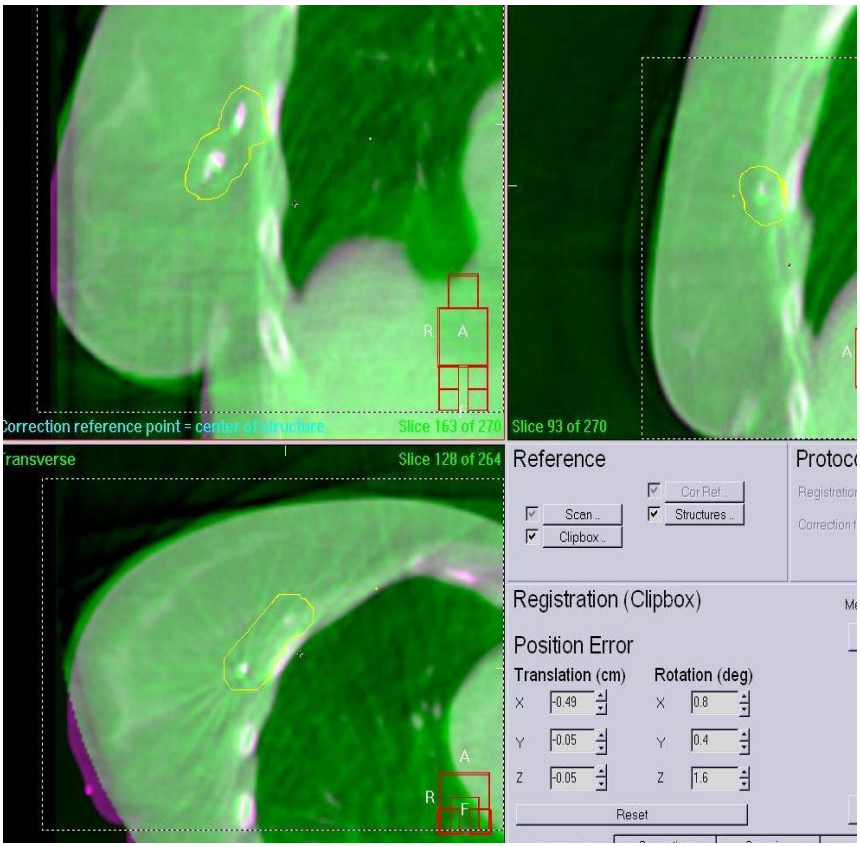


Figure 30 Example of KV CBCT imaging on Elekta Linac using grey anatomy matching and clips matching with PTV_{TB} structure.

6.5.4 Tomotherapy Verification Scan (Gold seeds or titanium clips)

It is recommended to use the imaging protocol (coarse mode) which minimizes the imaging dose. MVCT imaging is acquired daily for tomotherapy treatment verification.

6.5.4.1 Tomotherapy scanning volume selection (dependent on which arm the patient is randomised into)

Test arms: whole Breast with concomitant boost

On day 1 select scan slices to include the entire breast PTV (see Figure 1). If the patient position is stable after the first 3 days, the scan volume may be reduced. However this volume must include the boost volume PTV and sufficient breast tissue, in order to enable assessment of both external breast contours and internal chest walls registration.

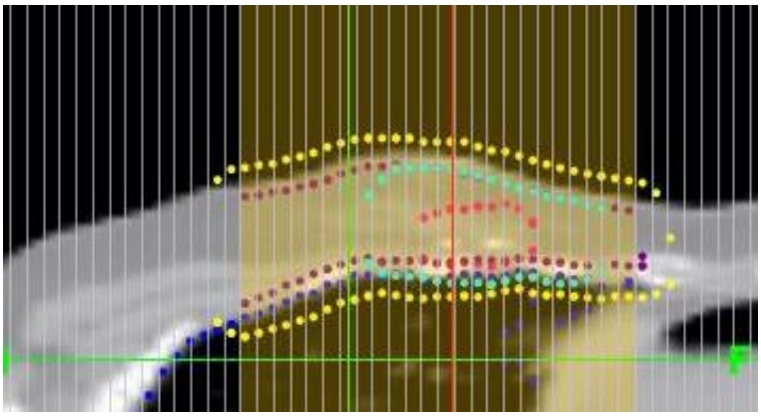


Figure 31: Test arm: slice selection includes the tumour bed PTV (red) including surgical clips and sufficient breast tissue for localisation. The breast PTV is shown in purple.

Control arm: sequential tumour bed boost.

On day 1 of the sequential tumour bed boost treatment select scan slices to include the entire boost volume PTV and sufficient breast tissues and bony anatomy for image matching (see Figure 2)

.

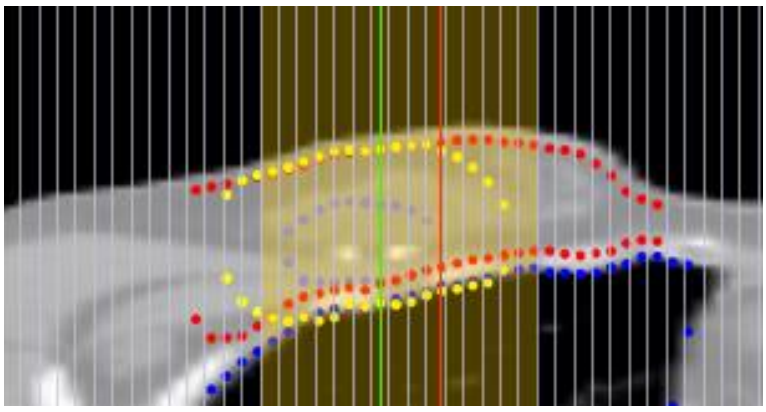


Figure 32: Control arm: slice selection includes the tumour bed PTV (purple) including surgical clips and sufficient anatomy to localise the volume accurately.

6.5.4.2 Tomotherapy Image matching

Registration of the MVCT scan to the planning CT scan is performed firstly to optimise the external contour and internal anatomy match. It is suggested to perform a 6 degrees of freedom (DoF) automatic match as a gross error check. If the automatic positional corrections are outside of the prescribed tolerance for gross error (see Table 7 for suggested values), the patient is repositioned and rescanned for a second 4 DoF (translations and roll) automatic registration. This registration is then manually optimised by radiographers using zero tolerance action level.

Corrective set-up position action level for gross error			
Translations (mm)			**Rotation (°)**
X	**Y**	**Z**	
10	**10**	**15**	**5**

Table 7 suggests gross error action levels to be used for re-positioning and rescanning IMPORT HIGH patients.

After the initial registration process, the treatment verification is performed by matching the clips from MVCT with planning KVCT. It is not always possible to have a perfect match with all clips on daily image registration between MVCT and planning KVCT. In these situations, it is recommended to ensure that the clips and any associated tumour bed seroma are covered by the 95% isodose (see Figure 3).

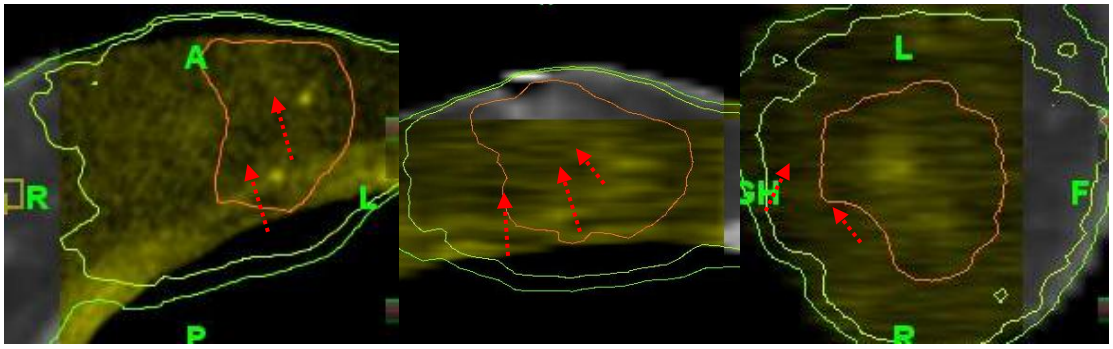


Figure 33: (a) represents the axial image, (b) Sagittal and (c) coronal. The 95% isodose coverage of the tumour bed is indicated by the orange outline. The surgical clips are indicated by the dashed arrows (seen optimally on the axial image).

A large discrepancy between external contours and internal anatomy of MVCT and planning KVCT scans may indicate a change in planned dosimetry. Where available, an assessment of the difference between the planned and delivered dose can be performed using the tomotherapy adaptive software. The daily MV CT scan can be exported into the planning system, whereby the dose distribution can be recalculated based on actual treated anatomical positions. Patients with significant dose differences

can be identified and referred to oncologists. Thus their treatment can be adapted to their needs (adaptive radiotherapy).

6.6 In-vivo Dosimetry

The use of in-vivo dosimetry within the first week of treatment is encouraged for patients in IMPORT HIGH. It is understandable that the situation may become quite difficult on the small partial breast and tumour bed fields. The measurements could be carried out at least for the tangential opposing whole breast fields which contribute majority of the treatment doses in both forward and inverse planning methods

7. Treatment gaps

A gap of up to 5 days is acceptable in the event of machine service or breakdown. If the treatment machine is unavailable for more than 5 days, or if you wish to move a patient to a machine with no imaging facilities before the initial correction for systematic error has taken place, please contact the QA team.